Epidemiological, Phenomenological, and Treatment Aspects of Trauma and Posttraumatic Stress Disorder in Children and Adolescents

Soraya Seedat

MB ChB (University of Natal), FC Psych, MMed Psych

(University of Stellenbosch)

Promotor: Prof RA Emsley

Co-Promotor: Prof DJ Stein

Dissertation presented for the Degree Doctor of Philosophy in the Faculty of Health Sciences, University of Stellenbosch

January 2005

Declaration

I, the undersigned, hereby declare that the work contained in this dissertation is my original work and that I have not previously in its entirety or in part submitted it at any university for a degree.

Signature: …… **Date:**……

SUMMARY

Many gaps remain in our current state of knowledge about the epidemiology, phenomenology, neurobiology, and psychopharmacology of posttraumatic stress disorder (PTSD) in children and adolescents. Empirical evidence, particularly in non-Western settings, is sparse and there is little convergent understanding of the inter-relationship of epidemiological factors, PTSD symptom expression, full and partial syndromes, disorders comorbid with PTSD, and pharmacotherapeutic interventions. Clinicians are faced with the difficult task of treating this often complicated and debilitating disorder in youth in the absence of data from well-controlled clinical trials. The studies detailed here are a point of departure for understanding the confluence that exists between epidemiological, phenomenological, and pharmacotherapeutic aspects of adolescent PTSD. Two studies were conducted to investigate the prevalence and effects of violence exposure and PTSD, clinical and functional correlates of full and partial syndromes, and associated gender differences in school and clinic samples, respectively. Two preliminary open-label trials assessed the efficacy and safety of a selective serotonin reuptake inhibitor (SSRI) in adolescents with at least moderate severity PTSD.

The results indicate that (i) partial PTSD is a common nosological entity in adolescents, (ii) gender-related differences in PTSD, even if not manifest in differences in prevalence (i.e., in the rates of trauma exposure and full and partial PTSD), may well manifest in symptom expression (i.e., higher symptom burden in girls), associated morbidity, and functional impairment, and (iii) SSRIs may be effective in treating core PTSD symptoms in this age group.

While not yet demonstrated, the partial subtype may have similar biological underpinnings to full PTSD in adolescents and may benefit from similar pharmacotherapeutic interventions. This is an area deserving of further investigation. Controlled SSRI data are needed to establish if these should be agents of choice for paediatric PTSD.

OPSOMMING

Daar is tans nog baie leemtes in ons kennis oor die epidemiologie, fenomenologie, neurobiologie en psigofarmakologie van post-traumatiese stressteuring (PTSS) in kinders en adolessente. Empiriese bewys, in die besonder in nie-Westerse omgewings, is yl gesaai en daar is min ooreenstemming wat betref begrip van die onderlinge verwantskap van epidemiologiese faktore, uitdrukking van PTSS-simptome, volledige en gedeeltelike sindrome, ongesteldhede wat komorbied tesame met PTSS voorkom, en farmakoterapeutiese intervensies. Klinici kom te staan voor die moeilike taak om hierdie dikwels gekompliseerde en uitmergelende ongesteldheid in jongmense te behandel ondanks die afwesigheid van data na aanleiding van goed gekontroleerde kliniese studies. Die studies wat hier opgesom word, is ’n vertrekpunt onderweg na begrip van die samesmelting tussen epidemiologiese, fenomenologiese, en farmakoterapeutiese aspekte van PTSS by adolessente. Twee studies is uitgevoer om die voorkoms en gevolge van blootstelling aan geweld en PTSS, kliniese en funksionele korrelate van volledige en gedeeltelike sindrome, en daarmee gepaardgaande geslagsverskille in skool- en kliniekseekproewe onderskeidelik te ondersoek. Twee voorlopige oop (‘open-label’) studies het die

doeltreffendheid en veiligheid van ’n selektiewe serotonien heropname-inhibeerder (SSHI) in adolessente met ten minste matig ernstige PTSS geassesseer.

Die resultate dui daarop dat (i) gedeeltelike PTSS ’n algemene nosologiese entiteit in adolessente is, (ii) geslagsverwante verskille in PTSS, selfs al is dit nie sigbaar in verskille ten opsigte van voorkoms nie (m.a.w. in die koers van blootstelling aan trauma en volledige en gedeeltelike PTSS), wel in die uitdrukking van simptome (m.a.w. ’n hoër simptoomlading in dogters), gepaardgaande morbiditeit en funksionele inkorting kan manifesteer, en (iii) SSHI’s doeltreffend kan wees in die behandeling van kern- PTSS-simptome in hierdie ouderdomsgroep.

Alhoewel dit nog nie aangetoon is nie, kan die gedeeltelike subtipe soortgelyke biologiese onderstutting as die volledige PTSS in adolessente hê en dit kan dus by soortgelyke farmakoterapeutiese intervensies baat. Hierdie veld bied geleentheid vir verdere ondersoek. Gekontroleerde SSHI-data is nodig om vas te stel of dit die middels van keuse by pediatriese PTSS behoort te wees.

PREVIOUS PUBLICATIONS

The contents of this dissertation have been published in part:

Seedat S, van Nood E, Vythilingum, Stein DJ, Kaminer D (2000) School survey of exposure to violence and posttraumatic stress symptoms in adolescents. South African *Journal of Child and Adolescent Mental Health*, **12(1),**38-44.

Seedat S, Stein DJ, Emsley RA (2000) Open trial of citalopram in adults with post-traumatic stress disorder. *Int J Neuropsychopharmacol,* **3(2),** 135-140.

Seedat S, Stein DJ, Ziervogel C, Middleton T, Kaminer D, Emsley RA, Rossouw W (2002) Comparison of response to a selective serotonin reuptake inhibitor in children, adolescents, and adults with posttraumatic stress disorder. *J Child Adolesc Psychopharmacol,* **12(1),** 37-46.

Seedat S, Nyamai C, Njenga F, Vythilingum B, Stein DJ (2004) Trauma exposure and post-traumatic stress symptoms in urban African schools. Survey in Cape Town and Nairobi. *Br J Psychiatry,* 184, **169-75.**

CONTENTS **Page**

1. INTRODUCTION: POSTTRAUMATIC STRESS DISORDER IN CHILDREN AND ADOLESCENTS

1.1 Epidemiology and Aetiology

Exposure to high-magnitude trauma occurs at alarmingly high rates in children and adolescents. Community studies in adolescents and young adults have documented trauma exposure rates (DSM-III R) ranging from 39% to 84% (Breslau et al., 1991; Vrana and Lauterbach, 1994). For example, in a community epidemiological study of adolescents, 43% had experienced at least one DSM-IIIR trauma by the age of eighteen and posttraumatic stress disorder (PTSD) was evident in 14,5% of adolescents who were exposed (Giaconia et al., 1995). In contrast, studies of at-risk children and adolescents (i.e., trauma-exposed) have reported PTSD prevalence rates of up to 100% (Frederick, 1985; Garrison et al., 1995; Perkonigg et al., 2000). Notably, events that may be reported as particularly upsetting are not always the most likely to lead to PTSD.

Rates for the development of PTSD in children and adolescents also vary widely according to the type of exposure (Kessler et al., 1995; Breslau et al., 1998). Interpersonal, high-intensity traumas, such as rape or

other types of sexual assault, are associated with the highest rates of PTSD, while exposure to natural disasters (such as floods and fires) are associated with much lower rates of the disorder (Yehuda, 2002).

While it is widely recognised that PTSD is more common in youth exposed to ‘external’, high magnitude life-threatening events, such as criminal assault (Pynoos et al., 1987), severe burns (Stoddard et al., 1989), hospitalisation following accidental injury (Daviss et al., 2000), motor vehicle accidents (Stallard et al., 2004), combat/war (Clarke et al., 1993; Durakovic-Belko et al., 2003), hostage taking (Schwarz and Kowalski, 1991), man-made disasters (March et al., 1997; Fremont, 2004, review) and natural disasters (Burke et al., 1986; Lee et al., 2004; Groome and Soureti, 2004); prevalence rates indicate that not all trauma-exposed children and adolescents develop PTSD. Factors such as severity of trauma exposure, duration of exposure, physical and emotional proximity, individual patient characteristics, and parental factors may influence the development of PTSD in children and adolescents (Silva et al., 2000; Foy et al., 1996, Pfefferbaum, 1997). Severity of trauma exposure and parental trauma-related distress have consistently produced

positive correlations with PTSD symptoms, while the length of time since trauma exposure in consistently negatively correlated with PTSD severity in this age group (Foy et al., 1996). Both the aforementioned findings are compatible with findings for adults (Foy et al., 1996). As is common with other psychiatric disorders, gender effects in exposure to trauma and PTSD have also been documented. For example, in an epidemiological sample (N=2,311) of young people who were recruited as participants at entry into first grade and then interviewed about a history of trauma and PTSD when their mean age was 21 years (Breslau et al., 2004) the lifetime occurrence of assaultive violence was significantly higher in males than females (62.6% vs. 33.7%), however females had higher rates of PTSD than males following assaultive violence (odds ratio of 4). Interestingly, gender differences in the rate of PTSD following other traumas were not observed. Thus, findings of higher rates of trauma exposure overall in boys, with higher rates of PTSD in girls (Cuffe et al., 1999; Giaconia et al., 1995; Breslau et al., 1997) have not been conclusive across all studies. Furthermore, many studies have not controlled for possible differences in lifetime trauma exposure between boys and girls.

Identification of etiological mechanisms and risk factors for development of the disorder has been an important recent thrust in PTSD research. Currently, it is viewed a complex disorder that is multifactorially mediated by biological dysregulation of noradrenergic, serotonergic, glutamatergic, dopaminergic, opioid and neuroendocrine pathways (among others) (Friedman and Southwick, 1995). In addition to neurobiological disturbances, etiological theories of PTSD have identified cognitive and behavioural factors as being contributory. Current evidence indicates that traumatized children, like traumatized adults, demonstrate altered hypothalamic-pituitary-adrenal (HPA) axis circadian rhythmicity, although there is little consensus on whether cortisol levels are elevated, reduced, or remain unchanged in paediatric PTSD. For example, a recent adolescent study did not find evidence for enhanced suppression of morning cortisol in multiply traumatized adolescents with or without PTSD (Lipschitz et al., 2003). In adults, recent data suggest that low cortisol levels may be an early predictor rather than a consequence of the disorder. For example, in a study examining cortisol responses in the acute aftermath of rape, low cortisol was associated with a prior rape or assault but not with the development of PTSD *per se* (Resnick et al., 1995). These

findings have not yet been replicated in children and adolescents.

Neuroimaging studies in posttraumatic stress disorder (PTSD) have also been largely restricted to adult populations. Structural and functional studies implicate the amygdala, hippocampus, anterior cingulate, Broca's area, medial prefrontal cortex, and visual cortex (Pitman et al., 2001, review). One published study to date assessed these neural correlates in adolescents (Yang et al., 2004). Brain activation was measured by functional magnetic resonance imaging during visual perception and imagery recall of an earthquake in adolescent earthquake survivors 14 months after the event. During earthquake imagery, the PTSD group showed activation in a number of limbic-paralimbic and visual regions, while the control group did not, generally consistent with findings in adults with PTSD.

Structural imaging studies that have specifically assessed the effects of childhood trauma and PTSD on brain volumes are, similarly, limited. De Bellis et al. (1999) found no evidence of reduced hippocampal or pituitary volumes (Thomas and De Bellis, 2004) in children with maltreatment-

related PTSD, but did demonstrate smaller intracranial, whole brain and corpus callosal volumes, which may suggest that PTSD has an impact on global brain development. In a follow-up analysis, controlling for socio-economic status (De Bellis et al., 2002), the authors found that brain volumes were positively correlated with the age of onset of PTSD but were negatively correlated with the duration of abuse. Debate continues on whether reduced hippocampal volumes predate or follow the development of PTSD, and to what extent this might predict the response to trauma. However, the findings of a recent study in twin-pairs discordant for trauma exposure and PTSD suggest that lower pre-existing hippocampal volumes may, in fact, predispose individuals to developing PTSD after trauma (Gilbertson et al., 2002).

Cognitive-behavioural theories have highlighted the involvement of information-processing and learning in the development of PTSD. Foa and colleagues (1989) have suggested that, following a trauma, a fear network that stores information about sources of threat is formed, and that these trauma-related representations are activated by external and internal cues. In children and adolescents with PTSD, this fear structure includes an especially large

number of stimuli elements and is therefore easily accessed. Similarly, it has been proposed (Keane et al., 1985) that PTSD fear responses develop through a process of classical conditioning, whereby fear comes to be associated with cues present during the actual trauma (e.g., gunfire), as well as through a process of stimulus generalization, whereby any stimulus associated with these cues (e.g., a car backfiring or a firecracker exploding) then produces a fear response. Continued avoidance of traumatic cues reinforces the fear response, which has no opportunity to be ‘un-learned’. In children and adolescents, subjective cognitive appraisals of traumatic events vary with the developmental level of the child, as does the way in which traumatic memories are encoded and recalled (Pynoos et al., 1996).

In summary, while much remains to be understood about the role of developmental, neurobiological, cognitive and other mechanisms that may create a vulnerability to PTSD, it is indisputable that the disorder poses significant challenges to the healthy physical, cognitive and emotional development of children and adolescents (Giaconia et al., 1995).

1.2 Phenomenology

The hallmark features of PTSD include a history of exposure to an index event that threatens the life or physical integrity of the child or others, induces a response of intense fear, helplessness, or horror, and temporally results in the development of symptoms from each of three symptom clusters: re-experiencing of the trauma, avoidance and numbing, and hyperarousal (APA, 2000). In children and adolescents, re-experiencing symptoms may involve recurrent frightening dreams or re-enactment of traumatic themes in play. Avoiding thoughts, feelings, or memories of the trauma, restriction of affect, and markedly diminished interest in activities may characterise avoidance and numbing, while symptoms of irritability, sleep dysregulation, anger outbursts and concentration difficulties are features of hyperarousal (AACAP, 1998). To make a diagnosis of PTSD, symptoms must cause significant distress and/ or functional impairment and persist for longer than one month. The disorder runs a longitudinal course, with progressive modification of symptoms occurring over time (Blank, 1993; McFarlane, 2000).

Partial symptomatology is not uncommon in children and adolescents and recent findings support the hypothesis that

children with subthreshold criteria may not differ significantly from children meeting all three cluster criteria (re-experiencing, avoidance, hyperarousal) with regard to functional impairment and distress. For example, in a study by Carrion and colleagues (2002), children with subthreshold PTSD had functional impairment that was specific to PTSD symptoms and was not due to comorbidity. This suggests that it might be more precise to make a diagnosis of PTSD in children and adolescents based on the intensity of symptoms and their relationship to functional impairment, than on the threshold number of symptoms.

While the applicability of DSM-IV nosological criteria to very young children is controversial, particularly as symptoms are often heterogeneous and developmentally-determined (Perry, 1994; Weisenberg et al., 1993; Nader et al., 1990), it does provide a useful framework for guiding the assessment and treatment of PTSD in older children and adolescents (AACAP, 1998; Perrin et al., 2000). Certainly, the frequency and severity of symptoms in the three symptom clusters constitute a primary target for pharmacotherapy. Important differences in clinical presentation may exist between acute (duration of symptoms less than 3 months) and chronic (duration of symptoms 3 months or more) subtypes in

children. Famularo et al. (1996), for example, described prominent re-experiencing, hyperarousal, and sleep difficulties in the acute subtype, and detachment, restricted affect, dissociation, and depressed mood in the chronic subtype. In addition, Terr (1991) has proposed a two-tiered classification of childhood traumas and their symptom subtypes: Type I (single-incident, sudden trauma, characterised by detailed memories and misperceptions) and Type II (chronic, recurrent, usually childhood physical and/or sexual abuse, characterised by denial/ numbing/ dissociation/ rage). These subtypes may be mediated by different psychobiological factors, and may require different treatment approaches (Donnelly et al., 1999). For example, symptom targets in patients with more chronic PTSD may, in addition to the core symptom clusters, need to include symptoms such as guilt and shame. Also, medications that theoretically decrease the ability of patients to respond to psychotherapeutic interventions aimed at resolving these issues (Risse et al., 1990; Gelpin et al., 1996) may be relatively contraindicated.

Childhood PTSD precedes, predisposes to, and co-occurs with other psychiatric disorders. While studies investigating the time-sequencing of PTSD and comorbid conditions have

yielded conflicting results, the high rates of comorbidity with mood, anxiety, and substance use disorders are comparable with adults and can significantly impact on prevention and treatment (Goenjian et al., 1995; Hubbard et al., 1995; Yehuda and McFarlane 1995; Brady, 1997; Kessler et al., 1995; Giaconia et al., 1995; McCloskey and Walker, 2000). Children with comorbid disorders (e.g., mood or anxiety disorders) will require interventions with broad-spectrum effects. In addition, certain medications (e.g. benzodiazepines) may be relatively contraindicated for patients with comorbid substance use disorders. Furthermore, children with PTSD have been shown to have more behavioral-emotional problems, interpersonal problems, academic failure, suicidal behavior, and health problems, than those without PTSD (Giaconia et al., 1995; Schwab-Stone et al., 1999, Mazza, 2000).

To date, a number of DSM-IV (APA, 1994) based child-adolescent structured interviews have been constructed to assist in diagnosis. At present, no ‘gold standard’ instrument exists. However, several reliable and valid assessment instruments are available to aid diagnosis, and a combination of both structured and unstructured child-adolescent and caregiver interviews is recommended (AACAP,

1998). Structured psychiatric interviews for children, such as the Schedule for Affective Disorders and Schizophrenia for School Age Children Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997), the Diagnostic Interview Schedule for Children-Version IV (DISC-IV) (Shaffer et al., 2000), and the Diagnostic Interview for Children and Adolescents (DICA) (Reich et al., 1991) contain a PTSD module. These instruments also assess disorders that that are frequently comorbid with PTSD (e.g., depressive disorders, anxiety disorders, substance use disorders, disruptive behaviour disorders). PTSD-specific interviews include the Clinician-Administered PTSD Scale-Child and Adolescent Version (CAPS-CA) (Nader et al., 1996), the Child PTSD Checklist (Newman and Amaya-Jackson, 1996), and the Child PTSD Symptom Scale (Foa et al., 2001). Finally, a number of scales are available for assessing the severity of PTSD symptoms in children, such as the Child Post-Traumatic Stress Reaction Index (Nader et al., 1993), the Child and Adolescent Trauma Survey (March, 1999) and the Trauma Symptom Checklist for Children (Briere, 1996). Direct reports from parents, teachers and other observers in the child's milieu are an important component of evaluation, although it should be borne in mind that parents often minimize a child's symptomatology (AACAP,

1998). Thus, the use of multiple assessment instruments and multiple informants to measure PTSD across different areas of functioning, is recommended. That said, nothing can replace a properly conducted and comprehensive clinical interview.

1.3 Pharmacotherapy

Despite better insights into the pathophysiology of PTSD and other anxiety disorders and compelling evidence that a number of key psychobiological systems are dysregulated, there is a relative dearth of rigorously designed pharmacotherapy trials for childhood anxiety disorders (March et al., 1996; Donnelly et al., 1999). Biological research in the field has been impeded by a plethora of ethical considerations peculiar to this population, for e.g., developmental immaturity, risks posed by treatment, and problems associated with ‘informed consent’ procedures. In the absence of definitive efficacy and effectiveness data to inform prescribing practices, clinicians are guided by clinical teaching and experience and extrapolation of efficacy and safety data from adults. This has encouraged the routine ‘off-label’ application of antianxiety drugs with US Food and Drug Administration (FDA) indications in adults, to disorders in children and adolescents (Labellarte et al., 1998). Currently, three selective serotonin reuptake inhibitor antidepressants (fluoxetine, sertraline, and fluvoxamine) have FDA approval for the treatment of another childhood anxiety disorder, obsessive-compulsive disorder. Fluvoxamine and fluoxetine have also demonstrated efficacy for generalised anxiety disorder,

separation anxiety disorder, and social phobia in youth but do not have FDA indications for these disorders in this age group (RUPP, 2001; Birmaher et al., 2003).

Treatment approaches for childhood posttraumatic stress disorder (PTSD) are diverse with little consensus on the effectiveness of many of the modalities in use. In a published survey of current practices of psychiatrists and non-medical therapists in the treatment of traumatised children and adolescents with PTSD; cognitive-behavior therapy (CBT) was endorsed as the most preferred first-line treatment among non-medical therapists and the second most preferred among psychiatrists for childhood PTSD (Cohen et al., 2001). Although only 17% of psychiatrists said they preferred psychotropic medications, the majority (95%) prescribed medications for the disorder. Both groups rated SSRIs as the most effective medications for treating overall PTSD symptoms.

Many of the symptoms of PTSD can be traced to core symptoms of physiological hyperarousal (viz., sleep difficulties, nightmares, night terrors, generalised anxiety symptoms) which, in turn, can trigger a cascade of interrelated problems, such as difficulties maintaining adult and peer

relationships, difficulties with intimacy, poor school performance, and poor self-esteem. Perry and Azad (1999) have suggested that successful treatment may require ‘modifying’ or ‘containing’ this physiological dysregulation, through the use of medication and/or psychotherapeutic treatment (to address mastery of specific fears and issues related to self-esteem, competence, and social skills).

While it is arguable that the treatment of anxiety disorders in youth needs to be multifaceted, pharmacotherapy may be an appropriate first-choice when dealing with (i) serious and disabling anxiety symptoms and (ii) older children and adolescents (Bernstein et al., 1996). Effective pharmacological agents for children and adolescents are ideally those which: a) will target disabling symptoms, b) improve the quality of life of the child/adolescent allowing for normal growth and development in the long-term, and c) facilitate the process of psychotherapy by allowing traumatised children to deal with emotionally distressing material and work through their distress (Donnelly and Amaya-Jackson, 2002). Pharmacologic agents that have been assessed in open trials have included clonidine (Harmon and Riggs, 1996), guanfacine (Horrigan,

1996), propranolol (Famularo et al., 1988), carbamazepine (Looff et al., 1995) and tricyclic antidepressants, and these are discussed here. To date, there are no published placebo-controlled trials of pharmacologic agents in children with PTSD.

1.3.1 Adrenergic agents

The finding that stress produces marked increases in brain noradrenergic function and that fear conditioning is related to alterations in noradrenergic activity may be important in understanding the pathophysiology of PTSD (Charney et al., 1993). Many of the symptoms experienced in PTSD (such as panic attacks, insomnia, exaggerated startle, and autonomic hyperarousal) are characteristic of increased noradrenergic function. Drugs like opiates and benzodiazepines either attenuate or decrease the stress-induced increases in norepinephrine release (Charney et al., 1993). Adrenergic agents (e.g. the α_2-adrenoreceptor antagonists clonidine and guanfacine, and the β-adrenoreceptor antagonist, propranolol) which reduce sympathetic arousal have been shown to be effective in treating the hyperarousal, re-experiencing, and impulsivity seen in PTSD. In two open-label trials, oral clonidine (0.05 to 0.1 mg/day) (Perry, 1994) and clonidine

transdermal patches (0.1 to 0.2 mg/day) (Harmon and Riggs, 1996) were effective in reducing PTSD symptoms in children, particularly anxiety, arousal, insomnia, impaired concentration, and impulsive and aggressive behaviour. Guanfacine was reported to be effective in reducing nightmares in a single case study (Horrigan, 1996), while propranolol significantly reduced intrusion and arousal symptoms over 5 weeks in 8 of 11 abused children with PTSD (Famularo et al., 1988).

1.3.2 Serotonergic agents

Animal models of PTSD suggest that serotonergic pathways may mediate certain avoidance behaviors, while clinical studies of paroxetine platelet binding and mCPP challenge tests further suggest a role for serotonin in PTSD (Southwick et al., 1997; Arora et al., 1993). For example, mCPP (a serotonin agonist) has been shown to induce panic attacks, flashbacks, and dissociative episodes in a significant number of adult combat veterans compared with a control group (Southwick et al.1997). In addition, veterans in the sample who had panic attacks induced by mCPP differed from patients who had panic attacks induced by yohimbine. Thus, it may be hypothesised that there are two distinct subgroups of PTSD: a group of patients with a

sensitised serotonergic system and another with a sensitised noradrenergic system. This finding, although not yet empirically tested in adults or children, may have implications for treatment in the clinical setting insofar as trying to match PTSD subtypes with appropriate pharmacological interventions.

Selective serotonin reuptake inhibitors (SSRIs) are widely used to treat adult PTSD. Two SSRIs, sertraline and paroxetine, are currently the only two FDA-approved pharmacological agents indicated for adult PTSD. In adults, several randomized, controlled acute treatment trials of sertraline, paroxetine, and fluoxetine have been conducted, as well as open trials of fluvoxamine and citalopram (Asnis et al., 2004). Studies in adult PTSD have predominantly included women with chronic PTSD (mean duration > 10 years) secondary to rape or physical assault. Fluoxetine was the first SSRI to be investigated in the treatment of PTSD. In contrast to several controlled studies that did not show a significant benefit for either fluoxetine or sertraline in male combat veterans, published studies in predominantly female, non-combat subjects have been positive. These studies have demonstrated that SSRIs are effective in the short-term (6-12 weeks) and that continuation and

maintenance treatment for 6-12 months decreases relapse rates (Asnis et al., 2004). Furthermore, meta-analyses of efficacy studies in adult PTSD suggest that the effect size of the SSRIs are moderate to strong compared with placebo (Penava et al., 1997; Stein et al., 2000).

The safety profile of the SSRIs, are also superior to those of the tricyclic antidepressants, they do not require the therapeutic drug monitoring required of the TCAs and are relatively safe in overdose. This factor is particularly important in children who are more susceptible to the toxic effects of TCAs, resulting from the increased production of cardiotoxic metabolites of these drugs, than adults (Leonard et al., 1997). Despite the lack of controlled trials of the SSRIs in childhood PTSD, they are currently recommended as a first-choice pharmacologic treatment in children and adolescents (AACAP, 1998; Donnelly and Amaya-Jackson, 2002). Serotonergic agents, other than SSRIs, such as nefazodone and cyproheptadine have been used in this age group but controlled data are lacking (Domon and Andersen, 2000; Gupta et al., 1998). Domon and Andersen (2000) found the serotonin-2 antagonist, nefazodone, to be effective in an open-label trial of adolescents with PTSD, particularly for symptoms of anger, aggression, insomnia, hyperarousal,

and concentration difficulties. *Mirtazapine*, a novel drug with both serotonergic and noradrenergic properties was used as augmentation in an 8-year old with PTSD and comorbid anxiety disorder not otherwise specified (Good and Petersen, 2001). The addition of *mirtazapine* (7.5 mg/day) to an SSRI resulted in improvement in PTSD symptoms. In adults with PTSD, a placebo-controlled, double-blind trial of mirtazapine demonstrated effects significantly in favor of mirtazapine and the drug was found to be well tolerated (Davidson et al., 2003).

1.3.3 Other agents

Randomised clinical trials have demonstrated efficacy of tricyclic antidepressants and monoamine oxidase inhibitors in adult PTSD, however no controlled studies have been reported in childhood PTSD. To date there has been one double-blind randomised study on the use of a low dose tricyclic antidepressant in the context of acute stress disorder in children with burn injuries. Imipramine was compared to chloral hydrate over a 7-day period in 25 children with ASD (Robert et al., 1999) and was found to be superior in treating ASD symptoms. In a more naturalistic study, Saxe et al. (2001) investigated the use of an opiate medication (morphine) as a possible preventive agent in

children with burns-related PTSD. The dose of morphine administered to children during hospitalisation for burn injuries was associated with a significant reduction in PTSD symptoms over a 6-month period.

Anticonvulsants have also been investigated in child and adult PTSD, their potential utility based on the premise that trauma exposure may induce sensitisation or kindling phenomena in limbic areas in the central nervous system. Looff et al. (1995) reported on the use of carbamazepine (300mg to 1200 mg/day) in 28 children and adolescents with sexual abuse histories. Twenty-two of these patients were asymptomatic at the end of treatment with regard to PTSD symptoms, while 6 continued to experience abuse-related nightmares. However, 50% of the sample had comorbid disorders (e.g., attention-deficit hyperactivity disorder, major depression, polysubstance abuse) and were being treated with concomitant medications (e.g., SSRIs, imipramine, methylphenidate, clonidine).

The utility of benzodiazepines for pediatric PTSD has not been established. In adults, alprazolam and clonazepam have been shown to reduce anxiety and insomnia but not to have significant effects on the PTSD symptom clusters (Braun et

al., 1990; Lowenstein et al., 1988). Controlled studies of benzodiazepines for childhood anxiety disorders other than PTSD (e.g., panic disorder, and school refusal) have shown superiority of these agents over placebo (Bernstein et al., 1990; Kutcher et al., 1992). While benzodiazepines may be a useful adjunct to antidepressant treatments, their potential for dependence and other adverse effects makes them less than an ideal choice in this population. Additionally they may negatively impact on behavioral therapy in children and adolescents. Antipsychotic agents, including the dopamine D2 receptor blocking agent risperidone (Horrigan, 1998) and the predominant D1 receptor blocking agent clozapine (Kant et al., 2004) have also demonstrated promise in small open studies of adolescents with chronic PTSD.

In summary, there is a growing database in children and adolescents that suggests that medication treatments for PTSD cannot be ignored. In particular, the SSRIs may be useful and research in the area is deserving of further attention. Furthermore, care needs to be taken in extrapolating data from adults to children, given that there is some preliminary evidence of developmental

alterations in the efficacy of these agents (Keller et al., 2001).

Finally, the absence of published open-label or controlled trials of SSRIs in childhood PTSD provided the impetus to conduct a preliminary open-label study of an SSRI in adolescent PTSD to evaluate its efficacy on PTSD symptom clusters. The study rationale, methods and results are described in chapter 4.

1.4 Questions for Further Study

In view of the questions raised concerning risk factors (e.g., the role of gender), clinical subtypes (e.g., the distinction between full and partial PTSD syndromes), and appropriate pharmacotherapy for this age group, a series of studies was undertaken: -

First, a community-based school survey was conducted to assess the: (i) type and extent of violent trauma exposure, (ii) prevalence and pattern of PTSD symptoms (including differentiation of full symptom & partial symptom PTSD), and (iii) interactional effects of gender with trauma and PTSD in two African cities (Cape Town and Nairobi). Approximately one thousand adolescents were selected from nine schools in each city using a stratified sampling, cross-sectional survey design. The key statistical variables of interest were type of trauma and socio-demographic factors(in particular gender) as potential risk factors for PTSD in the context of setting (Cape Town versus Nairobi). Prior to the initiation of this study, a preliminary survey conducted at three secondary schools (n=307) in Cape Town (Seedat et al., 2000) found high rates of PTSD (12.1%), with girls reporting more trauma exposures and PTSD symptoms than boys. Given these preliminary

findings and given the higher rates of current criminal violence in South Africa, it was hypothesised that higher rates of trauma exposure and posttraumatic stress disorder would be endorsed by South African adolescents; in addition, female adolescents in both South African and Kenyan samples would endorse considerably higher rates of PTSD than boys. The study is detailed in Chapter 2.

Second, characteristics of trauma and PTSD were assessed in a treatment-seeking clinic sample of trauma-exposed adolescents (described in Chapter 3). The aims were to: (i) examine the frequency of traumatic events, full and partial PTSD symptoms, other psychopathology (e.g., depression and anxiety), and functional impairment, (ii) differentiate which types of exposure were most likely to be associated with symptom expression, for example, PTSD and depression, as these are frequently comorbid and may have implications for treatment, and (iii) describe the profile of PTSD symptom clusters in a clinic-based sample. With respect to the study detailed in chapter 2, the objectives were to: (i) compare demographic and phenomenological differences in clinic-based and community-based adolescents presenting with violent trauma exposure, and (ii) clarify whether PTSD symptom cluster profiles in

trauma-exposed adolescent clinic attendees (i.e. a potentially ‘high-risk’ sample) were distinct from that in community-based trauma-exposed adolescents (i.e., a potentially ‘low risk’ sample).

Third, although SSRIs are a first line pharmacotherapy in adults with PTSD, the question arises as to whether this is appropriate pharmacotherapy for adolescents with the disorder. Chapter 4 details an open-label trial of a selective serotonin reuptake inhibitor (SSRI) in a sub-sample of treatment-seeking children and adolescents derived from the sample described in Chapter 3. Adolescents with moderate to severe PTSD were treated with the SSRI, citalopram, which has a high selectivity for serotonin reuptake inhibition and a low potential for drug interactions. Based on preliminary results of efficacy and safety emanating from this small sample study, a second 8-week trial of citalopram was undertaken in a larger sample of adolescents and, in this second trial, between-group differences in response to citalopram between adolescents and adults was also compared. It was hypothesised that citalopram would demonstrate efficacy in adolescents, as demonstrated by a significant reduction in all three PTSD symptom cluster scores (intrusive, avoidance,

hyperarousal). In a comparison with adults who would be treated with the same agent, it was hypothesized that both the magnitude of symptom reduction and the time to improvement would be in line with adult findings. A comparison of the two groups with respect to demographic features, index trauma type, multiplicity of exposure, and onset/duration of PTSD symptoms was also conducted and these findings are presented in Chapter 5.

1.5 References

American Academy of Child and Adolescent Psychiatry (1998) Practice parameters for the assessment and treatment of children and adolescents with posttraumatic stress disorder. *J Am Acad Child Adolesc Psychiatry*, **37 (Suppl),** 4S-26S.

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), 4th ed. *American Psychiatric Press*: Washington, DC.

American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), 4th ed. *American Psychiatric Press*: Washington, DC.

Arora FC, Fichtner CG, O'Connor F, Crayton JW (1993) Paroxetine binding in the blood platelets of posttraumatic stress disorder patients*. Life Sci*, **53,** 919-928.

Asnis GM, Kohn SR, Henderson M, Brown NL (2004) SSRIs versus non-SSRIs in post-traumatic stress disorder: an update with recommendations. *Drugs,* **64(4),** 383-404.

Bernstein GA, Garfinkel BD, Borchardt CM (1990) Comparative studies of pharmacotherapy for school refusal. *J Am Acad Child Adolesc Psychiatry*, **29**, 773-781.

Bernstein GA, Borchardt C.M, Perwien AR (1996) Anxiety disorders in children and adolescents. A review of the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry,* **35 (9),** 1110-1119.

Birmaher B, Axelson DA, Monk K, Kalas C, Clark DB, Ehmann M, Bridge J, Heo J, Brent DA (2003) Fluoxetine for the treatment of childhood anxiety disorders. *J Am Acad Child Adolesc Psychiatry,* **42(4),** 415-23.

Blank A (1993) The longitudinal course of posttraumatic stress disorder. In: Davidson J, Foa EB, eds. Posttraumatic Stress Disorder: DSM-IV and Beyond. Washington, DC: *American Psychiatric Press*, 3-22.

Brady KT (1997) Posttraumatic stress disorder and comorbidity: Recognizing the many faces of PTSD. *J Clin Psychiatry,* **58 (supplement),** 12-15.

Braun P, Greenberg D, Dasberg H, Lerer B (1990) Core symptoms of posttraumatic stress disorder unimproved by alprazolam treatment. *J Clin Psychiatry,* **51,** 236-238.

Breslau N, Davis GC, Andreski P, et al. (1991) Traumatic events and posttraumatic stress disorder in an urban population of young adults. *Arch Gen Psychiatry,* **48,** 216-222.

Breslau N, Davis GC, Andreski P, et al. (1997) Sex differences in posttraumatic stress disorder. *Arch Gen Psychiatry,* **54,** 1044-1048.

Breslau N, Kessler RC, Chilcoat HD, Schultz GC, Andreski P (1998) Trauma and posttraumatic stress disorder in the community: the 1996 Detroit Area Survey of Trauma. *Arch Gen Psychiatry,* **55 (7),** 626-632.

Breslau N, Wilcox HC, Storr CL, et al. (2004) Trauma exposure and posttraumatic stress disorder: a study of youths in urban America. *J Urban Health*, **81(4),** 530-44.

Briere J (1996) Trauma Symptom Checklist for Children (TSCC). Odessa, Psychological Assessment Resources.

Burke JD Jr, Moccia P, Borus JF, Burns BJ (1986) Emotional distress in fifth-grade children ten months after a natural disaster. *J Am Acad Child Psychiatry,* **25(4),** 536-41.

Carrion VG, Weems CF, Ray R et al. (2002) Toward an empirical definition of pediatric PTSD: The phenomenology of PTSD symptoms in youth. *J Am Acad Child Adolesc Psychiatry*, **41,** 166-173.

Charney DS, Deutsch AY, Krystal JH, Southwick SM, Davis M (1993) Psychobiological mechanisms of posttraumatic stress disorder. *Arch Gen Psychiatry,* **50,** 294-305.

Clarke G, Sack WH, Goff B (1993) Three forms of stress in Cambodian adolescent refugees. *J Abnorm Child Psychol,* **21(1),** 65-77.

Cohen JA, Mannarino AP, Rogal S (2001) Treatment practices for childhood posttraumatic stress disorder. *Child Abuse and Neglect,* **25,** 123-135.

Cuffe SP, Addy CL, Garrison CZ, et al. (1999) Prevalence of PTSD in a community sample of older adolescents. *J Am Acad Child Adolesc Psychiatry*, **37 (2),** 147-154.

Davidson JR, Weisler RH, Butterfield MI, et al. (2003) Mirtazapine vs. placebo in posttraumatic stress disorder: a pilot trial. *Biol Psychiatry*, **53(2),** 188-91.

Daviss WB, Mooney D, Racusin R, et al. (2000) Predicting posttraumatic stress after hospitalization for pediatric injury. *J Am Acad Child Adolesc Psychiatry,* **39(5),** 576-83.

De Bellis MD, Keshavan MS, Clark DB, et al. (1999) Developmental traumatology, part II: Brain development. *Biol Psychiatry*, **45,** 1271-1284.

De Bellis MD, Keshavan MS, Frustaci K, et al. (2002) Superior temporal gyrus volumes in maltreated children and adolescents with PTSD. *Biol Psychiatry*, **51,** 544-552.

Domon SE, Andersen MS (2000) Nefazodone for PTSD [letter]. *J Am Acad Child Adolesc Psychiatry*, **39,** 942-943.

Donnelly CL, Amaya-Jackson L, March JS (1999) Psychopharmacology of pediatric posttraumatic stress disorder. *Journal of Child and Adolescent Psychopharmacology,* **9 (3),** 203-220.

Donnelly CL, Amaya-Jackson L (2002) Post-traumatic stress disorder in children and adolescents. Epidemiology, diagnosis and treatment options. *Pediatr Drugs*, **4**, 159-170.

Durakovic-Belko E, Kulenovic A, Dapic R (2003) Determinants of posttraumatic adjustment in adolescents from Sarajevo who experienced war. *J Clin Psychol,* **59(1),** 27-40.

Famularo R, Kinscheiff R, Fenton T (1988) Propranolol treatment for childhood posttraumatic stress disorder: acute type: a pilot study. *American Journal of Diseases of Children,* **142,** 1244-1247.

Famularo R, Fenton T, Augustyn M, Zuckerman B (1996) Persistence of pediatric post traumatic stress disorder after 2 years. *Child Abuse and Neglect*, **20 (12),** 1245-1248.

Foa EB, Steketee G, Rothbaum BO (1989) Behavioral/cognitive conceptualisations of posttraumatic stress disorder. *Behavior Therapy*, **20,** 155-176.

Foa EB, Johnson KM, Feeny NC et al. (2001) The Child PTSD Symptom Scale: a preliminary examination of its psychometric properties. *J Clin Child Psychol*, **30,** 376-84.

Foy DW, Madvig BT, Pynoos RS, Camilleri AJ (1996) Etiologic factors in the development of posttraumatic stress disorder in children and adolescents. *J Sch Psychol,* **34,** 133-145.

Frederick CJ (1985) Children traumatized by catastrophic situations. In: Eth S, Pynoos RS (eds.). *Posttraumatic Stress Disorder in Children*. Washington, DC : American Psychiatric Press, pp 71-100.

Fremont WP (2004) Childhood reactions to terrorism-induced trauma: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry,* **43(4),** 381-92.

Friedman MJ, Southwick SM (1995) Towards pharmacotherapy for post-traumatic stress disorder. In: Friedman MJ, Charney DS, Deutch AY (eds.). *Neurobiological and Clinical Consequences of Stress: From Normal Adaptation to PTSD*. Philadelphia (PA): Lippincott-Raven Publishers, 465-481.

Garrison CZ, Bryant ES, Addy CL, Spurrier PG, Freedy JR, Kilpatrick DG (1995) Posttraumatic stress disorder in adolescents after Hurricane Andrew. *J Am Acad Child Adolesc Psychiatry 1995,* **34,** 1193-1201.

Gelpin E, Bonne O, Peri T, et al. (1996) Treatment of recent trauma survivors with benzodiazepines: a prospective study. *J Clin Psychiatry,* **57,** 390-394.

Giaconia RM, Reinherz HZ, Silverman AB et al. (1995) Traumas and posttraumatic stress disorder in a community population of older adolescents. *J Am Acad Child Adolesc Psychiatry*, **34,** 1369-1380.

Gilbertson MW, Shenton ME, Ciszewski A, et al. (2002) Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. *Nature Neurosci*, **5,** 1242-1247.

Goenjian AK, Pynoos RS, Steinberg AM, et al. (1995) Psychiatric comorbidity in children after the 1988 earthquake in Armenia. *J Am Acad Child Adolesc Psychiatry*, **34,** 1174-1184.

Good C, Petersen C (2001) SSRI and mirtazapine in PTSD. *J Am Acad Child Adolesc Psychiatry,* **40(3),** 263-4.

Groome D, Soureti A (2004) Post-traumatic stress disorder and anxiety symptoms in children exposed to the 1999 Greek earthquake. *Br J Psychol*, **95(Pt 3),** 387-97.

Gupta S, Austin R, Cali LA, Bhatara V (1998) Nightmares treated with cyproheptadine. *J Am Acad Child Adolesc Psychiatry*, **37(6),** 570-572.

Harmon RJ, Riggs PD (1996) Clonidine for posttraumatic stress disorder in preschool children. *Journal of the American Academy of Child and Adolescent Psychiatry,* **35,** 1247-1249.

Horrigan JP, Barnhill LJ (1996) The suppression of nightmares with guanfacine. *Journal of Clinical Psychiatry,* **57,** 371.

Horrigan JP (1998) Risperidone appears effective for children, adolescents with severe PTSD. *Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry*, Anaheim.

Hubbard J, Realmuto GM, Northwood AK, Masten AS (1995) Comorbidity of psychiatric diagnosis with posttraumatic stress disorder. *J Am Acad Child Adolesc Psychiatry,* **34,** 1167-1173.

Kant R, Chalansani R, Chengappa KN, Dieringer MF (2004) The off-label use of clozapine in adolescents with bipolar disorder, intermittent explosive disorder, or posttraumatic stress disorder. *J Child Adolesc Psychopharmacol*, **14(1),** 57-63.

Kaufman J, Birmaher B, Brent D et al. (1997) Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry*, **36,** 980-988.

Keane TM, Zimering RT, Caddell JM (1985) A behavioral formulation of posttraumatic stress disorder in Vietnam veterans. *The Behavior Therapist*, **8,** 9-12.

Keller MB, Ryan ND, Strober M, et al. (2001) Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial. *J Am Acad Child Adolesc Psychiatry,* **40(7),** 762-72.

Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB (1995) Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*, **52,** 1048-1060.

Kutcher SP, Reiter S, Gardner DM, et al. (1992) The pharmacotherapy of anxiety disorders in children and adolescents. *Psychiatr Clin North Am*, **15,** 41-67.

Labellarte MJ, Walkup JT, Riddle MA (1998) The new antidepressants. Selective serotonin reuptake inhibitors. *Pediatric Clinics of North America,* **45 (5),** 1137-1155.

Leonard HL, March J, Rickler KC, Allen AJ (1997) Pharmacology of the selective serotonin reuptake inhibitors in children and adolescents. *J Am Acad Child Adolesc Psychiatry*, **36(6),** 725-736.

Lee I, Ha YS, Kim YA, Kwon YH (2004) PTSD symptoms in elementary school children after Typhoon Rusa. *Taehan Kanho Hakhoe Chi*, **34(4),** 636-45.

Lipschitz DS, Rasmusson AM, Yehuda R, et al. (2003) Salivary cortisol responses to dexamethasone in adolescents with posttraumatic stress disorder. *J Am Acad Child Adolesc Psychiatry,* **42,** 1310-1317.

Looff D, Grimley P, Kuiler F, Martin A, Shunfield L (1995) Carbamazepine for posttraumatic stress disorder (letter). *Journal of the American Academy of Child and Adolescent Psychiatry,* **34,** 703-704.

Lowenstein RJ, Hornstein N, Farber B (1988) Open trial of clonazepam in the treatment of post- traumatic stress symptoms in multiple personality disorder. *Dissociation*, **1,** 3-12.

March JS, Amaya-Jackson L, Pynoos RS (1996) Pediatric posttraumatic stress disorder. In: J.M. Weiner (Ed.), *Textbook of Child and Adolescent Psychiatry, 2nd Edition.* Washington, DC: American Psychiatric Press.

March JS, Amaya-Jackson L, Terry R, Costanzo P (1997) Posttraumatic symptomatology in children and adolescents after an industrial fire. *J Am Acad Child Adolesc Psychiatry,* **36(8),** 1080-8.

March J (1999) Assessment of pediatric posttraumatic stress disorder. In: P Saigh and D Bremner (eds.), *Posttraumatic Stress Disorder*:199-218.

Mazza JJ (2000) The relationship between posttraumatic stress symptomatology and suicidal behavior in school-based adolescents. *Suicide Life Threat Behav,* **30 (2),** 91-103.

McCloskey LA, Walker M (2000) Posttraumatic stress in children exposed to family violence and single-event trauma. *J Am Acad Child Adolesc Psychiatry*, **39(1),** 108-115.

McFarlane AC (2000) Posttraumatic stress disorder: a model of the longitudinal course and the role of risk factors. *J Clin Psychiatry*, **61 (suppl 5),** 15-20.

Nader K, Pynoos R, Fairbanks LA et al., (1993) A preliminary study of PTSD and grief among the children of Kuwait following the Gulf Crisis. *Br J Clin Psychol*, **32,** 407-416.

Nader K, Pynoos R, Fairbanks L, Frederick C (1990) Children's PTSD reactions one year after a sniper attack at their school. *Am J Psychiatry*, **147,** 1526-1530.

Nader KO, Kriegler JA, Blake DD et al. (1996) Clinician Administered PTSD Scale, Child and Adolescent Version (CAPS-C). White River Junction, National Center for PTSD, 1994.

Newman E, Amaya-Jackson L (1996) Assessment of trauma instruments for children. Paper presented at the Scientific Proceedings of the 12th International Conference for Traumatic Stress Studies, San Francisco, CA.

Penava SJ, Otto MW, Pollack MH, et al. (1997) Current status of pharmacotherapy for PTSD: an effect size analysis of controlled studies. *Depression Anxiety*, **4,** 240-242.

Perkonigg A, Kessler RC, Storz S, Wittchen HU (2000) Traumatic events and post-traumatic stress disorder in the community: prevalence, risk factors and comorbidity. *Acta Psychiatr Scand*, **101(1),** 46-59.

Perrin S, Smith P, Yule W (2000) The assessment and treatment of Post-traumatic Stress Disorder in children and adolescents. *J Child Psychol Psychiatry*, **41(3),** 277-289.

Perry BD (1994) Neurobiological sequelae of childhood trauma: PTSD in children. In: Murburg MM (ed.). *Catecholamine Function in Post-Traumatic Stress Disorder: Emerging Concepts.* Washington, DC: American Psychiatric Press, 233-255.

Perry BD, Azad I (1999) Posttraumatic stress disorder in children and adolescents. *Curr Opin Pediatr,* **11(4),** 310-6.

Pfefferbaum B (1997) Posttraumatic stress disorder in children: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry*, **36,** 1503-1511.

Pitman RK, Shin LM, Rauch SL (2001) Investigating the pathogenesis of posttraumatic stress disorder with neuroimaging. *J Clin Psychiatry*, **62 Suppl 17,** 47-54.

Pynoos RS, Frederick C, Nader K, et al. (1987) Life threat and posttraumatic stress in school-age children. *Arch Gen Psychiatry,* **44(12),** 1057-63.

Pynoos R, Steinberg AM, Goenjian A (1996) Traumatic stress in childhood and adolescence: recent developments and current controversies. In: B van der Kolk, AC McFarlane, L Weisaeth (eds.). *Traumatic Stress: The Effects of Overwhelming Experience on Mind, Body and Society*. New York, Guilford, 331-358.

Reich W, Shayka JJ, Taibelson C (1991) Diagnostic Interview for Children and Adolescents (DICA). St Louis, Washington University.

Resnick HS, Yehuda R, Pitman RK, et al. (1995) Effect of previous trauma on acute plasma cortisol following rape. *Am J Psychiatry*, **152,** 1675-1677.

Risse SC, Whitters A, Burke J, et al. (1990) Severe withdrawal symptoms after discontinuation of alprazolam in eight patients with combat-induced posttraumatic stress disorder. *J Clin Psychiatry*, **51,** 206-209.

Robert R, Blackeney PE, Villareal C, et al. (1999) Imipramine treatment in pediatric burn patients with symptoms of acute stress disorder. *J Am Acad Child Adolesc Psychiatry*, **38,** 873-882.

RUPP Anxiety Study Group (2001) An eight-week placebo-controlled trial of fluvoxamine for anxiety disorders in children and adolescents. *N Engl J Med*, **344,** 1279-1285.

Saxe G, Stoddard F, Courtney D, et al. (2001) Relationship between acute morphine and the course of PTSD in children with burns. *J Am Acad Child Adolesc Psychiatry*, **40(8),** 915-921.

Shaffer D, Fisher P, Dulcan M et al. (2000) The NIMH Diagnostic Interview Schedule for Children (DISC-2.3): description, acceptability, prevalences and performance in the MECA study. *J Am Acad Child Adolesc Psychiatry*, **39,** 28-38.

Schwab-Stone M, Chen C, Greenberger E, et al. (1999) No safe haven II: the effects of violence exposure on urban youth. *J Am Acad Child Adolesc Psychiatry*, **38 (4),** 359-367.

Schwarz ED, Kowalski JM (1991) Posttraumatic stress disorder after a school shooting: effects of symptom threshold selection and diagnosis by DSM-III, DSM-III-R, or proposed DSM-IV. *Am J Psychiatry*, **148(5),** 592-7.

Silva RR, Alpert M, Munoz DM, Singh S, Matzner F, Dummit S (2000) Stress and vulnerability to posttraumatic stress disorder in children and adolescents. *Am J Psychiatry,* **157(8),** 1229-35.

Southwick SM, Krystal JH, Bremner JD (1997) Noradrenergic and serotonergic function in posttraumatic stress disorder. *Arch Gen Psychiatry,* **54,** 749-758.

Stallard P, Salter E, Velleman R (2004) Posttraumatic stress disorder following road traffic accidents - a second prospective study. *Eur Child Adolesc Psychiatry,* **13(3),** 172-8.

Stein DJ, Seedat S, van der Linden GJ, Zungu-Dirwayi N (2000) Selective serotonin reuptake inhibitors in the treatment of post-traumatic stress disorder: a meta-analysis of randomized controlled trials. *Int Clin Psychopharmacol*, **15 Suppl 2,** S31-9.

Stoddard FJ, Norman DK, Murphy JM (1989) A diagnostic outcome study of children and adolescents with severe burns. *J Trauma,* **29(4),** 471-7.

Terr LC (1991) Childhood traumas: An outline and overview. *Am J Psychiatry*, **148,** 10-20.

Thomas LA, De Bellis MD (2004) Pituitary volumes in pediatric maltreatment-related posttraumatic stress disorder. *Biol Psychiatry*, **55(7),** 752-8.

Vrana S, Lauterbach D (1994) Prevalence of traumatic events and posttraumatic psychological symptoms in a nonclinical sample of college students. *J Traumatic Stress*, **7,** 289-302

Yang P, Wu M-T, Hsu C-C, Ker JH (2004) Evidence of early neurobiological alterations in adolescents with posttraumatic stress disorder: a functional MRI study. *Neuroscience Letters,* **370 (1),** 13-18.

Yehuda R, McFarlane AC (1995) Conflict between current knowledge about posttraumatic stress disorder and its original conceptual basis. *Am J Psychiatry*, **152,** 1705-1713.

Yehuda R (2002) Post-traumatic stress disorder. *N Engl J Med,* **346(2),**108-14.

Weisenberg M, Schwarwzald J, Waysman M, Solomon Z, Klingman A (1993) Coping of school-age children in the sealed room during scud missile bombardment and postwar stress reactions. *J Consult Clin Psychol*, **61,** 462-467.

2. EPIDEMIOLOGY AND PHENOMENOLOGY OF POSTTRAUMATIC STRESS DISORDER IN A COMMUNITY SAMPLE

Trauma Exposure and Posttraumatic Stress Symptoms in Adolescents: A Schools' Survey in Cape Town (South Africa) and Nairobi (Kenya)

2.1 Study Summary

There is a lack of comparative data on the prevalence and effects of violence exposure in African youth. This study assessed trauma exposure, posttraumatic stress symptoms, and gender differences in adolescents from two African countries. Two thousand and forty one boys and girls from 18 schools in Cape Town and Nairobi completed anonymous self-report questionnaires.

More than 80% reported exposure to severe trauma, either as victims or witnesses. Kenyan adolescents, compared with South African adolescents, had significantly higher rates of exposure to witnessing violence (69% vs. 58%), serious accidents (33% vs. 26%), physical assault by a family member (27% vs. 14%) and sexual assault (18% vs. 14%). However, rates of current full symptom PTSD (22.2% vs.4.7%) and current partial symptom PTSD (11.9% vs. 8.2%) were

significantly higher in the S.A. sample. Boys were as likely as girls to meet PTSD symptom criteria.

While lifetime exposure to trauma was comparable across both settings, Kenyan adolescents had much lower rates of PTSD. This difference may be attributable to cultural and other trauma-related variables. High rates of sexual assault and PTSD, traditionally documented in girls, may also occur in boys and warrants further study.

2.2 Background

Globally great variability exists in the estimates of violence exposure in community samples of adolescents. Surveys in the United States have consistently observed high rates of violence and victimisation among urban adolescents, with some studies reporting rates ranging from 9% to 42% for experiencing and witnessing serious violence (American School Health Association, 1989; Center for Disease Control and Prevention, 1992; Schubiner et al., 1993). In a national telephone sample of youth aged 10 to 17 years in the United States, over one third reported being victims of assault and victimised adolescents displayed significantly more psychological and behavioural symptomatology than nonvictimised respondents (Boney-McCoy and Finkelhor, 1995).

The phenomenon of community violence exposure is conceptually complex as it applies not only to direct personal exposure, but also exposure through witnessing and vicarious means (Foy and Goguen, 1998). Community violence exposure has been reliably linked with diverse mental health and behavioural sequelae including depression, anxiety, posttraumatic stress, low self-esteem, self-destructive behaviour and aggression (Richters & Martinez,

1993; Fitzpatrick & Boldizar, 1993; Giaconia et al., 1995). The constructs of community violence exposure and psychological sequelae appear to be directly related, with exposure to violence positively and linearly related to psychological distress, and more exposure to violence associated with more self-reported posttraumatic stress disorder (PTSD) and depressive symptomatology (Rosenthal and Wilson, 2001; Ozer and Weinstein, 2004). Indeed, both direct (e.g. being victimised) and indirect (e.g., witnessing violence) violence exposure have demonstrated independent (as well as overlapping) relationships with traumatic symptoms (Rosenthal, 2000), and it has been suggested that not only are PTSD symptoms significantly associated with exposure to violence, but that PTSD symptoms may in fact mediate the relationship between exposure to violence and other forms of psychological distress, such as depression and suicidal ideation (Mazza and Reynolds, 1999).

While many adolescents have to contend with chronic and high levels of violence exposure, specific factors relating to risk and resilience in adolescents remain unclear. Risk for community violence exposure is higher among the poor, non-white, and those who live in densely populated urban

areas (Fitzpatrick and Boldizar, 1993). Studies have also found that late adolescence (ages 15-19) represents the period of highest risk for community violence exposure (Foy and Goguen, 1998). With respect to the risk for PTSD, a review of 55 studies on youth found that 85% of studies that examined linkages between trauma exposure severity and PTSD symptomatology demonstrated significant relationships (McLain et al., 1998). Prior trauma exposure was also consistently associated with increased PTSD symptomatology. Age, gender, and ethnicity were significantly related to PTSD in some studies but the authors suggested that more studies are needed before definitive patterns can be discerned. More recent work suggests that social support alone may not be sufficient to “buffer’ the effect between exposure to community violence and psychological distress (Paxton et al., 2004). Furthermore, gender may be an important determinant of later trauma-related distress in adolescents. Studies have demonstrated higher rates of mood and anxiety symptoms in girls than boys (Pynoos et al., 1993; Green et al., 1994). For example, in a study of African-Americans aged between 7 and 18 years (Fitzpatrick and Boldizar, 1993), boys were more likely than girls to be victims of, and witnesses to, violent acts, but PTSD symptoms were more severe in victimized girls.

As yet, there are no national large-scale epidemiological surveys of the prevalence of PTSD among children and adolescents in the general population; however, community studies in the United States have consistently indicated that approximately 40% of high school students have experienced some form of domestic or community violence and 3% to 6% have PTSD (Giaconia et al., 1995; Cuffe et al., 1998). Furthermore, few surveys have described the extent of violence exposure and its associated psychological outcomes in African youth. One recent survey (Ward et al., 2001) involving four secondary schools (n=104) in Cape Town (South Africa) found that the majority of adolescents (more than 70%) were exposed to at least one type of violent event either as victims or witnesses, with 5.8% likely to meet criteria for post-traumatic stress disorder (PTSD). PTSD symptoms and depression were related to most types of violence exposure. In other cross-sectional studies of youth in rural and urban settings in South Africa (S.A.), high rates of violence exposure ranging from 67% to 95% have been documented, with 8.4% to 40% of children less than seventeen years of age fulfilling PTSD diagnostic criteria (Peltzer, 1999; Ensink et al., 1997). A significant positive relationship has also been identified

between the extent of exposure and the development of PTSD (Peltzer, 1998).

To date, there has been only one randomised controlled school-based study on the effectiveness of psychological interventions for children with symptoms of PTSD resulting from, personal experience of, or exposure to, violence (Stein et al., 2003). Students at 2 large middle schools in Los Angeles (USA), who had reported exposure to violence and had clinical symptoms of PTSD, were randomly assigned to a 10-session school-based standardised cognitive-behavioural therapy (CBT) early intervention or to a wait-list delayed intervention comparison. The group who received the brief CBT intervention, delivered by school mental health clinicians on school premises, had significantly fewer reported symptoms of PTSD and depression than the wait-listed delayed intervention group. Notably, the magnitude of effect on child- and parent-reported outcomes was comparable to that of other child psychotherapy intervention trials for disorders other than PTSD, suggesting that such an intervention, incorporated into existing community-based programs and delivered by school-based psychologists, could be useful in settings

where accessibility to mental health services might be limited.

With these data underscoring the high risk that adolescents are at for being victims of violent crime and with the apparent need for a better understanding of how specific violent experiences may or may not lead to adverse psychological experiences such as PTSD and depression within particular populations of youth, the aim of this survey was to compare trauma exposure and its sequelae, in particular rates of full and partial current PTSD symptoms, in grade 10 adolescents in public and private schools from two African cities. The key statistical differences of interest were type of trauma, gender, and risk for PTSD in the context of setting. In a preliminary survey conducted at three secondary schools (n=307) in Cape Town (Seedat et al., 2000), we noted high rates of PTSD (12.1%), with girls reporting more trauma exposures and PTSD symptoms than boys. Given these preliminary findings and given the high rates of current criminal violence in the country (Victims of Crime Survey, 1998), it was hypothesised that South African respondents, especially females, would endorse considerably higher rates of trauma and PTSD compared with Kenyan respondents. It was also hypothesised that in the

sample as a whole (i) exposure to violence in adolescents would have a positive and significant association with posttraumatic stress disorder symptoms; (ii) exposure to multiple traumas would have a stronger association with PTSD symptoms, and (iii) gender effects in response to violent crime would be evident, with girls responding to violence with more PTSD symptoms than boys.

2.3 Methods

2.3.1 Subjects

The sampling pool comprised grade 10 students from 18 schools in Cape Town (South Africa) and Nairobi (Kenya) who were surveyed during the 2000 school year. Seven public schools and two private urban schools were selected in each city to be representative of the ethnic and socio-economic make-up of the population. A stratified sampling procedure was used to select students in grade 10 at public and private high schools in Cape Town and Nairobi. Schools were stratified according to geographic area. One thousand one hundred and forty South African students and 901 Kenyan students participated. Their mean age was 15.8 years (SD = 0.98 years, range 10.5 to 22 years).

2.3.2 Procedures

The protocol was approved by the institutional review board (University of Stellenbosch) and the Departments of Education in Cape Town and Nairobi. Students and parents were notified in advance of the study. Participation was entirely voluntary and no student or parent opposed participation. All grade 10 students present on the day of the survey completed anonymous self-report questionnaires in English under the supervision of classroom teachers and

research assistants (master's level) during a 45-60 minute classroom period at their schools. Within each school, all grade 10 adolescents who were present on the day of the survey participated. No attempt was made to substitute students if a class had absentees.

2.3.3 Instruments

(i) Demographics Questionnaire

A demographics questionnaire was devised by the authors and included demographic information on age, gender, ethnicity, composition of the home, parental marital status, parental occupation, family income and substance use (cigarette smoking, alcohol, and other drug use).

(ii) Trauma Checklist

The Trauma Checklist, a list of DSM-IV qualifying traumas (e.g. being robbed or mugged, being physically hurt or attacked, being raped) was adapted from the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997). Respondents were also required to circle the most frightening or upsetting event that ever happened to them.

(iii) Child PTSD Checklist

After ascertaining the event that was the most frightening or upsetting, the Child PTSD Checklist (Newman and Amaya-Jackson, 1996), a 28-item child-adolescent PTSD structured interview, was administered. The Child PTSD Checklist was developed to diagnose child-adolescent PTSD, however information about its psychometric properties have not been reported in the literature. For this survey, the scale was administered as a self-rated measure. The Child PTSD Checklist which rates the presence of each of the 17 PTSD symptoms (American Psychiatric Association, 2000) in the past month, was used to assess for current PTSD. The PTSD checklist yields 3 composite scores (for the 3 PTSD symptom clusters) and an overall score. The scale uses a 4-point Likert format with ‘0’ corresponding to “not at all” and ‘3’ to “all of the time”. For the purpose of the study, respondents were asked to rate PTSD symptoms according to the most upsetting event endorsed on the Trauma Checklist. A conservative threshold of ‘2’ (i.e. “most of the time”) was used to endorse the presence of a symptom. Partial symptom PTSD was defined as having at least one symptom in each DSM-IV symptom criterion category (Stein et al., 1997; Marshall et al., 2001).

(iv) Life Events Questionnaire-Adolescent version (LEQ-A)

The LEQ-A (Masten et al., 1994), a 45-item measure of negative and positive life events, was used to measure non-PTSD events that can happen in the life of any adolescent or in any family. Respondents were required to indicate (‘yes’ or ‘no’) if an event had happened to them or their families in the past year. Discrete, negative life events included school failure and suspension, pregnancy, legal difficulties, and trouble with drugs and alcohol.

(v) Beck Depression Inventory (BDI)

The BDI is a widely used 21-item self-report measure of cognitive, affective, somatic and behavioural symptoms of depression with excellent psychometric properties (Beck & Steer, 1987). Internal consistency of the BDI has been reported to range from .73 to .92 with a mean of .86 (Beck et al., 1988). Meta-analysis of the scale’s psychometric properties suggest high content validity, and validity in differentiating between depressed and non-depressed individuals (Richter et al., 1998). Each item comprises four statements rated from 0 to 3. A total score for the 21 items is obtained, with the lowest possible score being 0 and the highest possible total being 63. High scores indicate more severe depression. In a school sample of adolescents who were screened with the BDI, a screening

score of 16 produced 100% sensitivity and 93% specificity (Barrera & Garrison-Jones, 1988).

2.4 Statistical Analyses

All data was analysed using SPSS (version 10.0) for Windows. Demographic characteristics, exposure by trauma type, posttraumatic stress and depressive symptoms were assessed using frequency and descriptive statistics. Chi-squared tests (and odds ratios) for categorical variables and student t-tests for numeric variables were used to explore the relationship between country, gender, trauma exposure, PTSD and depression. Pearson's correlation statistics were used to correlate PTSD symptoms with BDI total scores. Fisher's exact tests were done in place of chi-squared tests for independence when one or more cells in a 2 X 2 table had an expected count of less than 5. All tests were two-tailed and significance was set at $p < .05$.

2.5 Results

2.5.1 Demographic characteristics

Table 1 compares the demographic characteristics of S.A. and Kenyan respondents. There was a preponderance of girls in both groups. The majority of Kenyan respondents were Black while the majority of S.A. students were of mixed descent, representing the majority ethnic groups in these two cities (Nairobi & Cape Town). 38% of S.A. students were from homes characterized by single, divorced or widowed parents compared with 19% of Kenyan students.

2.5.2 Pattern of trauma exposure

More than 80% of all respondents (n=2041) reported lifetime exposure to at least one DSM-IV trauma (APA, 2000). The mean number of trauma exposures was 2.49 (SD=1.99, range= 0 to 11). Results of comparisons by country were not statistically significant. For both S.A. and Kenyan respondents, the commonest traumas were witnessing community violence (63%), being robbed or mugged (35%) and witnessing a family member being hurt or killed (33%). However, significantly more Kenyan than S.A. respondents had witnessed violence, been in a bad accident, been physically hurt/ beaten by a family member or been sexually assaulted (Table 2).

2.5.3 PTSD symptoms

The most common PTSD symptoms in descending order were: (i) avoidance of activities, places or people that aroused recollections of the trauma [***S.A.:*** 33.3%, ***Kenya:*** 53.2%], (ii) avoidance of thoughts, feelings, or conversations associated with the trauma [***S.A.:*** 32.4%, ***Kenya:*** 50.5%], (iii) irritability or outbursts of anger [***S.A.:*** 31.1%, ***Kenya:*** 23.1%] and (iv) intense psychological distress at exposure to traumatic reminders [***S.A.:*** 21.3%, ***Kenya:*** 28.0%].

S.A respondents had higher scores across all the 3 symptom clusters (re-experiencing, avoidance, hyperarousal) and more PTSD symptoms than Kenyan respondents [***S.A.:*** 4.9 (±5.5); ***Kenya:*** 2.3 (±2.9), t=13.2, *p* <.001).

14.5% [n=295] of adolescents met symptom criteria for full PTSD while an additional 10.3% [n=210] met symptom criteria for partial PTSD. Notably, 22.2% of S.A. adolescents had a full PTSD symptom diagnosis compared with only 4.7% of Kenyan adolescents (*p* <. 001) *and* 11.9% met symptom criteria for partial PTSD compared with 8.2% in the Kenyan group (*p* <.01).

2.5.4 Relationship between trauma exposure & PTSD symptoms

Adolescents meeting symptom criteria for full PTSD (n=295) endorsed more traumas on the Trauma Checklist than adolescents without PTSD [3.5 (± 2.6) vs. 2.3 (± 1.8), t=-9.7, *p* <.001). These differences remained significant in the analysis by country [**PTSD+** vs. **PTSD-: *Kenya:*** 2.9 (±2.1) vs. 2.4 (±1.7) mean exposures, t=-2.1, *p* <. 05; S.A*.:* 3.6 (± 2.7) vs. 2.2 (± 1.9) mean exposures, t=-9.1, *p* <. 001] and by gender [**PTSD+** *vs.* **PTSD-: *Males:*** 3.7 (± 2.6) vs. 2.5 (± 1.9) mean exposures, t=-6.3, *p* <. 001; ***Females:*** 3.2 (±2.5) vs. 2.2 (±1.8) mean exposures]. Respondents with full symptom PTSD were more likely to endorse a higher number of traumas (mean ± SD =3.7 ± 2.5) than those with partial symptom PTSD (mean ± SD = 2.9 ± 1.9) or no PTSD (mean ± SD = 2.3 ± 1.8) (F = 58.9, *p* <. 001).

2.5.5 Gender & trauma exposure

Boys had a higher mean number of trauma exposures than girls (2.7 ± 2.0 vs. 2.3 ± 1.9, t=3.7, p <. 002). Boys were also significantly more likely than girls to have witnessed community violence (67% vs. 60%, Fisher’s exact test, p <. 001), to have been robbed or mugged (39% vs. 33%, Fisher’s exact test, p <0.03), to have been beaten by a non-family

member (26% vs. 15%, Fisher's exact test, p <. 001), and to have been victims of sexual assault (19% vs.13%, Fisher's exact test, p <. 002) (Table 3). "Sexual assault' was operationalised in the survey as 'any unwanted and forceful sexual experience that made you feel uncomfortable'. When boys and girls were analysed by country, these differences remained significant in the Kenyan sample but not in the S.A. sample.

2.5.6 Gender & PTSD Symptoms

Boys and girls were equally likely to meet symptom criteria for full PTSD (χ^2 = .96, *p*< .18, *ns* [not significant]) and partial PTSD (Fisher's exact test, *p* < .07, *ns*). In the sample as whole, PTSD symptom clusters (re-experiencing, avoidance and hyperarousal symptoms) also did not differ significantly by gender. However, in the S.A. sample girls reported more re-experiencing and avoidance symptoms than boys (Table 4). S.A. girls also had higher mean scores on the Child PTSD Checklist (indicative of greater symptom severity) (*Females:* 20.5 (± 15.6) vs. *Males*: 17.2 (± 14.4), t= -3.2, *p* < 0.001).

2.5.7 Lifetime trauma exposure, PTSD & ethnicity

Table 5 shows lifetime trauma exposure rates and rates of PTSD across the major ethnic groups in the sample. Among the majority ethnic grouping in the sample (mixed descent), 85% reported exposure to trauma with 25% of those exposed meeting criteria for a PTSD symptom diagnosis. In the Kenyan sample, 75% of the majority ethnic grouping (Black) endorsed trauma exposure. However, only 5% met PTSD symptom criteria.

2.5.8 Trauma type & PTSD risk

Based on respondents' selection of the most frightening or upsetting event, the 3 traumas most likely to be associated with a PTSD symptom diagnosis were: sexual assault (χ^2 = 38.9, p <. 001, odds ratio [OR] = 2.5, 95% CI [1.8-3.3]), physical assault by a family member (χ^2 = 43.3, p <. 001, OR=2.3, 95% CI [1.8-2.9]), and serious accidents (χ^2 = 33.5, p <. 001, OR=2.2, 95% CI [1.7-2.9]). The risk of PTSD following sexual assault was the same for girls (24% of sexually assaulted girls, Fisher's exact test, p <. 001, OR=2.3) as it was for boys (25% of sexually assaulted boys, Fisher's exact test, p <. 001, OR=2.3).

2.5.9 Regression analysis

All trauma exposures were then entered as independent variables into a stepwise regression equation to examine the relationship between type of trauma exposure and the risk for PTSD. The dependent variable was a PTSD (full) symptom diagnosis. Traumas that constituted independent predictors for PTSD were: (i) sexual assault (p < .001, exp (B) =. 53, 95% CI [0 .39 -.72]), (ii) witnessing family members injured, beaten, hurt or killed (p<. 001, exp (B) =. 55, 95% CI [0.42 - 0.72]), (iii) being in a bad accident (p <. 001, exp (B) = .56, 95% CI [0.41 - 0.75]), (iv) being robbed or mugged (p <. 04, exp (B) = .74, 95% CI [0.56 - 0.98]), (v) being beaten or physically hurt by a family member (p <. 03, exp (B) = .69, 95% CI [0.63 – 1.22]) and, (vi) witnessing violence in the street, neighbourhood or school (p < .02, exp (B) = 1.47, 95% CI [1.09-1.97]). Physical attack by a non-family member (p < .432) and natural disasters (p < .096) were not independently predictive of a PTSD symptom diagnosis.

2.5.10 Depression

For the sample as a whole, mean BDI scores were in the 'mild' range for depression (11.5 ± 16.7). No significant country [***Kenya:*** 12.2 (± 23.2); ***S.A.:*** 11.1 (± 10.5)] or

gender [***Males:*** 10.8 (± 9.7) vs. ***Females:*** 11.4 (± 10.0)] differences were observed. In the Kenyan group, but not in the S.A. group, girls reported more depressive symptoms and had significantly higher scores on the BDI than boys [***Females:*** 12.4 (± 9.3) vs. ***Males:*** 9.5 (± 7.9), t = -3.6, *p* <. 001] (Table 4).

2.5.11 Correlation between PTSD & depression

Number of PTSD symptoms endorsed on the PTSD Checklist (Newman and Amaya-Jackson, 1996) correlated significantly with total BDI scores (*r* = .29, *p* <. 001). Statistical significance was retained in the analyses by country [***Kenya:*** *r* = .20, *p* <. 001; S.A.*:* *r*= .52, *p* <. 001] and gender [***Males:*** *r* = .48, *p* <. 001; ***Females:*** *r* =. 51, *p* <. 001]. Respondents with full symptom PTSD also had higher mean BDI scores (mean ± SD = 20.0 ±11.4) than those with partial symptom PTSD (mean ± SD=13.6 ± 9.6) and those with no PTSD (mean ± SD = 9.4 ± 17.8) (F=37.5, *p* <. 001).

2.5.12 Substance use

More S.A. adolescents than Kenyan adolescents reported smoking cigarettes (≥ 10 cigarettes per day) (5.3% vs. 0.4%, *p* <. 001) and cannabis (10.6 % vs. 1.7%, *p* < .001). In the

sample as a whole, more boys than girls reported cannabis use (8.7% vs. 4.6%, $p < .001$). However, no significant gender differences were noted for cigarette and alcohol use. Use of these substances did not correlate significantly with PTSD symptoms.

2.5.13 Negative life events

S.A. respondents reported a higher number of past year exposures to negative life events on the Life Events Questionnaire (**S.A.:** mean=9.2 ± 5.2, **Kenya:** mean=8.3 ± 4.7, t=4.2, $p <. 001$), that included doing much worse than expected in a test/ examination and breaking up with a boyfriend/girlfriend. Negative life event exposure was not significantly associated with PTSD symptoms (**total sample**: $p =. 170$; **S.A.**: $p =. 372$; **Kenya** = $p =. 562$). Further, adolescents who endorsed 1 or more traumas plus 1 or more negative life events were not more likely to meet PTSD symptom criteria ($\chi^2 = .66$, $p = .363$).

2.6 Discussion

2.6.1 PTSD & trauma

14.5% of adolescents (i.e. 14.8% of those traumatized) fulfilled criteria for a full symptom diagnosis of PTSD while an additional 10.3% (i.e. 11.4% of those traumatized) fulfilled partial PTSD criteria. These rates are strikingly similar to rates previously documented in trauma samples. In study by Giaconia et al. (1995), 14.5 % of affected youth (6.3% of the total sample) met DSM-III-R criteria for PTSD, while Lipschitz et al., 2000) found that 14.4% and 11.6% of traumatized girls met DSM-IV symptom criteria for full and partial PTSD, respectively. It is noteworthy that recent findings support the hypothesis that children with partial/ subthreshold criteria may not differ significantly from children meeting all three cluster criteria (re-experiencing, avoidance, hyperarousal) with regards to functional impairment and distress. For example, in a study by Carrion and colleagues (2002), children with subthreshold PTSD had functional impairment that was specific to PTSD symptoms and was not due to comorbidity. This suggests, therefore, that it might be more precise to make a diagnosis of PTSD in children and adolescents based on the intensity of symptoms and their relationship to

functional impairment than on the threshold number of symptoms.

Both countries had high rates of trauma exposure with 83 % of S.A adolescents and 85% of Kenyan adolescents reporting at least one DSM-IV trauma in their lifetime, echoing the findings of other local (South African) and international studies (Ensink et al., 1997; Peltzer, 1999 American School Health Association, 1989; Giaconia et al., 1995). A noteworthy finding was that both direct (i.e., direct victimisation) and indirect (e.g., witnessing violence) types of violence exposure were predictive of PTSD symptom status.

2.6.2 Differences between S.A. & Kenyan respondents

The most striking finding was the discrepancy in the rate of PTSD between S.A. and Kenyan adolescents in the context of equally high rates of trauma exposure (and even higher rates for specific types of trauma in the Kenyan sample). The lower rate of PTSD in Kenyan adolescents is difficult to explain. The assessments did not measure the severity or chronicity of trauma exposure or past PTSD, variables that may contribute to PTSD risk. For example, differences in toxicity of exposure between the samples (much higher

levels of exposure to violent crime in South African adolescents) may be operant here accounting to some extent for the difference in PTSD rates.

Could cultural factors be responsible? Cultural differences are known to exist in the way that concepts of ‘trauma’, trauma exposure, and PTSD symptoms are operationalised and understood in different ethnic groups. Our survey questionnaires were not culturally validated in the various ethnic groups in which they were used and the likelihood of cultural response bias to questionnaire items cannot be excluded. Further, compared with the S.A. sample in which the cultural contexts of the different communities were diverse, the ethnic composition of the Kenyan sample was relatively homogenous. More than 97% of Kenyan students were Black compared with only a fifth of South African students.

2.6.3 Gender

In this study, boys had a higher mean number of trauma exposures and higher rates of exposure to certain types of assaultive violence (e.g. robbing or mugging, beating by a non-family member, sexual assault) compared with girls. Not all studies have noted gender differences in trauma

exposure. Giaconia et al. (1995), in a community study of 18 year-olds, found that overall rates of trauma were the same for both boys and girls. Other studies have reported a greater incidence of trauma exposure in boys (Breslau et al., 1991; Vrana and Lauterbach, 1994; Schwab-Stone et al., 1999).

A surprising finding was the absence of a gender difference in the overall rate of PTSD. Several studies have demonstrated a much greater risk for PTSD (up to 6-fold) in females (Breslau et al., 1991; Green et al., 1994; Giaconia et al., 1995; Berton and Stabb, 1996; Curle and Williams, 1996; March et al., 1997; Jaycox et al., 2002). For example, Singer et al. (1995) surveyed a diverse sample of high-school students (n=3735) selected from large-city, small-city, and suburban schools, and reported that female gender was the strongest demographic predictor of trauma symptoms, including posttraumatic stress, depression, anxiety, anger, dissociation and total trauma symptoms. In another recent study of adolescents exposed to a disaster (fire), increases in self-reported anxiety, depression, aggression, and self-reported excessive use of alcohol were seen, with increases in all these effects larger in girls than boys (Reijneveld et al., 2003).

Similarly, in a national household probability sample of 4,023 telephone-interviewed adolescents ages 12-17 in the USA, the 6-month prevalence of PTSD was 3.7% for boys and 6.3% for girls (Kilpatrick et al., 2003).

The findings reported here are consistent with those described by Silva et al. (2000) who, in a clinic sample of traumatized inner-city youth (n=59), found no significant differences in terms of the interaction of trauma (including sexual abuse) and gender, and no difference in the mean number of PTSD symptoms. 22% of 59 traumatised children met full criteria for PTSD, 32% had partial symptoms and 46% had no PTSD symptoms.

Another unexpected finding was that while boys and girls were equally likely to have experienced at least one lifetime trauma, more boys than girls endorsed sexual trauma. While studies of young adolescent males in developing countries have shown that they are also not uncommonly subject to various forms of sexual assault (for example, a chart review study in the Cameroon of 5,082 children presenting at a medical clinic found that boys comprised 4.8% of those abused) (Menick and Ngoh, 1998), most studies would suggest that girls are far more likely

than boys to be sexually assaulted (i.e., to be victims of completed or attempted rape) (Fehon et al., 2001; Fergusson et al., 2002; Walker et al., 2004). Indeed, this is consistent with the findings of a recent study in adolescent high school students in Cape Town, which found that girls are about four times more likely than boys to have been victims of sexual abuse (King et al., 2004).

The risk of developing PTSD following sexual assault was the same for both sexes (OR= 2.3). Sexual assault, compared with all other traumas, was also associated with the highest risk of PTSD. This finding parallels that of other workers who have found a relatively higher risk for PTSD (up to 12-fold) following rape or sexual assault compared with other types of trauma (Breslau et al., 1991; Green et al., 1994; Giaconia et al., 1995).

We found that depression, but not substance use, correlated with PTSD. Girls had higher depression scores than boys, consistent with previous work (Lewinsohn et al., 1993; Schraedley et al., 1999). Further, respondents with more PTSD symptoms (i.e. those with full PTSD) tended to have more depressive symptoms than those with partial symptoms or no PTSD. In contrast, the only published paediatric

study to compare the constructs of full and partial/subthreshold PTSD found no significant differences in comorbidity (e.g., major depressive disorder) or functional impairment between children (aged 7 to 14 years) with full or PTSD (Carrion et al., 2002).

2.6.4 Clinical implication of findings

- High rates of full symptom PTSD (14.5%) and partial symptom PTSD (10.3%) characterise African youth, mirroring findings in Western settings.
- Discrepant rates of PTSD between Kenyan and S.A. adolescents in the presence of comparable rates of trauma exposure, suggest that other factors (e.g. differences in trauma toxicity, cultural variables) may be operant in contributing to risk.
- Boys in the sample endorsed more sexual traumas than girls. Compared with all other traumas, sexual assault was associated with the highest risk for PTSD.
- The above findings lend support to the growing literature on the positive relationship between exposure to violence and psychological distress and should be a consideration in designing school-based violence prevention programs in African community settings.

2.6.5 Limitations

Several limitations are worth mentioning. First, while we used a relatively high symptom threshold of “most of the time’ to establish PTSD criteria, diagnoses of current PTSD (full and partial) were based solely on symptom status and not on functional impairment. For partial PTSD, the presence of at least 1 symptom from each symptom category (criteria sets B, C, and D) was employed (Stein et al., 1997; Marshall et al., 2001). Second, as the age of onset and duration of PTSD were not documented, we were not able to establish symptom chronicity. Third, exposure to trauma was measured as a count of the type of trauma, rather than as the number of exposures or the severity of exposure to a particular trauma. This may have impacted, to some extent, on the failure to detect significant differences between the samples, particularly as cumulative and toxic trauma exposure is associated with a higher PTSD risk. It does not, however, account for higher rates of PTSD in S.A. youth, despite higher rates of exposure in Kenyan youth to both sexual assault and physical assault by a family member as these are traumas that, if present, are likely to be repeated. These traumas were also the ones most likely to be associated with a PTSD symptom diagnosis. This discrepancy is one for which we do not have an adequate

explanation. Finally, survey questionnaires were not culturally validated and all questionnaires were administered in English (i.e., to be eligible participants had to be able to read and write English at 10th grade level), although English was not the home language of the majority of respondents.

2.7 Conclusion

In conclusion, replication across other ethnic and cultural settings in the African context is required to more clearly establish the nature and extent of trauma exposure and its psychological repercussions in African youth. Nevertheless, these findings share many similarities with studies undertaken in Western countries. They highlight the high rates of violence exposure and PTSD in both boys and girls and suggest a need for health care professionals to be more vigilant in screening for victimization and trauma-related distress. In view of a paucity of mental health interventions that can be effectively delivered within the constraints of community settings, these findings further highlight the need for such programs and the important role that could be played by school-based clinics in providing such services.

TABLE 1: Demographic Characteristics

Demographic Variables	**S.A. (n=1140)**	**KENYA (n=901)**
Age in years (SD) *	15.9 (1.1)	15.6 (0.8)
Gender		
Male	43.3 %	41.9 %
Female	56.7 %	58.1 %
*Ethnicity**		
•White	32.1 %	0.3 %
•Mixed descent	42.2 %	----
•Black	21.3 %	97.7 %
•Asian	2.1 %	0.6 %
•Other	2.3 %	1.4 %
Habits (current use)		
Cigarettes: ≥ 10 per day*	5.3 %	0.4 %
Alcohol > 3 times per week	1.2 %	1.1 %
Cannabis*	10.6 %	1.7 %
*Parental Marital Status**		
Married/living together	62.0 %	81.0 %
Single/divorced/widowed	38.0 %	19.0 %
Parental Unemployment		
Mother	27.6 %	16.6 %
Father	14.6 %	4.9 %
Total (N)	**1140**	**901**

* denotes significant differences ($p < .001$) between the countries

TABLE 2: Trauma Exposure Type and PTSD Symptom Diagnosis

Common Trauma Types	**S.A. (n=1140)** % (count)	**KENYA (n=901)** % (count)	***p***
Exposure to ≥ 1 trauma	83 % (943)	85 % (764)	*ns*
Exposure to ≥ 3 traumas	44 % (499)	45 % (406)	*ns*
Witnessing violence in the street, neighbourhood, or school	58 % (660)	69 % (619)	<. 001
Being robbed or mugged	34 % (386)	37 % (331)	*ns*
Being in a bad accident	26 % (291)	16 % (140)	<. 001
Being in an earthquake, fire, flood, or other natural disasters	16 % (184)	16 % (139)	*ns*
Seeing family members injured, beaten, hurt, or killed	33 % (377)	32 % (286)	*ns*
Being beaten or physically hurt yourself by a family member	14 % (161)	27 % (246)	<. 001
Being physically hurt or attacked by a non-family member	18 % (202)	21 % (188)	*ns*
Sexual assault	14 % (157)	18 % (161)	<. 02
PTSD symptom diagnosis			
Full	22 % (253)	5 % (42)	<. 001
Partial	12 % (136)	8 % (74)	<. 01

statistic = chi-squared
ns = not statistically significant

TABLE 3: Trauma Exposure by Gender

Common Trauma Types	**S.A. (n=1021)**			**KENYA (n-887)**		
	Girls %(count)	**Boys** %(count)	***p***	**Girls** %(count)	**Boys** %(count)	***p***
Exposure to ≥ 1 trauma	82 (472)	84 (371)	*ns*	83 (429)	87 (324)	*ns*
Witnessing violence in the street, neighbourhood, or school	55 (321)	60 (265)	*ns*	64 (330)	75 (278)	<. 001
Being robbed or mugged	33 (190)	37 (162)	*ns*	34 (174)	41 (151)	<. 02
Being in a bad accident	24 (140)	28 (123)	*ns*	15 (76)	17 (61)	*ns*
Being in an earthquake, fire, flood, or other natural disasters	15 (87)	17 (74)	*ns*	15 (76)	16 (60)	*ns*
Seeing family members injured, beaten, hurt, or killed	32 (185)	33 (145)	*ns*	35 (182)	28 (102)	<. 02
Being beaten or physically hurt yourself by a family member	12 (71)	15 (67)	*ns*	27 (136)	29 (107)	*ns*
Being physically hurt or attacked by a non-family member	16 (93)	20 (88)	*ns*	13 (65)	33 (121)	<. 001
Sexual assault	12 (72)	15 (64)	*ns*	14 (71)	24 (87)	<. 001

'missing' gender: *South Africa* n=119, *Kenya* n=14
statistic = chi-square
ns = not statistically significant

TABLE 4: PTSD, Depression by Gender

Symptom Profile	S.A. (n=1021)			KENYA (n=887)		
	Girls (n=579)	**Boys (n=442)**	***p***	**Girls (n=515)**	**Boys (n=372)**	***P***
Intrusive symptoms *Mean (SD)*	1.6 (2.1)	1.2 (1.9)	<.003	0.6 (1.3)	0.5 (1.3)	*ns*
Avoidance symptoms *Mean (SD)*	2.2 (2.3)	1.9 (2.1)	<.02	1.2 (1.4)	1.1 (1.3)	*ns*
Hyperarousal symptoms *mean (SD)*	1.7 (2.1)	1.5 (2.0)	*ns*	0.5 (0.9)	0.5 (0.9)	*ns*
No. of PTSD symptoms *mean (SD)*	4.7 (5.4)	5.1 (5.5)	*ns*	2.3 (2.9)	2.2 (2.9)	*ns*
Full PTSD symptoms *N (%)*	122 (21)	107 (24)	*ns*	26 (5)	16 (4)	*ns*
Partial PTSD symptoms *N (%)*	68 (12)	57 13)	*ns*	43 (8)	28 (8)	ns
Depressive symptoms *mean (SD)*	10.7(10.4)	11.7(10.7)	*ns*	12.4 (9.3)	9.5 (7.9)	<.0001

missing gender: *South Africa* n=119, *Kenya* n=14
ns = not statistically significant

TABLE 5: Lifetime Trauma Exposure & PTSD Symptom Diagnosis by Ethnicity

Ethnicity	Lifetime Trauma Exposure		PTSD with Lifetime Exposure	
	S.A. % (count)	Kenya % (count)	S.A. % (count)	Kenya % (count)
Asian	86% (19/22)	60% (3/5)	21% (6/19)	0% (0/5)
Black	75% (166/221)	85% (734/867)	27% (56/166)	5% (40/734)
Mixed Descent	85% (371/437)	-----	25% (108/371)	-----
White	86% (285/333)	100% (3/3)	20% (58/285)	0% (0/3)

2.8 References

American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders-Text Revision (DSM-IV-TR), 4th ed. *American Psychiatric Press*: Washington, DC

American School Health Association (1989) *The National Adolescent Student Health Survey: A Report on the Health of America's Youth*. Oakland, Calif: Third Party Publishing Co.

Barrera M Jr, Garrison-Jones CV (1988) Properties of the Beck Depression Inventory as a screening instrument for adolescent depression. *Journal of Abnormal Psychology*, **16(3)**, 263-273.

Beck AT, Steer RA (1987) *Beck Depression Inventory Manual*. San Antonio, TX: Psychological Corporation.

Beck AT, Steer RA, Garbin MG (1988) Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clinical Psychology Review,* **8 (1),** 77-100.

Berton MW, Stabb SD (1996) Exposure to violence and post-traumatic stress disorder in urban adolescents. *Adolescence*, **21(122),** 489-498.

Boney-McCoy S, Finkelhor D (1995) Psychosocial sequelae of violent victimization in a national youth sample. *Journal of Consulting and Clinical Psychology,* **63(5),** 726-736.

Breslau N, Davis GC, Andreski P, et al. (1991) Traumatic events and posttraumatic stress disorder in an urban population of young adults *Archives of General Psychiatry*, **48**, 216-222.

Carrion VG, Weems CF, Ray R, et al. (2002) Toward an empirical definition of pediatric PTSD: The phenomenology of PTSD symptoms in youth. *Journal of the American Academy of Child and Adolescent Psychiatry*, **41(2)**, 166-172.

Center for Disease Control and Prevention (1992) Violence-related attitudes and behaviors of high school students-New York City. *MMWR Morbidity and Mortality Weekly Report*, **42**, 773-777.

Cuffe SP, Addy CL, Garrison CZ et al. (1998) Prevalence of PTSD in a community sample of older adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, **37**, 147-154.

Curle CE, Williams C (1996) Post-traumatic stress reactions in children: gender differences in the incidence of trauma reactions at two years and examination of factors influencing adjustment. *British Journal of Clinical Psychology,* **35(Pt 2),** 297-309.

Ensink K, Robertson BA, Zissis C, et al. (1997) Post-traumatic stress disorder in children exposed to violence. *South African Medical Journal*, **87(11)**, 1526-1530.

Fehon DC, Grilo CM, Lipschitz DS (2001) Gender differences in violence exposure and violence risk among adolescent inpatients. *J Nerv Ment Dis*, **189(8),** 532-40.

Fergusson DM, Swain-Campbell NR, Horwood LJ (2002) Does sexual violence contribute to elevated rates of anxiety and depression in females? *Psychol Med,* **32(6),** 991-6.

Fitzpatrick KM, Boldizar JP (1993) The prevalence and consequences of exposure to violence among African-American youth. *Journal of the American Academy of Child and Adolescent Psychiatry*, **32**, 424-430.

Foy DW, Goguen CA (1998) Community-violence related PTSD in children and adolescents. *PTSD Research Quarterly*, **9(4),** 1-8.

Giaconia RM, Reinherz HZ, Silverman AB, et al. (1995) Traumas and posttraumatic stress disorder in a community population of older adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, **34**, 1369-1380.

Green B, Grace MC, Vary MG, et al. (1994) Children of disaster in the second decade: A 17-year follow-up of Buffalo Creek survivors. *Journal of the American Academy of Child and Adolescent Psychiatry*, **33**, 721-729.

Jaycox LH, Stein BD, Kataoka SH, et al. (2002) Violence exposure, posttraumatic stress disorder, and depressive symptoms among recent immigrant schoolchildren. *Journal of the American Academy of Child and Adolescent Psychiatry,* **41(9),** 1104-1110.

Kaufman J, Birmaher B, Brent D, et al. (1997) Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child and Adolescent Psychiatry*, **36**, 554-565.

Kilpatrick DG, Ruggiero KJ, Acierno R, et al. (2003) Violence and risk of PTSD, major depression, substance abuse/dependence, and comorbidity: results from the National Survey of Adolescents. *J Consult Clin Psychol*, **71(4),** 692-700.

King G, Flisher AJ, Noubary F, et al. (2004) Substance abuse and behavioral correlates of sexual assault among South African adolescents. *Child Abuse Negl*, **28(6),** 683-96.

Lewinsohn PM, Hops H, Roberts RE, et al. (1993) Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *Journal of Abnormal Psychology*, **102**, 133-144.

Lipschitz DS, Rasmusson AM, Anyan W, et al. (2000) Clinical and functional correlates of posttraumatic stress disorder in urban adolescent girls at a primary care clinic. *J Am Acad Child Adolesc Psychiatry,* **39(9),** 1104-11.

March JS, Amaya-Jackson L, Terry R, et al. (1997) Posttraumatic stress symptomatology in children and adolescents after an industrial fire. *Journal of the American Academy of Child and Adolescent Psychiatry,* **36(8)**, 1080-1088.

Marshall RD, Olfson M, Hellman F, et al. (2001) Comorbidity, impairment, and suicidality in subthreshold PTSD. *American Journal of Psychiatry*, **158**, 1467-1473.

Masten AS, Neeman J, Andenas S (1994) Life events and adjustment in adolescents: the significance of event dependence, desirability, and chronicity. *J Res Adolesc*; **4:** 71-87.

Mazza JJ, Reynolds WM (1999) Exposure to violence in young inner city adolescents: Relationships with suicidal ideation, depression, and PTSD symptomatology*. J Abnorm Child Psychol,* **27,** 203-213.

McLain SL, Morland LA, Shapiro JA, Foy DW (1998) Etiologic factors in posttraumatic stress disorder in children: Comparing child abuse to other trauma types. *Family Violence and Sexual Assault Bulletin,* **14(1-2),** 27-30.

Menick DM, Ngoh F (1998) Sexual abuse in children in Cameroon. *Med Trop (Mars,.* **58(3),** 249-52.

Newman E, Amaya-Jackson L (1996) *Assessment of trauma instruments for children*. Presented at the 12th International Conference for Traumatic Stress Studies, San Francisco, November 1996.

Ozer EJ, Weinstein RS (2004) Urban adolescents' exposure to community violence: the role of support, school safety, and social constraints in a school-based sample of boys and girls. *Journal of Clinical Child and Adolescent Psychology,* **33(3)**, 463-476.

Paxton KC, Robinson WL, Shah S, Schoeny ME (2004) Psychological distress for African-American adolescent males: exposure to community violence and social support as factors. *Child Psychiatry Hum Dev*, **34(4),** 281-95.

Peltzer K (1998) Traumatic experiencing and post traumatic psychological symptoms in South African University students. *Central African Journal of Medicine*, **44 (11)**, 280-283.

Peltzer K (1999) Posttraumatic stress symptoms in a population of rural children in South Africa. *Psychological Reports*, **85(2)**, 646-650.

Pynoos RS, Goenjian A, Tashjian M, et al. (1993) Post-traumatic stress reactions in children after the 1988 Armenian earthquake. *British Journal of Psychiatry*, **163**, 239-247.

Reijneveld SA, Crone MR, Verhulst FC, et al. (2003) The effect of a severe disaster on the mental health of adolescents: a controlled study. Lancet, **362(9385),** 691-6.

Richter P, Werner J, Heerlien A, et al. (1998) On the validity of the Beck Depression Inventory: A review. *Psychopathology,* **31 (3),** 160-168.

Richters JE, Martinez P (1993) The NIMH community violence project: children as victims of and witnesses to violence. *Psychiatry*, **56**, 7-21.

Rosenthal BS (2000) Exposure to community violence in adolescence: trauma symptoms. *Adolescence,* **35(138)**, 271-284.

Rosenthal BS, Wilson WC (2001) Relationship between exposure to community violence and psychological distress: linear or curvilinear? *Psychological Reports,* **88 (3 Pt 1)**, 635-640.

Schraedley PK, Gotlib IH, Hayward C (1999) Gender differences in correlates of depressive symptoms in adolescents. *Journal of Adolescent Health*, **25**, 98-108.

Schubiner H, Scott R, Tzelepsis A (1993) Exposure to violence among inner-city youth. *Journal of Child and Adolescent Health*, **14**, 214-219.

Schwab-Stone M, Chen C, Greenberger E, et al. (1999) No Safe Haven II. The effects of violence exposure on urban youth. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38, 359-367.

Seedat S, van Nood E, Vythilingum B, et al. (2000) School survey of exposure to violence and posttraumatic stress symptoms in adolescents. Southern African Journal of Child and Adolescent Mental Health, **12 (1)**, 38-44.

Silva RR, Alpert M, Munoz DM, et al. (2000) Stress and vulnerability to posttraumatic stress disorder in children and adolescents. *American Journal of Psychiatry*,**157**, 1229-1235.

Singer MI, Anglin TM, Song Yu L, et al. (1995) Adolescents' exposure to violence and associated symptoms and psychological trauma. *Journal of the American Medical Association*, **273 (6)**, 477-482.

Stein BD, Jaycox LH, Kataoka SH, et al. (2003) A mental health intervention for schoolchildren exposed to violence: a randomized controlled trial. *JAMA*, **290(5),** 603-11.

Stein MB, Walker JR, Hazen AL, et al. (1997) Full and partial posttraumatic stress disorder: Findings from a community survey. *American Journal of Psychiatry*, **154 (8)**, 1114-1119.

Victims of Crime Survey (1998). Statistics South Africa, http://www.statssa.gov.za.

Vrana S, Lauterbach D (1994) Prevalence of traumatic events and post-traumatic psychological symptoms in a nonclinical sample of college students. *Journal of Traumatic Stress*, **7**, 289-302.

Walker JL, Carey PD, Mohr N, Stein DJ, Seedat S (2004) Gender differences in the prevalence of childhood sexual abuse and in the development of pediatric PTSD. *Arch Women Ment Health*, **7(2),** 111-21.

Ward CL, Flisher AJ, Zissis C, et al. (2001) Exposure to violence and its relationship to psychopathology in adolescents. *Injury Prevention: Journal of the International Society for Child and Adolescent Injury Prevention*, **7(4)**, 297-301.

3. EPIDEMIOLOGY AND PHENOMENOLOGY OF POSTTRAUMATIC STRESS DISORDER IN A CLINIC SAMPLE

Clinical Correlates, Differential Symptom Patterns and Gender Differences in Traumatised Adolescents With and Without Posttraumatic Stress Disorder

3.1 Study Summary

Few studies have focused on the assessment of full and partial PTSD in trauma-exposed adolescents in clinic settings. This study examined the prevalence of violence exposure and PTSD, clinical and functional aspects of full/ subsyndromal forms of the disorder and gender differences in a sample of treatment-seeking adolescents exposed to at least one PTSD-qualifying event.

170 consecutively referred adolescents (58% female) with a mean age of 13.8 years (SD=2.9 years) completed an assessment battery comprising a clinician-administered diagnostic interview (Kiddie-Schedule for Affective Disorders and Schizophrenia [K-SADS]) and several self-report measures of community violence exposure, childhood abuse, and PTSD symptom severity.

More than half the sample had been exposed to at least three traumatic events, with the commonest index traumas reported being witness to serious domestic violence (48.2%) and sexual abuse (45.9%). 47% met criteria for full PTSD while a further 19% met partial symptom criteria. Of note, no significant differences were observed in adolescents with full or subsyndromal forms, either in symptom persistence (duration of PTSD) or in school, family, or social impairment. Adolescents with full PTSD were significantly more likely to be depressed than those with partial PTSD or no disorder. While no gender differences in the rate of trauma exposure or PTSD (full and partial) were observed, girls suffered more severe childhood abuse, community violence, and exposure to negative life events.

These data support the utility of assessing for partial PTSD in traumatised adolescents who, despite exhibiting fewer PTSD symptoms, may experience significant impairment and distress.

3.2 Background

Several lines of evidence suggest that treatment-seeking children and adolescents exposed to various traumatic events have far higher prevalence rates of PTSD than general population samples, ranging from 15% to more than 90% (Pfefferbaum, 1997, review). More importantly, clinic referred adolescents compared with community sampled adolescents may be two times more likely to report a traumatic event and, depending on the index trauma, 25 times more likely to report symptoms of posttraumatic stress (Costello et al., 1998). While studies among adults suggest that approximately 25% of individuals exposed to trauma develop symptoms of PTSD (Breslau et al., 1991; Green, 1994, review), the situation differs somewhat in children and adolescents where many factors (e.g., trauma severity, time lapsed since the trauma, and definition of outcome) may produce greater variability in estimates (Pine and Cohen, 2002, review). For example, in a study of school-age children from three cities at increasing distances from the epicenter of the 1988 Armenian earthquake, rates of PTSD-like reactions in those living closest to the epicenter exceeded 90% (Goenjian et al., 1995). Much lower rates have been documented in children exposed to less extreme and relatively brief stressors,

particularly if some time has lapsed since the trauma (Laor et al., 2001; Keppel-Bendson et al., 2002; Zink and McCain, 2003).

In a study that was conducted at an inner-city child and adolescent psychiatry clinic, 27% of children and adolescents exposed to a PTSD qualifying trauma (principally physical abuse, sexual abuse and witnessing domestic violence) met criteria for a diagnosis of PTSD, while a further 32% had partial or subthreshold symptomatology (Silva et al., 2000). Identification of symptoms of posttraumatic stress and other psychopathology in traumatised adolescents who present to primary, secondary and tertiary health care settings may lead to timely psychiatric intervention, at a critical transitional stage into adulthood (Lipschitz et al., 2000). However, the evaluation and assessment presents a constellation of complex and unique challenges, in part owing to ongoing developmental issues in this group. The nature of the stress-inducing event and the adolescent’s subjective experience of a traumatic event are both influential factors in PTSD symptom expression (Drake et al., 2001).

The 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (APA, 1994) was notable for its revision of the stressor criterion from a traumatic event that is outside the range of usual human experience and would be markedly distressing to almost anyone, to a traumatic event that involves actual or threatened death or serious injury and incites a response of intense fear, horror, or helplessness. This criterion recognises that in many locations around the world (including South Africa) violence is endemic, such that traumatic events cannot be considered as outside of the range of usual human experience.

That said, while there is a rich body of literature on community-related precipitating events (e.g., school shootings, bombings, physical assault, war) for PTSD and other psychopathology, the literature focusing on the assessment of trauma-exposed children and adolescents with and without PTSD, in clinical contexts, is somewhat limited. The current analysis was undertaken to supplement previous findings of trauma and PTSD characteristics in a community sample by examining a clinic sample of adolescents. It was envisaged that evaluation of this population using a structured, psychometrically sound,

clinician-administered diagnostic interview (in addition to adolescent self report measures used in the community survey) would provide more extensive data on diagnostic morbidity and comorbidity, and more careful delineation of the nature of trauma/ violence exposure, full and partial PTSD symptoms (and other psychopathology) and gender effects. It would also provide some means of comparison of demographic and phenomenological differences in clinic-based and community-based adolescents and would serve to clarify whether PTSD symptom cluster profiles in trauma-exposed adolescent clinic attendees (i.e., a potentially ‘high-risk’ sample) differ significantly from trauma-exposed community-based adolescents (i.e., a potentially ‘low- risk’ sample).

3.3 Methods

3.3.1 Subjects

Consecutive referrals who presented to the Bathuthuzele Youth Stress Clinic at the MRC Research Unit on Anxiety and Stress Disorders (Department of Psychiatry, University of Stellenbosch, Tygerberg) were included in the analysis. The clinic offers a screening evaluation, assessment, medication, and referral service for traumatised adolescents. A research psychologist conducted initial telephonic screening interviews with prospective subjects to identify individuals who had experienced a traumatic event meeting the A1 criterion for PTSD (APA, 1994). The study was approved by the University of Stellenbosch ethics committee. Prior to the administration of study procedures, written informed consent for participation was obtained from parents or legal guardians in addition to written assent being obtained from adolescents.

The study sample comprised 170 adolescents (n=170), with a mean age of 13.75 years (standard deviation (SD)=2.9 years, range: 10 to 18 years). There were 99 females (58%) and 71 males (42%) and the majority (78.8%) were of mixed race (Table 1).

3.3.2 Procedures

Participants were administered an assessment battery by a clinical psychologist which included a demographics questionnaire (as used in chapter 2), a clinician-administered diagnostic interview (Kiddie Schedule for Affective Disorders and Schizophrenia [K-SADS]) (Kaufman et al., 1997) and self-report measures of PTSD, depression and other psychopathology, violence exposure and childhood trauma.

3.3.3 Instruments

(i) The Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-PL)-Present and Lifetime version

The K-SADS-PL (Kaufman et al., 1997) was used to evaluate for the presence of psychiatric diagnoses (current and lifetime), and as the 'gold standard' for the diagnosis of PTSD. The K-SADS-PL includes an initial 82-item screen interview that surveys key symptoms for current and past episodes in 20 different diagnostic areas, skip-out criteria that determine whether additional interviewing is necessary, and supplemental diagnostic sections to be completed, as indicated (Kaufman et al., 2000). The screen interview is initially administered and based on the results of the screen interview, the interviewer moves on

to five diagnostic supplements, which include affective disorders, anxiety disorders, psychotic disorders, behavioural disorders, substance abuse, tic and eating disorders covered in the DSM-IV (APA, 1994). Thus, detailed symptomatic data are not obtained in non-diagnosed disorders because of the extensive use of symptom "skip-outs" (Ambrosini, 2000). The interview takes approximately 45-75 minutes to conduct, and is administered to both parent/guardian and child. The K-SADS-PL has been shown to have excellent interrater reliability and concurrent validity (Ambrosini, 2000). It is arguably the primary diagnostic manual in use for the assessment of DSM-IV diagnoses.

(ii) Child PTSD Checklist

The Child PTSD Checklist (Newman and Amaya-Jackson, 1996), a 28-item symptom status measure of PTSD, has been described in chapter 2. For this study, as in other studies (Lipschitz et al., 2000), DSM-IV symptom criteria (minimum of 1 re-experiencing, 3 avoidance, 2 hyperarousal symptoms) were applied to determine the number of PTSD cases (based on symptom criteria alone).

(iii) Child Exposure to Violence Checklist (CEVC)

The CEVC (Amaya-Jackson, 1998) is a self-report, 33 item checklist adapted from Richters and Martinez's "Things I've

Seen and Heard” (Richters, 1990). It assesses various types of violence that may have been experienced, witnessed or heard about. Examples of violence rated include shootings, stabbings, sexual assault, and family violence. Responses are coded on a 5-point Likert scale ranging from “never” to “more than 10 times”. Total scores are obtained with higher scores indicating higher levels of violence exposure. Although there is limited published psychometric information on this survey, it has been shown to have good internal consistency with coefficient alphas ranging from .51 to .90 for each violence category (Fehon et al., 2001). In a subgroup of 31 inpatients, the kappa coefficients for agreement ranged from .47 to .85 for the different categories of violence.

(iv) Beck Depresssion Inventory (BDI)

The BDI (Beck et al., 1961) is a 21-item self-report scale (described in chapter 2). A total score for the 21 items was obtained, with higher scores indicating more depressive symptoms.

(v) Childhood Trauma Questionnaire (CTQ)

The CTQ (Bernstein and Fink, 1998), a 28-item measure that assesses five domains of childhood abuse and neglect: physical abuse, sexual abuse, emotional abuse, physical neglect and emotional neglect, was used as the primary

measure of childhood trauma severity. The reliability of 5 CTQ subscales range from 0.66 to 0.92 in psychiatric outpatients, and content, concurrent, and construct validity have been established. While it was originally developed for adults, various modifications have been made for use down to 12 years of age and it reportedly functions as well with adolescents as it does with adults (Ohan et al., 2002).

(vi) Life Events Questionnaire for Adolescents (LEQ-A)

The LEQ-A (Masten et al., 1994), as described in chapter 2, is a 45-item measure of negative and positive life events. It was used in the study to measure non-PTSD events. These events, while defined as psychologically challenging, are generally distinguishable from PTSD-defined traumatic events by their lesser intensity. The LEQ-A was developed by Project Competence at the University of Minnesota. The negative life event items in the scale were summed to compute a total score for negative life events experienced by adolescents in the past year.

3.4 Statistical Analyses

Statistical analysis, using SPSS software version 11.0, proceeded from descriptive statistics to a series of univariate and multivariate analyses to examine the relationship among demographic, trauma exposure, and clinical characteristics. The analyses focused on current rather than lifetime PTSD, to be consistent with the assessments and analyses that were conducted in the community sample (Chapter 2). Adolescents with exposure to traumatic events were assigned to one of 3 outcome groups (i) those without any symptoms of PTSD (ii) those with subthreshold PTSD and (iii) those who met full criteria for PTSD. Demographic and psychopathological differences were assessed among the groups using a series of x^2 tests and one-way analyses of variance with Tukey post hoc comparisons. Chi-square and student's t-tests were used to compare boys and girls in the sample. All tests were 2-tailed with significance set at $p < 0.05$, unless otherwise specified.

3.5 Results

3.5.1 Demographic characteristics

Table 1 shows the demographic characteristics of the total sample and the distribution by gender. Girls were significantly older than boys (mean age ± SD in years for boys: 12.6 ± 2.8, for girls: 14.6 ± 14.6, t= -4.7, df=168, p<0.001) and girls were also more likely than boys to be in a higher grade at school (28 boys vs. 63 girls were in grades 7 to 12, Fisher's Exact Test (FET), p <0.003). There were no significant gender differences with respect to substance use (cigarette smoking, alcohol and cannabis) and also no differences between the groups (boys/girls) with respect to parents' marital, living or employment status.

3.5.2 Pattern of trauma exposure

Tables 2 and 3 illustrate the pattern of exposure by trauma type, frequency of occurrence, and age of onset. More than half the sample (55.3%) was assessed on the K-SADS as having had lifetime exposure to at least three PTSD qualifying traumas (Table 3). The commonest traumatic events reported were, in order of frequency: (i) being a witness to serious domestic violence (48.2%), (ii) sexual abuse (45.9%), (iii) being confronted with extremely

traumatic news (42.4%), witnessing a violent crime (41.2%), and (v) being a victim of a violent crime (25.9%).

3.5.3 PTSD diagnosis, Partial PTSD & PTSD symptoms

47.1 % of adolescents (n=80) met criteria for a current diagnosis of PTSD on the K-SADS and 33.1 % met criteria for a lifetime diagnosis. 19.4% (n=33) met criteria for a current partial/subthreshold diagnosis (Table 3) while 22.9% (n=39) had neither the full nor partial syndrome (i.e., did not fulfil criteria of at least 1 re-experiencing, 1avoidance, and 1 hyperarousal symptom). Adolescents who met criteria for full PTSD endorsed significantly more symptoms from criteria sets B, C, and D compared with those who had a subthreshold syndrome (Table 4).

Table 5 outlines the percentage of adolescents in the sample who endorsed each of DSM-IV based symptoms for PTSD (K-SADS). The most commonly endorsed symptoms were, in descending order, efforts to avoid thoughts or feelings and activities/places linked to the events (53.2%), exaggerated startle responses (52.7%), hypervigilance (51.1%), difficulty concentrating (51.1%) and insomnia (49.5%).

There were no significant differences between those with full PTSD and those with partial PTSD with respect to the rate at which impairments in school functioning (FET, *p* <1.00), social functioning (FET, *p* < .84) and family functioning (FET, *p* < .52) were endorsed. Although adolescents with full PTSD tended to have a longer duration of symptoms (current episode) than those with the subthreshold form, differences between the 2 groups did not reach statistical significance (full PTSD vs. partial PTSD = 6.9 ± 18.4 vs. 4.6 ± 12.0, t = -0.63, *p* = 0.45).

3.5.4 PTSD caseness: Agreement between clinician-administered & self-report measures

Caseness for PTSD in the study was determined from three sources: (i) the K-SADS (the primary diagnostic measure), (ii) the Child PTSD Checklist, and (iii) a clinician-based PTSD diagnosis. Clinicians, following administration of the K-SADS, were also asked to say whether based on their clinical judgment alone they would consider making a PTSD diagnosis. Using this method, clinicians documented a diagnosis of PTSD in 56.5% of adolescents (n=96, missing: N=13). The rate of PTSD was also computed on the self-report Child PTSD Checklist by applying DSM-IV symptom criteria (minus the 'clinically significant

distress/impairment' criterion which is not measured by the checklist). This measure yielded a PTSD rate of 34.7% (n=59).

To achieve consistency with a symptom-based diagnosis of PTSD on the Child PTSD Checklist, identical criteria were then applied to the K-SADS (i.e., the presence of 1 intrusive, 3 avoidance, 2 hyperarousal symptoms in the absence of the 'functional impairment/distress' criterion) to compute a separate PTSD 'symptom diagnosis'. This yielded an almost identical rate (47.6%, n=81) to when routine criteria were applied.

Chi-square tests were then used to determine if there was a significant difference in PTSD diagnosis between the K-SADS and Child PTSD Checklist. Cohen's kappa coefficients (Cohen, 1960) were also used to assess the level of agreement. The level of agreement between the measures was only 60%: 60% of PTSD cases were correctly diagnosed on both measures (kappa=. 21, p = .006). However, 24% were misclassified with PTSD on Child PTSD Checklist, while 54% of adolescents who received a diagnosis of PTSD on the K-SADS were not classified as such on the Child PTSD Checklist. The level of agreement was higher between

clinician assessments of PTSD and the K-SADS (76%, kappa =.51, p = 0.000).

3.5.5 Trauma type & PTSD risk

Contrary to expectation, no significant associations were found between the type of trauma (on the K-SADS Traumatic Events screen) and the risk for PTSD (K-SADS), using Pearson chi-square and odds ratio calculations. Similarly no significant association emerged when the sample was stratified by gender.

3.5.6 Trauma exposure, PTSD & ethnicity

With respect to ethnic differences, 63.6% of White adolescents, 52.2% of Coloured adolescents, and 77% of Black adolescents reported lifetime exposure to at least 3 traumas. The low number of White respondents in the sample precluded meaningful comparisons. Preliminary analysis revealed no significant differences in the number of traumatic event exposures (grouped as those with <3 lifetime exposures and those with ≥3 lifetime exposures) between White and non-White adolescents (FET, p=0.76) and also no difference among the 3 groups (Black, mixed ethnicity, White) (x^2=5.1, df=2, p < 0.08).

44% of White adolescents, 54% of mixed race adolescents and 47% of Black adolescents met K-SADS PTSD criteria. Again, there appeared to be no significant difference in the rate of PTSD caseness between White and non-White adolescents (FET, p=0. 74) and no difference among the 3 groups (x^2=0.6, df=2, p =0.76).

3.5.7 Other diagnoses on the K-SADS

The most common K-SADS 'current' diagnoses (occurring at a frequency of ≥5% in the sample) were: major depressive disorder (MDD) (20 %), acute stress disorder (ASD) (19%), enuresis (12%), specific phobia (8%), oppositional defiant disorder (ODD) (7%) and attention deficit/hyperactivity disorder (ADHD) (5%) (Table 6). Four adolescents also met criteria for a lifetime diagnosis of MDD. Among adolescents with current MDD, 11 (32%) reported current suicidal ideation while 8 adolescents (24%) endorsed past suicidal ideation. Five (15%) had committed suicidal acts in the past. Other disorders occurring at a slightly lower frequency included panic disorder (4%), generalised anxiety disorder (3%), alcohol abuse (2.9%) and dysthymic disorder (2%).

Chi-square tests were conducted to determine psychopathological differences (using diagnoses that occurred at ≥5% frequency in the sample) among adolescents with full PTSD, adolescents with partial PTSD, and adolescents with no PTSD. Adolescents with full PTSD were significantly more likely to be depressed (i.e., to have comorbid MDD) compared with the other two groups: 79% of adolescents with full PTSD also met criteria for depression compared with 4% of adolescents with partial PTSD, and 17% with no PTSD, $x^2 = 7.2$, $p < 0.03$). As noted in Table 6, with the exception of specific phobia, all other co-occurring disorders in the sample were most likely of post-traumatic onset, and either concurrent with or proceeding the onset of PTSD.

3.5.8 Gender & trauma exposure

There were no gender differences in the number of exposures (lifetime) to PTSD-qualifying traumatic events (Table 3). Girls had significantly higher rates of sexual abuse than boys (63.9% vs. 23.5%), FET, $p < 0.001$). However, there were no significant gender differences in the rate of exposure to other PTSD qualifying traumas including being a victim of physical abuse or being a victim/witness to violent crime (Table 3).

3.5.9 Gender, PTSD diagnosis & PTSD symptom clusters

Boys and girls had similar rates of current full PTSD (K-SADS diagnosis) (53.5% vs. 51.5% respectively, FET, $p < 0.88$) and current subthreshold/partial PTSD (21.2% vs. 21.8% respectively, FET, $p < 1.00$). There were also no significant differences in the rate of full PTSD when a clinician-based diagnosis of PTSD (instead of a diagnosis on the K-SADS) was subjected to chi-square analysis (FET, $p < .42$). With respect to specific PTSD symptoms as elicited on the K-SADS, girls were significantly more likely to endorse symptoms of (i) irritability (63.3% vs. 44.8%) and (ii) detachment/numbing (54.9% vs. 45.4%) than boys (Table 5). Girls were also significantly more likely than boys to report clinically significant interference from PTSD symptoms in current social (51% of girls vs. 32% of boys, FET, $p = 0.04$) and family domains (58% of girls vs. 37% of boys, FET, $p < 0.046$).

In the sample (irrespective of PTSD diagnosis), there were no significant gender differences in the mean number of intrusive symptoms (boys vs. girls 2.2 ± 1.6 vs. 2.4 ± 1.5, $t = -0.75$, $df = 144$, $p < 0.46$), avoidance symptoms (boys vs. girls: 3.2 ± 2.1 vs. 3.4 ± 1.7, $t = -0.83$, $df = 146$, $p < 0.42$), or hyperarousal symptoms (boys vs. girls: 2.7 ± 1.8 vs. 3.1

± 1.8, t=-1.22, df = 151, $p < 0.23$) on the K-SADS. However, a different picture emerged on the Child PTSD Checklist, where girls endorsed significantly more PTSD symptoms overall (*indicative of greater PTSD severity*) and also more symptoms in each symptom domain (re-experiencing, avoidance, hyperarousal) (Table 7).

3.5.10 Gender & comorbidity

Girls were significantly more likely than boys to meet criteria for MDD (79% of adolescents who fulfilled MDD criteria were girls vs. 21% who were boys, $x^2 = 6.5$, $p < 0.02$) but not for the other disorders examined (ASD, ADHD, ODD, enuresis, specific phobia). The mean number of K-SADS diagnoses in the sample was 1.2 ± 1.3 (range 0 to 7) and there were no significant gender differences in the number of co-occurring disorders (Table 6).

3.5.11 Gender & childhood trauma

As a group, females reported significantly higher levels of childhood trauma (CTQ total and on all 5 clinical scales). Gender differences were especially significant for sexual and emotional abuse (Table 7). Scores in these 2 clinical domains were suggestive of moderate to severe levels of

sexual abuse and low to moderate levels of emotional abuse in the female group (Bernstein and Fink, 1998).

3.5.12 Gender & negative life events

On the LEQ-A, the mean number of negative life events reported overall was 8.4 ± 5.8 (range 0 to 33) (Table 7), with girls reporting significant more mean negative life event exposures in the past year than boys (9.2 ± 6.6 vs. 7.3 ± 4.5, t= -2.23, df=168, $p < 0.03$).

3.5.13 Gender & depressive symptoms

On the self-report BDI, although girls endorsed higher levels of depressive symptoms than boys (mean ± SD: 23.3 ± 13.9 vs. 9.8 ± 11.9), this did not reach significance ($p < 0.07$) (Table 7).

3.5.14 Correlation of PTSD symptoms with other self-report measures

Scores on the Child PTSD checklist were positively correlated with exposure to community violence (CECV) ($r = .45$, $p < 0.001$), exposure to childhood trauma (CTQ) ($r = .55$, $p < 001$), exposure to negative life events ($r = .36$, $p <0.001$), and depressive symptoms ($r = .46$, $p < .05$)

Statistical significance for all of these variables was maintained in the analysis by gender. With respect to the relationship between CTQ and LEQ-A scores, a stronger positive relationship was found within the male group (r = 0.64, p < 0.001) compared with the female group (r =0.45, p < 0.001).

3.5.15 PTSD versus non-PTSD groups

In comparing PTSD (N=80) and non-PTSD (N=72) groups respectively, there were no significant differences in demographic characteristics: mean age (14.0 ± 3.2 vs. 13.2 ± 2.7 years, t= -1.6, df=150, p < 0.12); gender (58% female vs.56% female, FET, p< .88); ethnicity (95% non-White vs.93% non-White). There were also no significant differences between adolescents with and without PTSD with respect to personal psychoactive substance use (nicotine, alcohol, cannabis), family characteristics (e.g. parental marital status/ employment/substance use). However, as mentioned above, there was a significant difference in the rate of major depression among the groups. Table 8 compares some of the clinical correlates of PTSD (total number of PTSD traumatic events and CECV, CTQ, LEQ-A scores) in adolescents with full, partial, and no PTSD. No significant differences in these measures were observed across the

groups and there were also no significant differences when the sample was stratified by gender.

3.6 Discussion

3.6.1 Rates of trauma & PTSD

These results demonstrate that the vast majority of treatment-seeking adolescents in the sample had multiple exposures to PTSD-qualifying traumatic events (including community and domestic violence). Severity of exposure to one type of trauma (e.g. community violence) was highly correlated with severity of exposure to other types of trauma (e.g. childhood abuse). The commonest traumatic events reported were, in order of frequency: being a witness to serious domestic violence, sexual abuse, being confronted with extremely traumatic news, and being witness to a violent crime. Witnessing serious domestic violence, the commonest type of trauma documented here, is known to be associated with increasing morbidity in children and adolescents and may be an especially potent factor in the development of PTSD (Silva et al., 2000). It has also been shown to be a common index event for PTSD in other studies. For example, in a clinic study of traumatised adolescent girls (Lipschitz et al., 2000), witnessing domestic violence was reported as one of the “most distressing or upsetting” index events.

It is notable that traumatic experiences (including sexual assault) did not differ in their association with the development of PTSD in this sample. Sexual assault, in particular, has been shown to be associated with a high risk for PTSD (Breslau et al., 1991; Giaconia et al., 1995), however, the lack of a significant association in this population who were multiply traumatised and presented with compounded community and domestic trauma suggests perhaps that, in this context, sexual assault may have a high likelihood of co-occurrence with other factors. Thus, sexual assault *per se* was not significantly related to PTSD but may have worked synergistically with other traumatic events to give rise disorder.

3.6.2 Full versus Partial PTSD

47% of traumatised adolescents met full DSM-IV criteria for PTSD while a further 19% met partial criteria. These rates, both of full PTSD and partial PTSD, are considerably higher than those reported in other clinic/ hospital adolescent samples (in the range of 11 to 24%). For example, one study of female adolescent clinic attendees found that 14.4 % and 11.6% of traumatised girls met criteria for full and partial PTSD, respectively (Lipschitz et al., 2000), while

in another study of youth hospitalised for accidental injuries (7 to 17 years), full PTSD was documented in 12.5 % and partial symptoms in a further 16.7% (Daviss et al., 2000). In a more recent sample of clinic-referred youth (7 to 14 years of age) with histories of trauma, the rate of full PTSD (as measured on the Clinician-Administered PTSD Scale for Children and Adolescents) was 24% (Carrion et al., 2002).

It is perhaps notable that the rates of full and partial PTSD were high even when other methods of determination were used (viz., the Child PTSD Checklist and clinician assessment). The 19% rate of partial PTSD is higher than expected considering the relatively strict definition of partial PTSD compared with other studies (Giaconia et al., 1995; Stein et al., 1997, Lipschitz et al., 2000). Only one study has documented a higher rate of partial PTSD (32%) in a similar sample (i.e., traumatised adolescent clinic cohort) (Silva et al., 2000). The high rates in this study may, in part, be a reflection the relatively stringent admission criteria to our clinic. The clinic is located within a tertiary academic centre and only recruits traumatised adolescents who are presumed, at screening, to have emotional and/or behavioural problems. It is,

therefore, likely that only the most symptomatic adolescents are referred for evaluation.

3.6.3 Comorbidity

In comparing the groups (full PTSD, partial PTSD, no PTSD), the only significant difference that emerged was in the rate of major depression; adolescents with full PTSD were far more likely than those with the subthreshold syndrome or no syndrome to be depressed. Higher rates of major depressive disorder have consistently been documented in individuals with PTSD. For example, Giaconia and colleagues (1995) reported that more than 41% of adolescents with PTSD met criteria for major depression by the age of eighteen, compared with 8% of those without PTSD. Physically and sexually maltreated youth with PTSD have similarly demonstrated significantly more mood and anxiety comorbidity than maltreated youth without PTSD (Linning and Kearney, 2004). Furthermore, differences in clinical presentation have been documented in youth with PTSD (with and without comorbidity). In a study comparing abused children with PTSD, nonabused children with PTSD and concurrent MDD, and nonabused children with MDD only (Runyon et al., 2002), those children with both disorders were more likely to report flashbacks and difficulty

sleeping while those with PTSD-only tended to experience more episodes of psychological amnesia. It has been suggested that youth with both disorders may be less likely to mentally avoid their emotional distress which, in turn, may lead to an increase in feeling out of control and flashbacks (Runyon et al., 2002). Not all studies have found higher rates of concurrent depression in adolescent PTSD. Silva et al. (2000) found similar rates of comorbidity, with the exception of disruptive behaviour disorders (oppositional defiant disorder and conduct disorder) which were more frequently observed in the subthreshold and non-PTSD groups.

With regard to comorbid substance use, few adolescents met criteria for a substance use disorder on the K-SADS. This may partly reflect recruitment bias as adolescents with comorbid substance use disorders are more likely to be referred within the tertiary hospital setting directly to child psychiatry services. That said, the co-occurrence of PTSD and substance use disorders has been fairly extensively documented in both adolescents (Simkin, 2002, review) and adults (Brady et al., 2000, review). For example, a recent study comparing traumatised, inner-city adolescent girls with and without PTSD (Lipschitz et al.,

2003), found that both those with full PTSD and partial PTSD were more likely to use nicotine, cannabis, and/or alcohol on a regular basis than those without. In fact, it has been suggested that the association between PTSD and substance use may be especially salient for girls. Lipschitz et al. (2000) found that PTSD symptoms were significantly associated with problematic drug and alcohol use in girls but not in boys.

3.6.4 Clinical & functional correlates

The three groups (full PTSD, partial PTSD, no PTSD) were not discriminated on the mean number of PTSD-related events, level of child abuse, degree of exposure to community violence, or negative life experience. In contrast, one study has reported higher levels of prior psychopathology, higher parental acute distress and higher rates of prior sexual abuse in adolescents with the full syndrome compared with those who had partial PTSD or no disorder (Daviss et al., 2000). It is arguable that the failure to detect group differences in this study relates to sample size (i.e., there were relatively small numbers within each group). Despite this, an important finding emerged: adolescents with subthreshold syndrome were not significantly different from children meeting full criteria

when the level of impairment in key areas of functioning (school, social, and family) was looked at. Of note, too, was the absence of a group difference with respect to PTSD symptom duration, suggesting that symptom persistence and rate of functional interference may not be too dissimilar across these syndromes. This supports the work of Carrion et al. (2002) who suggested that impairment in PTSD might be attributable to the effects of PTSD symptoms rather than to other clinical characteristics. In adolescents with full and partial PTSD, the most commonly occurring PTSD symptom endorsed was ‘avoidance of thoughts, feelings, and conversations associated with the trauma’. Interestingly, this symptom has been documented as being one of the most frequently occurring manifestations in adolescents with PTSD in several studies (Lipschitz et al., 2000; Carrion et al., 2002; Cuffe et al., 1998).

3.6.5 Gender effects for trauma & PTSD

Also notable, were lack of gender differences in the rate of exposure to trauma and in the rates of PTSD (full and subthreshold). With the exception of sexual assault (which was more prevalent in girls), there were no gender differences with respect to other types of exposure, including physical assault. This is contrary to what was

hypothesised in the study, namely, that boys would be more likely to endorse higher levels of violence exposure, in particular physical assault. As noted in an earlier chapter, some community-based studies have noted a greater incidence of trauma in adolescent/young adult males (Breslau et al., 1991; Norris, 1992; Vrana and Lauterbach, 1994) while others have found few gender differences in rates of specific traumas (Giaconia et al., 1995). Consistent with the higher rate of sexual assault in girls, girls compared with boys endorsed more childhood abuse (including childhood sexual assault) and, in fact, gender differences for sexual and emotional abuse were highly significant on the CTQ. This is in keeping with the findings of a validation study of the CTQ in an adolescent population (12-17 years of age), where girls scored higher on sexual and emotional abuse subscales (Bernstein et al., 1997). Fehon et al. (2001) also reported significantly higher mean levels of childhood trauma on the CTQ in adolescent girls compared with boys. Further, it has been suggested that the CTQ may have a lower threshold for detection of sexual abuse, particularly in boys but this warrants further study (Lipschitz et al., 1999).

With respect to gender specificity in PTSD, very few clinic-based paediatric studies have examined or found gender differences. For example, in one study of hospitalised adolescents (Fehon et al., 2001a), those with PTSD were more likely to be female. Higher rates of PTSD in girls were confirmed in a follow-up study by the same authors (Fehon et al., 2001b). However, in the aforementioned study girls with PTSD could not be differentiated from boys on other socio-demographic variables, for example age, ethnicity, religion, parental marital status, family income or household composition (Fehon et al., 2001a), consistent with the findings here. It is important to note that although there were no significant gender differences in the number of PTSD cases in the current study, girls reported more severe PTSD symptoms than boys. This has also been the finding in another adolescent study, using the same PTSD symptom severity measure (Child PTSD Checklist) (Fehon et al., 2001b).

Another interesting observation is that while no significant differences were observed in the frequency of functional impairment reported by full and partial PTSD groups, significant gender differences were seen. Girls

were more likely than boys to report current social and family (but not school) impairments than boys, suggesting that event though rates of PTSD may be similar, girls may experience more functional interference than boys.

3.6.6 Comparisons with the school sample

In comparing these results with that of the school survey (Cape Town cohort only), some striking similarities emerge. First, in both of these samples the rate of full and partial PTSD was comparable in boys and girls. The higher number of cases of PTSD (full and partial) in the 'high-risk' treatment-seeking group compared with the 'low-risk' school sample (47% vs. 22% for full PTSD; 19% vs. 12% for partial PTSD) is consistent with expectation.

Second, no significant gender effect was seen with respect to the rate of exposure to different trauma types, with the exception of sexual assault. In contrast to the school sample where no gender difference in the rate of sexual assault was observed, more girls than boys reported sexual assault in this study. One explanation for this might be the different formats used to elicit traumatic events (self-report in the school survey, clinician interview

here), which could have produced some degree of measurement artefact.

Third, multiple trauma exposure (defined as exposure to ≥ 3 traumas) was common in both samples (55% in this study and 44% in school cohort), and in line with expectation occurred at a higher frequency in the clinic sample. Fourth, the two PTSD symptoms that were reported most commonly by adolescents (efforts to avoid thoughts, feelings, or conversations associated with the trauma and efforts to avoid activities, places or people that arouse recollections of the trauma) were consistent in the studies. Lastly, there were no differences between boys and girls in depression severity (as measured on the BDI), and the severity of PTSD symptoms (as measured on the Child PTSD checklist) correlated positively with the severity of depression, in both samples.

One notable difference deserves mention. While in the school sample some traumas (sexual assault, physical assault by a family member, serious accidents) were associated with a significant risk for PTSD, this was not a finding here and may be accounted for by a Type II error, in view of the comparatively smaller clinic sample.

3.6.7 Study limitations and strengths

Several caveats in this study limit the interpretation of results and should be mentioned. First, this was a relatively small sample of adolescents. A larger sample size would have provided more power for the detection of group differences (full PTSD/partial PTSD/no PTSD; boys/girls). Second, as the study was cross-sectional in design, longitudinal assessment of the disorder (full and partial PTSD) in these groups was not possible. Third, while data on the number of traumatic events was obtained, information on the severity and duration of each traumatic event and their relation to PTSD was not. Fourth, there was a reliance on patient self-report for some measures of violence exposure and psychopathology (viz. PTSD and depression symptom severity, community violence, and childhood abuse). It has been suggested that the relative privacy of the self-report format might produce an overreporting of traumatic events and symptoms (Cuffe et al., 1998), however, this does not appear to be the case here as lower PTSD symptom rates were obtained on the self-report Child PTSD checklist compared with the clinician-administered interview. While on the one hand it can also be argued that the validity of self-reports in adolescents must be viewed with caution as negative mood states and

individual response styles in adolescents introduce bias, self-report scales may make disclosure of sensitive or embarrassing material easier for some youth.

One of the strengths of the study was the emphasis on multi-method, multi-score assessments across a variety of diagnostic and symptom domains. The sample also comprised of adolescents with heterogeneous and compounded trauma exposure, comparable to youth populations who present to primary care clinics, trauma clinics, and psychiatry outpatient settings. Finally, the study groups (PTSD and non-PTSD) were ascertained from the same traumatised sample, eliminating a variety of selection and sampling confounds (du Fort et al., 1993).

3.7 Conclusion

In conclusion, this study is of interest not least because it provides descriptive data on violence exposure and its considerable impact on the evolution of PTSD and other DSM-IV disorders in treatment-seeking adolescents. The findings indicate that adolescent boys may be just as likely as adolescent girls to develop PTSD, irrespective of the kind of traumatic event that is experienced, and that once developed, there may be little to distinguish full and subthreshold syndromes in either gender.

Furthermore, adolescents with partial and full PTSD may have comparable rates of interference with respect to school, family and social functioning. To date, this finding has been documented in only one other youth study, comprising a smaller sample (n=59) of children with a mean age of 10.6 years (Carrion et al., 2002). It is, therefore, fair to say that this is the first such replication in a substantially larger sample of older adolescents.

That partial PTSD may be just as disabling, raises important clinical issues for professionals working in the field of trauma. Detection and provision of appropriate and

timely care to adolescents who are exposed to traumatising experiences and who meet criteria for partial disorder may be just as critical as providing these services to those individuals with the full disorder.

Although not yet demonstrated, adolescents who fall short of meeting the full criteria set may arguably also benefit from pharmacotherapeutic and/ or psychotherapeutic intervention. Considering that partial PTSD is a relatively common entity in both youth and adult populations, this is certainly an area in which further research is needed. Treatment of PTSD in adolescents who present to primary care and specialised trauma clinic settings needs to be sensitive to potential gender-related differences, which even if not manifest in differences in prevalence, may well manifest in symptom expression, associated morbidity, or functional impairment.

The following chapter covers pharmacological intervention in a subset of adolescents with full PTSD, who were derived from the sample under discussion here.

3.8 References

Amaya-Jackson L (1998) Child exposure to Violence Checklist (adapted from Richters Things I've Seen and Heard). Durham, NC: Trauma Evaluation, Center for Child and Family Health.

Ambrosini PJ (2000) Historical development and present status of the schedule for affective disorders and schizophrenia for school-age children (K-SADS). *J Am Acad Child Adolesc Psychiatry,* **39(1),** 49-58.

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), 4th ed. *American Psychiatric Press*: Washington, DC.

American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders-Text Revision (DSM-IV-TR), 4th ed. *American Psychiatric Press*: Washington, DC

Beck AT, Ward CH, Mendelson M, et al. (1961) An inventory for measuring depression. *Arch Gen Psychiatry,* **4,** 561-571.

Beck AT, Steer RA, Garbin MG (1988) Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clinical Psychology Review,* **8 (1),** 77-100.

Bernstein DP, Ahluvalia T, Pogge D, Handelsman L (1997) Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. *J Am Acad Child Adolesc Psychiatry,* **36(3),** 340-8.

Bernstein DP, Fink L (1998) Childhood Trauma Questionnaire: A retrospective self-report. San Antonio, TX: Psy6chological Corporation.

Brady KT, Killeen TK, Brewerton T, Lucerini S (2000) Comorbidity of psychiatric disorders and posttraumatic stress disorder. *J Clin Psychiatry,* **61 Suppl 7,** 22-32.

Breslau N, Davis GC, Andreski P, Peterson E (1991) Traumatic events and posttraumatic stress disorder in an urban population of young adults. *Arch Gen Psychiatry,* **48(3),** 216-22.

Cohen J (1960) A coefficient of agreement for nominal scales. *Educational and Psychological Measurement,* **10,** 156-164.

Costello EJ, Angold A, March J, Fairbank J (1998) Life events and post-traumatic stress: the development of a new measure for children and adolescents. *Psychol Med,* **28(6),** 1275-88.

Cuffe SP, Addy CL, Garrison CZ et al. (1998) Prevalence of PTSD in a community sample of older adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, **37**, 147-154.

Daviss WB, Mooney D, Racusin R, et al. Predicting posttraumatic stress after hospitalization for pediatric injury. *J Am Acad Child Adolesc Psychiatry,* 39(5), 576-83.

Drake EB, Bush SF, van Gorp WG (2001) Evaluation and assessment of PTSD in children and adolescents. In: Eth S (ed.). PTSD in Children and Adolescents, Review of Psychiatry Vol 20, pp 1-27.

du Fort GG, Newman SC, Bland RC (1993) Psychiatric comorbidity and treatment seeking sources of selection bias in the study of clinical populations*. J Nerv Ment Dis*, 181: 467-474.

Fehon DC, Grilo CM, Lipschitz DS (2001a) Correlates of community violence exposure in hospitalized adolescents. *Compr Psychiatry,* **42(4),** 283-90.

Fehon DC, Grilo CM, Lipschitz DS (2001b) Gender differences in violence exposure and violence risk among adolescent inpatients. *J Nerv Ment Dis,* **189(8),** 532-40.

Goenjian AK, Pynoos RS, Steinberg AM, et al. (1995) Psychiatric comorbidity in children after the 1988 earthquake in Armenia. *J Am Acad Child Adolesc Psychiatry,* **34(9),** 1174-84.

Green BL (1994) Psychosocial research in traumatic stress: an update. *J Trauma Stress,* **7(3),** 341-62.

Horowitz K, Weine S, Jekel J (1995) PTSD symptoms in urban adolescent girls: compounded community trauma*. J Am Acad Child Adolesc Psychiatry,* **34(10),** 1353-61.

Kaufman J, Birmaher DB, Brent D, et al. (1997) Schedule for Affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime Version (K-SADS-PL): Initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry,* **36(7),** 980-988.

Kaufman J, Birmaher B, Brent DA, et al (2000) K-SADS-PL. *J Am Acad Child Adolesc Psychiatry,* **39(10),** 1208.

Keppel-Benson JM, Ollendick TH, Benson MJ (2002) Post-traumatic stress in children following motor vehicle accidents. *J Child Psychol Psychiatry*, 43(2), 203-12.

Laor N, Wolmer L, Cohen DJ (2001) Mothers' functioning and children's symptoms 5 years after a SCUD missile attack. *Am J Psychiatry,* **158(7),** 1020-6.

Linning LM, Kearney CA (2004) Post-traumatic stress disorder in maltreated youth: a study of diagnostic comorbidity and child factors. *J Interpers Violence,***19(10),**1087-101.

Lipschitz DS, Winegar RK, Hartnick E, et al. (1999) Posttraumatic stress disorder in hospitalized adolescents: psychiatric comorbidity and clinical correlates. *J Am Acad Child Adolesc Psychiatry,* **38(4),** 385-92.

Lipschitz DS, Bernstein DP, Winegar RK, Southwick SM (1999) Hospitalized adolescents' reports of sexual and physical abuse: a comparison of two self-report measures. *J Trauma Stress,* **12(4),** 641-54.

Lipschitz DS, Rasmusson AM, Anyan W, et al. (2000) Clinical and functional correlates of posttraumatic stress disorder in urban adolescent girls at a primary care clinic. *J Am Acad Child Adolesc Psychiatry,* **39(9),** 1104-11.

Lipschitz DS, Grilo CM, Fehon D, et al. (2000) Gender differences in the associations between posttraumatic stress symptoms and problematic substance use in psychiatric inpatient adolescents. *J Nerv Ment Dis*, **188(6),** 349-56.

Lipschitz DS, Rasmusson AM, Anyan W, et al. (2003) Posttraumatic stress disorder and substance use in inner-city adolescent girls. *J Nerv Ment Dis,***191(11),**714-21.

Masten AS, Neeman J, Andenas S (1994) Life events and adjustment in adolescents: the significance of event dependence, desirability, and chronicity. *J Res Adolesc,* **4,** 71-87.

Newman E, Amaya-Jackson L (1996) *Assessment of trauma instruments for children*. Presented at the 12th International Conference for Traumatic Stress Studies, San Francisco, November 1996.

Norris FH (1992) Epidemiology of trauma: frequency and impact of different potentially traumatic events on different demographic groups. *J Consult Clin Psychol,* **60(3),** 409-18.

Ohan JL, Myers K, Collett BR (2002) Ten-year review of rating scales. IV: scales assessing trauma and its effects. *J Am Acad Child Adolesc Psychiatry,* **41(12),** 1401-22.

Pine DS, Cohen JA (2002) Trauma in children and adolescents: risk and treatment of psychiatric sequelae. *Biol Psychiatry*, **51(7),** 519-31.

Pfefferbaum B (1997) Posttraumatic stress disorder in children: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry*, **36,** 1503-1511.

Richter P, Werner J, Heerlien A, et al. (1998) On the validity of the Beck Depression Inventory: A review. *Psychopathology,* **31 (3),** 160-168.

Richters JE (1990) *Screening Survey of Exposure to Community Violence*, Self-Report Version. Rockville, MD: NIMH, Child and Adolescent Research Branch.

Runyon MK, Faust J, Orvaschel H (2002) Differential symptom pattern of post-traumatic stress disorder (PTSD) in maltreated children with and without concurrent depression. *Child Abuse Negl*, **26(1),** 39-53.

Silva RR, Alpert M, Munoz DM, et al (2000) Stress and vulnerability to posttraumatic stress disorder in children and adolescents. *Am J Psychiatry*, **157(8),** 1229-35.

Simkin DR (2002) Adolescent substance use disorders and comorbidity. *Pediatr Clin North Am,* **49(2),** 463-77.

Stein MB, Walker JR, Hazen AL, et al. (1997) Full and partial posttraumatic stress disorder: Findings from a community survey. *American Journal of Psychiatry*, **154 (8)**, 1114-1119.

Vrana S, Lauterbach D (1994) Prevalence of traumatic events and post-traumatic psychological symptoms in a nonclinical sample of college students. *J Trauma Stress,***7(2),** 289-302.

Zink KA, McCain GC (2003) Post-traumatic stress disorder in children and adolescents with motor vehicle-related injuries. *J Spec Pediatr Nurs*, **8(3),** 99-106.

TABLE 1: Demographic Characteristics

Demographic Variables	**Total Sample (N=170)**	**Boys (N=71)**	**Girls (N=99)**
Age in years (SD)**	13.8 (2.9)	12.6 (2.8)	14.6 (2.8)
Ethnicity % (N) White Non-White •Coloured •Black	 6.5% (11) 91.8% (156) 78.8% (134) 12.9% (22) *(missing value: N=3)*	 7.4 % (5) 92.6 % (63) 80.3% (57) 8.5% (6)	 6.1 % (6) 93.9% (93) 77.8% (77) 16.2% (16)
School Grade % (N) ** Grade 1 to 6 Grade 7 to 12	 40.6% (69) 53.5% (91) *(missing value: N=10)*	 32.9% (31) 67.0% (63)	 57.6% (38) 42.4% (28)
Habits (current use) Cigarettes: ≥ 10 per day Alcohol > 3 times per week Cannabis	 8.3% (14) 10.6% (18) 4.1% (7) *(missing value: N=1)*	 10.1% (10) 10.1% (10) 4.1% (4)	 5.7% (4) 11.3% (8) 4.2% (3)
Parents' deceased Mother Father	 10.6% (18) 16.5% (28) *(missing value: N=2 for mother and N=4 for father)*	 7.2% (7) 16.8% (16)	 15.5% (11) 16.9% (12)
Parents' marital status Married/living together Single/divorced/separated/ widowed	 42.4% (72) 56.7% (94) *(missing value: N=4)*	 40.6% (39) 59.4% (57)	 47.1% (33) 52.9% (37)
Unemployment Mother Father	 12.4% (21) 7.1% (12) *(missing values: N=33 for father, and N=19 for mother)*	 16.2% (16) 10.1% (10)	 7.0% (5) 2.8% (2)

** denotes significant gender differences at p <0.05*
*** denotes significant gender differences at p < 0.01*

Note: For analysis by gender, percentages are expressed as per gender group

TABLE 2: Trauma Type, Age of Occurrence, and Number of Exposures

DSM-IV Traumatic Events *(K-SADS PTSD module)*	**Age of Occurrence in Years** *mean ± SD*	**Number of Exposures** *mean ± SD range*
Significant car accident in which child/ other individual in car was injured and required medical intervention	10.8 ± 4.2	1.3 ± 0.9 *(0 to 4)*
Other significant accident involving injury and requiring medical intervention	9.2 ± 3.7	***0.9 ± 0.4*** *(0 to 2)*
Witness to fire that caused significant property damage or moderate to severe physical injuries	9.3 ± 3.6	***1.1 ± 0.3*** *(1 to 2)*
Witness of a natural disaster (e.g., flood, hurricane, other natural disaster)	11.5 ± 2.1	1.0 ± 0.7 *(0 to 2)*
Witness of a violent crime	11.8 ± 3.5	1.4 ± 1.4 *(0 to 5)*
Victim of violent crime	12.3 ± 3.6	1.1 ± 0.9 *(0 to 4)*
Confronted with extremely traumatic news	11.0 ± 3.6	1.2 ± 0.7 *(0 to 4)*
Witness to domestic violence	8.0 ± 3.4	3.2 ± 2.0 *(0 to 10)*
Physical abuse	8.6 ± 3.3	2.9 ± 1.9 *(0 to 10)*
Sexual abuse (isolated/ repeated incidents of genital fondling, oral sex, or vaginal or anal intercourse) *(missing values, N=5)*	10.7 ± 3.8	1.6 ± 1.4 *(0 to 4)*
Other very traumatic event	11.8 ± 4.1	1.6 ± 1.1 *(1 to 4)*

TABLE 3: Trauma Type and PTSD Diagnosis

DSM-IV Traumatic Events (K-SADS PTSD module)	**Total (N=170)** % (count)	**Boys (N=71)** % (count)	**Girls (N=99)** % (count)	***p***
Significant car accident *(missing values, N=6)*	11.8% (20)	17.5% (12)	8.3% (8)	.09
Other significant *(missing values, N=6)*	13.5% (23)	17.5% (12)	11.6% (11)	***.36***
Witness to fire *(missing values, N=6)*	5.3% (9)	2.9% (2)	7.4% (7)	***.31***
Witness of a natural *(missing values, N=8)*	2.9% (5)	2.9% (2)	3.2% (3)	1.00
Witness of a violent crime *(missing values, N=5)*	41.2% (70)	44.1% (30)	41.2% (40)	.75
Victim of violent crime *(missing values, N=5)*	25.9% (44)	33.3% (23)	21.9% (21)	.11
Confronted with traumatic news *(missing, N=4)*	42.4% (72)	40.6% (28)	45.4% (44)	.63
Witness to domestic violence *(missing, N=6)*	48.2% (82)	50% (34)	50.0% (48)	1.00
Physical abuse *(missing values, N=6)*	25.9% (44)	26.5% (18)	27.1% (26)	1.00
Sexual abuse *(missing values, N=5)*	45.9% (78)	23.5% (16)	63.9% (62)	.000**
Other very traumatic event	20.0% (34)	25.0% (17)	17.7% (17)	.17
Mean (SD) number of PTSD qualifying events *(range: 1 to 7)*	2.8 ± 1.5	2.7 ± 1.7	2.9 ±1.4	.50
Exposure to ≥ 3 traumas	55.3%	50.7%	58.6%	.19
PTSD symptom diagnosis (current)				
Full (*missing values: N=18*)	47.1%	51.5%	53.5%	.87
Partial (*missing values: N=18*)	19.4%	21.2%	21.8%	1.00
Mean duration (SD) in weeks of PTSD symptoms (irrespective of PTSD diagnosis or not)	5.48 (14.6)	3.7 (10.9)	6.6 (16.5)	.19

******* *denotes significant gender differences at* ***p < 0.01***

Note: Full diagnosis of PTSD based on K-SADS (DSM-IV) criteria. Partial PTSD diagnosis based on the presence of 1 re-experiencing, 1 avoidance and 1 hyperarousal symptom. For the analysis by gender, percentages are expressed as per gender group.

TABLE 4: Number of Diagnostic Symptoms in Adolescents Meeting Full Criteria for PTSD and those not meeting Full Criteria

K-SADS Criteria	**Full PTSD**	**No PTSD**	***P***
Number of Intrusive Symptoms *(mean ± SD)*	3.3 ± 1.0	1.1 ± 1.1	.000**
Number of Avoidance Symptoms *(mean ± SD)*	4.6 ± 1.1	1.9 ± 1.6	.000**
Number of Hyperarousal Symptoms *(mean ± SD)*	4.0 ± 1.0	1.7 ± 1.8	.000**

significant gender differences at* ***p < 0.01

TABLE 5: Frequency of PTSD Symptoms: Gender Differences

Symptom Endorsed on K-SADS	Total (N=170) %	Boys (N=71) %	Girls (N=99) %	*P*
Re-experiencing (Cluster B)				
B1 Intrusive thoughts	48.9	55.9	60.7	.62
B2 Nightmares	47.3	53.7	60.2	.51
B3 Reliving	37.2	50.0	43.0	.42
B4 Psychological distress	47.3	56.7	57.9	1.00
B5 Physiological reactivity	45.7	53.0	57.9	.62
Avoidance cluster (cluster C)				
C1 Avoids thoughts	53.2	58.8	67.4	.32
C2 Avoids people, places	53.2	62.7	63.0	1.00
C3 Amnestic	39.9	50.0	47.8	.87
C4 Diminished interest	44.1	50.0	54.9	.63
C5 Detachment/numbing	47.3	45.4	54.9	.02*
C6 Restricted range of affect	48.4	50.0	61.9	.15
C7 Foreshortened future	45.2	54.5	54.4	1.00
Hyperarousal cluster (cluster D)				
D1 Sleep difficulties	49.5	54.5	63.3	.32
D2 Irritability	46.3	44.8	63.3	.02*
D3 Concentration problems	51.1	58.8	61.5	.75
D4 Hypervigilance	51.1	61.8	61.5	.87
D5 Exaggerated startle	52.7	56.7	67.0	.24

** denotes significant gender differences at p< 0.05*

TABLE 6: Other Psychiatric Diagnoses: Gender Differences

Psychiatric Diagnosis and Onset	**Total (N=170)** % (count)	**Boys (N=71)** % (count)	**Girls (N=99)** % (count)	***P***
Major Depressive Episode *Pre-trauma: N=1* *Posttrauma: N=33*	20.0% (34)	9.9% (7)	27.3% (27)	.02*
Acute Stress Disorder *(posttrauma onset in all)*	19.4% (33)	16.9% (12)	21.2% (21)	.56
Enuresis *Pre-trauma: N=8* *Posttrauma: N=12*	11.8% (20)	12.7% (9)	11.1% (11)	.81
Specific Phobia *Pre-trauma: N=8* *Posttrauma: N=5*	7.6% (13)	5.6% (4)	9.1% (9)	.56
Oppositional Defiant Disorder *Pre-trauma: N=1* *Posttrauma: N=10*	6.5% (11)	8.5% (6)	5.1% (5)	.52
Attention Deficit Disorder *Pre-trauma: N=3* *Posttrauma: N=5*	4.7% (8)	8.5% (6)	2.0% (2)	.07
Mean no. of diagnoses *mean ± SD* *range*	1.2 ± 1.3 *(0 to 7)*	0.9 ± 1.1	1.3 ± 1.3	.05

* *denotes significant gender differences at p <0.05*

For the analysis by gender, percentages are expressed as per gender group

TABLE 7: Mean Scores on Self-Report Measures: Gender Comparisons

Measure	Total (N =170)	Boys (N=71)	Girls (N=99)	F
Child PTSD Checklist				
Intrusive score	18.7 ± 8.9	16.5 ± 8.5	20.3 ± 8.9	0.09*
Avoidance score	18.2 ± 8.5	16.5 ± 8.2	19.4 ± 8.6	0.17*
Hyperarousal score	14.6 ± 7.0	12.9 ± 6.2	15.7 ± 7.4	2.52*
Total score	55.9 ± 26.7	48.5 ± 24.4	60.5 ± 27.2	0.11**
Beck Depression Inventory (BDI)	19.9 ± 14.4	9.8 ± 11.9	23.3 ± 13.9	0.8
Child Exposure to Violence Checklist (CEVC) *Total score*	29.3 ± 23.2	29.3 ± 26.6	29.3 ± 20.6	4.9
Life Events Questionnaire for Adolescents (LEQ-A) *Total number of negative life events*	8.4 ± 5.8	7.3 ± 4.5	9.2 ± 6.6	4.5*
Childhood Trauma Questionnaire (CTQ)				
Physical Abuse	7.0 ± 4.8	6.1 ± 3.9	7.6 ± 5.2	6.0*
Sexual Abuse	7.4 ± 5.9	5.7 ± 4.4	8.6 ± 6.5	18.5**
Emotional Abuse	9.5 ± 6.0	7.8 ± 4.9	10.8 ± 6.4	7.4**
Physical Neglect	8.3 ± 4.8	7.4 ± 4.1	8.9 ± 5.1	1.3*
Emotional Neglect	10.5 ± 6.3	9.1 ± 5.7	11.4 ± 6.5	2.7*
Total Score	42.7 ± 22.3	36.2 ± 18.0	47.3 ± 23.9	4.1**

Gender differences denoted as * $p < 0.05$, ** $p < 0.01$

TABLE 8: Clinical Correlates in Trauma-Exposed Adolescents with PTSD, Partial PTSD and No PTSD

Measure (Total scores)	Mean	SD	F value	Group Differences
Number of PTSD-qualifying traumas				
Full PTSD	4.6	4.2		
Partial PTSD	4.2	3.7	0.4	
No PTSD	3.8	2.9		*ns*
Child Exposure to Violence Checklist (CEVC)				
Full PTSD				
Partial PTSD	30.4	22.9		
No PTSD	22.8	21.7	1.1	*ns*
	31.1	26.0		
Negative Life Events (LEQ-A)				
Full PTSD	8.3	4.9		
Partial PTSD	8.1	6.2	0.5	*ns*
No PTSD	9.3	7.2		
Childhood Trauma Questionnaire (CTQ)				
Full PTSD	42.2	20.7		
Partial PTSD	39.5	25.1	0.6	
No PTSD	44.8	18.2		*ns*

Analysis of variance (ANOVA) using Tukey post hoc tests.
Groups: Full PTSD (n=80), Partial PTSD (n=33), and No PTSD (n= 39), missing: n=18
ns=Group differences were not significant

4. PHARMACOTHERAPY OF ADOLESCENT POSTTRAUMATIC STRESS DISORDER

Pilot Study of Treatment with the Selective Serotonin Reuptake Inhibitor, Citalopram, in Adolescents with Posttraumatic Stress Disorder (PTSD)

4.1 Study Summary

In this preliminary 12-week open-label study, eight adolescents with moderate to severe PTSD were treated with citalopram (the most selective of the SSRIs) in a fixed daily dose of 20mg, and rated at 2-week intervals. The Clinician-Administered PTSD Scale (Child and Adolescent Version) was the primary variable used to assess treatment outcome.

Core PTSD symptoms (re-experiencing, avoidance, and hyperarousal symptoms) showed statistically significant improvement at week 12 on the Clinician-Administered PTSD Scale (Child and Adolescent Version) (CAPS), with a 38% reduction in total CAPS scores between baseline and endpoint. Citalopram failed to effect improvement on self-reported depressive symptoms. All 7 adolescent completers were rated as much improved or very much improved on

Clinical Global Impression-Improvement scores. Citalopram was well-tolerated overall with reported adverse experiences being relatively benign.

The differential improvement on PTSD symptom clusters but not on depression suggests that citalopram might be a promising treatment for PTSD in adolescents, independent of its antidepressant effects.

4.2 Introduction

As has been highlighted in previous chapters, PTSD is a prevalent, and often disabling consequence of trauma exposure in children and adolescents (Berman et al., 1996; Breslau et al., 1991). Empirical data, gleaned primarily from adult populations, reinforces the specific neurobiological basis of PTSD, its diagnostic validity, and responsiveness to both pharmacotherapeutic and psychotherapeutic strategies (van der Kolk, 1997). More recently, the role of serotonin in underlying the pathophysiology of PTSD has been highlighted by a wealth of preclinical and clinical data (Connor and Davidson, 1998). Results of animal and clinical studies (paroxetine binding, pharmacologic challenge tests, and neuroimaging techniques) suggest that serotonergic agents, specifically, selective serotonin reuptake inhibitors (SSRIs) might be beneficial in ameliorating PTSD symptoms (Connor and Davidson, 1998), and several authors have postulated that SSRIs may exert their effects indirectly rather than directly, through modulation of non-serotonergic neurobiologic systems (Friedman, 1998; Friedman, 2000; Donnelly et al., 1999).

In adults, the safety and efficacy of SSRIs in treating both core and secondary PTSD symptoms has been borne out by

several open and randomised controlled trials (Davidson et al., 1998; Marshall et al., 1998; Meek and Kablinger, 1998; Brady et al., 1995; Fichtner et al., 1997). For example, in a seminal study leading to the SSRI, sertraline's indication for the treatment of adult PTSD, Brady et al. (2000) demonstrated effectiveness over placebo in 94 patients treated with sertraline (versus 93 with placebo) on 3 of 4 primary outcome measures. While the SSRIs may act in a fairly rapid, broad spectrum fashion in PTSD, optimal results may entail relatively high doses for 8 to 12 weeks (Donnelly and Amaya-Jackson, 2002).

In children with PTSD, the few pharmacological studies have reported benefits from clonidine patches (n=7 children) (Harmon and Riggs, 1996), propranolol (n=11 children) (Famularo et al., 1988), carbamazepine (n=28 children) (Looff et al., 1995), and guanfacine (n=1 child) (Horrigan, 1996). None of these studies utilised a control group. In addition, anecdotal evidence exists for using antidepressants (tricyclics and SSRIs) in children with PTSD characterised by prominent depressive or panic symptoms (Brent et al., 1995).

The efficacy of the SSRIs in paediatric depression and anxiety has only recently been supported by controlled data (Emslie et al., 1997; Jensen et al., 1999; Pine, 2001). With their “broad spectrum” of activity, the SSRIs are receiving more diverse application in child and adolescent disorders, including depression, obsessive-compulsive disorder, social anxiety disorder, and selective mutism, and fluoxetine, sertraline and fluvoxamine are both FDA-approved for use in paediatric OCD. (Black and Uhde, 1994; Allen et al., 1995; Kutcher 1997; Beidel et al., 1999; Emslie et al., 1999; Murphy et al., 2000; Kastelic et al., 2000; Ziervogel, 2000).

Despite the lack of open and controlled trials in children and adolescents with PTSD, SSRIs have been recommended as first-line agents in clinical practice (Cohen et al., 1998). However, some authors recommend that their use in child and adolescent PTSD be reserved for comorbid or disabling symptoms (Marmar et al., 1994). Considering their favourable side-effect profile and broad therapeutic index, SSRIs offer specific advantages over tricyclic antidepressants in paediatric populations (Leonard et al., 1997). In childhood PTSD, the SSRIs may have two distinct roles: first, in targeting disabling symptoms to allow for

a normal growth and developmental trajectory and second, to facilitate confrontation with emotionally traumatic material in psychotherapy and in day-to-day life (Donnelly et al., 1999).

This preliminary study undertook to treat a sample of adolescents presenting with PTSD with the highly selective SSRI, citalopram. Citalopram is a bicyclic phthalane derivative, with no effect on the uptake of noradrenaline, dopamine, or GABA. Moreover, neither citalopram nor its metabolites have significant antidopaminergic, antiadrenergic, antiserotonergic, antihistaminergic, or anticholinergic properties (Milne and Goa, 1991). With respect to citalopram, both controlled studies in adult mood and anxiety disorders (Tan and Levin, 1999; Wade et al., 1997; Lepola et al., 1998; Birmaher et al., 2003) and open-label studies in child and adolescent OCD (Thomsen, 1997; Mukaddes et al., 2003) suggest favourable efficacy and tolerability. In a recent placebo-controlled study of citalopram (20mg to 40mg/day) for paediatric patients (12-17 years) with major depression, mean child-Depression Rating Scale-Revised scores decreased significantly more from baseline in the citalopram treatment group than in the placebo treatment group, with differences already evident

in the first week (Wagner et al., 2004). Citalopram has also demonstrated short-term efficacy and safety as a treatment for impulsive aggression in children and adolescents (aged 7 to 15 years) (Armenteros and Lewis, 2002) and in preliminary data from children and adolescents with autism treated with citalopram, it was suggested that this agent was useful in the reduction of symptom domains such as repetitive behaviours and anxiety and mood symptoms (Namerow et al., 2003). Finally, in a retrospective chart review of child and adolescent outpatients treated with citalopram for depressive or anxiety disorders and a high degree of comorbidity, citalopram appeared to be effective and well-tolerated (Baumgartner et al., 2002).

This trial investigated (i) the preliminary efficacy of citalopram in treating PTSD symptoms in adolescents and (ii) the tolerability of this agent in this age group.

4.3 Methods

Adolescents aged 12-18 years meeting DSM-IV criteria for PTSD, as determined by the CAPS-CA (Clinician Administered Posttraumatic Stress Disorder Scale-Child and Adolescent version) (Nader et al., 1996) were entered into a treatment protocol approved by the ethics committee of the University of Stellenbosch Medical School, Cape Town. Adolescents were recruited from the Bathuthuzele Clinic, an outpatient unit for children and adolescents exposed to traumatic experiences. Written informed consent for study inclusion was obtained from a parent or legal guardian. A criterion for entry into the study was a Clinical Global Impression (CGI) severity score of ≥ 4 (at least moderate severity PTSD) (Guy, 1976).

The presence of comorbid mood and anxiety disorders was not an exclusion criterion, provided these disorders did not precede the PTSD diagnosis. Comorbidity was screened for with the K-SADS (Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version) (Kaufman et al., 1997). K-SADS interviews were conducted by a clinical psychologist.

Adolescents who had been treated with SSRIs at therapeutic antidepressant doses for at least 4 weeks prior to study entry were excluded, as were adolescents meeting DSM-IV criteria for psychotic, bipolar, or organic disorders. Adolescents with a substance abuse/dependency diagnosis in the preceding 6 months, or an unstable medical condition, were also excluded. Prior to study entry, adolescents were kept medication-free for at least 2 weeks. Concomitant psychotropic medications and formal psychotherapies (excluding supportive psychotherapy) were contraindicated for the duration of the trial.

The primary outcome variable was a mean change from baseline in PTSD symptoms, as assessed by the CAPS-CA. All CAPS-CA interviews were performed by the treating psychiatrist. The CAPS-CA was used both as a reference standard to establish PTSD caseness and treatment outcome. Modelled after the adult CAPS (Blake et al., 1990), the CAPS-CA provides scalar and categorical assessment of PTSD and PTSD-related psychopathology, such as hostility and school problems (Nader et al., 1996). The CAPS-CA measures 17 PTSD symptoms based on DSM-IV criteria. Symptoms are grouped into categories of: (1) re-experiencing symptoms (items 1-5, maximum score 40), (2) avoidance/numbing

symptoms (items 6-12, maximum score 56), and (3) hyperarousal symptoms (items 13-17, maximum score 40). The CAPS-CA is useful in children aged 8 through to adolescence. Besides establishing a current and/or lifetime diagnosis of PTSD; the scale measures overall severity of PTSD symptoms, frequency and severity of each symptom, and impact of symptoms on developmental, social, and scholastic functioning.

Secondary outcome measures of depression, and PTSD symptom severity and improvement, were assessed using the Zung Depression Self-Rating Scale, and Clinical Global Impression-Severity and Improvement Scales (CGI-S and CGI-I) (Guy, 1976). CGI-Improvement scores at endpoint distinguished responders from non-responders. A final CGI-I score of 1 or 2 (much or very much improved) defined "response", while a final CGI-I score of ≥ 3 (minimally improved or worse) defined "non-response". Adolescents were assessed at 2 weekly intervals over 12 weeks of open treatment with citalopram. Citalopram was initiated at 20mg, and this dose was fixed throughout the 12 week period. At every visit, the CAPS-CA (clinician-rated), Zung Depression Scale (patient-rated), and CGI (clinician-

rated), were administered. Adverse events were documented at visits.

4.4 Results

4.4.1 Sample

Eight adolescents entered the study, and seven completed 12 weeks of treatment. One subject was withdrawn at 2 weeks due to adverse events (nose bleeds). The mean age of subjects was 14.8 years (SD=2.7), with a mean level of schooling of 8.75 years (SD=2.4). There were 7 girls and 1 boy, their racial composition being: mixed race (4), Black (2), White (1), and Asian (1). The majority presented with chronic PTSD, with mean duration of PTSD symptoms 16.5 months (SD=16.4, range 2 to 48 months, median 14 months). Only 2 of the 8 adolescents met criteria for "acute PTSD"(duration of symptoms $<$ 3 months). Four adolescents had a "delayed onset" (symptoms $\geq$ 6 months after the traumatic event).

Traumatic events reported included: rape (3), childhood sexual abuse (3), physical abuse (2), physical injury from a gunshot (1), witnessing sudden death of a friend (1), and witnessing domestic violence (1) (Table 1). Six had directly experienced trauma, while two had been witnesses to trauma. Five of the eight had been victims of multiple traumas leading to the development of PTSD. 6 of the 8 met criteria for current major depressive episodes (which were

mild in severity), while none met criteria for a past (lifetime) diagnosis. 1 adolescent had comorbid panic disorder (current) and separation anxiety disorder (past).

4.4.2 Outcome

All 7 subjects were responders to citalopram on the CGI-Improvement Scale at endpoint (week 12), with 3 completers much improved (CGI-I=2), and 4 very much improved (CGI-I=1).

Paired t-tests (n= 7 completers) demonstrated significant differences between baseline and endpoint CAPS scores for all three symptom clusters (Table 2). There was a mean reduction of 50 points (38%) in total CAPS scores between baseline and endpoint (Table 3 and Figure 1). There was also a significant difference between baseline and endpoint CGI severity scores (t=6.97, p=0.0004). There was no significant difference between baseline and endpoint Zung depression scores.

Citalopram (20mg) was well tolerated, and reported adverse effects were mild and self-remitting. Common adverse effects experienced were increased sweating (n=3), nausea (n=2), headache (n=2), and tiredness (n=2). 1 adolescent

experienced akathisia (of moderate severity), which resolved without any intervention, 3 weeks into the trial. The only adolescent who did not complete the trial was withdrawn at 2 weeks (at the request of his parents) after 3 episodes of nose bleeding (epistaxis) on day 10. He had 1 further episode two weeks after citalopram discontinuation. All 4 nose bleeds were mild, and did not require medical intervention. Physical examination at the time revealed no abnormalities. In retrospect, the nose-bleeds did not appear to be related to the study drug.

4.5 Discussion

These findings suggest that citalopram may be an effective agent in adolescents with PTSD, as demonstrated by a 38% mean symptom reduction score between baseline and endpoint, as well as significant reduction in all 3 PTSD symptom cluster scores (intrusive, avoidance, hyperarousal) over 12 weeks. Both the magnitude of symptom reduction and the time-to-improvement, are in line with open trials of SSRIs in adults (van der Kolk et al., 1994; Hertzberg et al., 1998). Despite the low placebo response in a number of controlled trials of adult PTSD (5-10%); placebo response rate has tended to be higher in non-veteran samples. The small sample size of this trial, and absent placebo arm, are limiting factors. Findings of this study will need to be confirmed in larger-sample, controlled trials.

Six adolescents satisfied criteria for comorbid depression (MDD) at study entry. Interestingly, while 5 of the 6 no longer met criteria for MDD at study end; depressive symptoms as measured by the self-report Zung Scale (paired t-tests of means) did not improve. These differences might reflect depression severity at baseline (mild severity, low Zung scores). Co-morbidity between PTSD and depression has been well documented in the literature (Goenjian et al.,

1995; Hubbard et al, 1995), and it has been hypothesized that PTSD might precede and predispose to the onset of depression (Goenjian et al., 1995).

Citalopram was well tolerated overall. This is consistent with studies of citalopram in child and adolescent obsessive-compulsive disorder (Thomsen and Mikkelsen, 1995; Thomsen, 1997).

4.6 Conclusion

This preliminary open trial of citalopram in eight adolescents is the first published trial of SSRI use in adolescent PTSD. Interestingly, the findings suggest that the beneficial effects of citalopram on PTSD symptoms might not necessarily be a function of its antidepressant effects.

Given the approved safety and tolerability of the SSRIs, and given the morbidity associated with PTSD, the findings of this study hold promise for the treatment of this disorder in this population.

4.7 References

Allen JA, Leonard H, Swedo SE (1995) Current knowledge of medications for the treatment of childhood anxiety disorders. *J Am Acad Child Adolesc Psychiatry,* **34(8),** 976-986.

Armenteros JL, Lewis JE (2002) Citalopram treatment for impulsive aggression in children and adolescents: an open pilot study. *J Am Acad Child Adolesc Psychiatry*, **41(5),** 522-9.

Baumgartner JL, Emslie GJ, Crismon ML (2002) Citalopram in children and adolescents with depression or anxiety. *Ann Pharmacother*, **36(11),** 1692-7.

Beidel DC, Turner SM, Morris TL (1999) Psychophathology of childhood social phobia. *J Am Acad Child Adolesc Psychiatry*, **38,** 643-650.

Berman SL, Kurtines WM, Silverman WK, et al. (1996) The impact of exposure to crime and violence on urban youth. *Am J Orthopsychiatry,* **66,** 329-336.

Birmaher B, Axelson DA, Monk K, et al. (2003) Fluoxetine for the treatment of childhood anxiety disorders. *J Am Acad Child Adolesc Psychiatry,* **42(4),** 415-23.

Black B, Uhde TW (1994) Treatment of elective mutism with fluoxetine: double-blind, placebo-controlled study. *J Am Acad Child Adolesc Psychiatry,* **33,** 1000-1006.

Blake DD, Weathers FW, Nagy LM, et al.(1990) A clinician rating scale for assessing current and lifetime PTSD: the CAPS-1. *Behaviour Therapist*, **13,** 187-188.

Brady KT, Sonne SC, Roberts JM (1995) Sertraline treatment of comorbid posttraumatic stress disorder and alcohol dependence. *J Clin Psychiatry,* **56(11),** 502-505.

Brady K, Pearlstein T, Asnis GM, et al. (2000) Efficacy and safety of sertraline treatment of posttraumatic stress disorder: a randomized controlled trial. *JAMA*, **283(14),** 1837-44.

Brent DA, Perper JA, Moritz G, et al. (1995) Posttraumatic stress disorder in peers of adolescent suicide victims. *J Am Acad Child Adolesc Psychiatry,* **34,** 209-215.

Breslau N, Davis CG, Andreski P, et al. (1991) Traumatic events and posttraumatic stress disorder in an urban population of young adults. *Arch Gen Psychiatry,* **48,** 216-222.

Cohen JA, Bernet W, Dunne JE, et al. (1998) Practice parameters for the assessment and treatment of adolescents with posttraumatic stress disorder. *J Am Acad Child Adolesc Psychiatry,* **37(suppl 10),** 4S-26S.

Connor KM, Davidson RT (1998). The role of serotonin in posttraumatic stress disorder: neurobiology and pharmacotherapy. *CNS Spectrums,* **7S2**, 41-43.

Davidson JRT, Weisler RH, Malik ML, Connor KM (1998) Treatment of posttraumatic stress disorder with nefazodone. *Int Clin Psychopharm*, **13(3),** 111-113.

Donnelly CL, Amaya-Jackson L, March JS (1999) Psychopharmacology of pediatric posttraumatic stress disorder. *Journal of Child and Adolescent Psychopharmacology,* 9 (3), 203-220.

Donnelly CL, Amaya-Jackson L (2002) Post-traumatic stress disorder in children and adolescents. Epidemiology, diagnosis and treatment options. *Pediatr Drugs*, **4**, 159-170.

Emslie GJ, Rush AJ, Weinberg WA, et al. (1997) A double-blind, randomized, placebo-controlled trial of fluoxetine in children and adolescents with depression. *Arch Gen Psychiatry*, **54 (11),** 1031-1037.

Emslie GJ, Walkup JT, Pliszka SR, Ernst M (1999) Nontricyclic antidepressants: Current trends in children and adolescents*. J Am Acad Child Adolesc Psychiatry,* **38 (5),** 517-528.

Famularo R, Kinscheiff R, Fenton T (1988) Propranolol treatment for childhood posttraumatic stress disorder, acute type: a pilot study. *Am J Psychiatry,* **142,** 1244-1247.

Fichtner CG, Poddig BE, DeVito RA (1997) Posttraumatic stress disorder: pathophysiological aspects and pharmacological approaches to treatment. *CNS Drugs*, **8(4),** 293-322.

Friedman MJ (1998) Current and future drug treatment for post-traumatic stress disorder patients. *Psychiatric Annals*, **28(8),** 461-468.

Friedman MJ (2000) What might the psychobiology of posttraumatic stress disorder teach us about future approaches to pharmacotherapy ? *J Clin Psychiatry,* **61(suppl 7),** 44-51.

Goenjian AK, Pynoos RS, Steinberg AM, et al. (1995) Psychiatric comorbidity in children after the 1988 earthquake in Armenia. *J Am Acad Child Adolesc Psychiatry,* **34,** 1174-1184.

Guy W (1976) ECDEU Assessment Manual for Psychopharmacology, 2nd ed (DHEW Publication ABM 76-388). Washington DC: US Government Printing Office.

Harmon RJ, Riggs PD (1996) Clinical perspectives: clonidine for posttraumatic stress disorder in preschool children. *J Am Acad Child Adolesc Psychiatry,* **35,** 1247-1249.

Hertzberg MA, Feldman ME, Beckham JC, et al. (1998) Open trial of nefazodone for combat-related posttraumatic stress disorder. *J Clin Psychiatry,* **59(9),** 460-463.

Horrigan JP (1996) Guanfacine for posttraumatic stress disorder nightmares (letter). *J Am Acad Child Adolesc Psychiatry,* **35,** 975-976.

Hubbard J, Realmuto GM, Northwood AK, et al. (1995) Comorbidity of psychiatric diagnoses with posttraumatic stress disorder in survivors of childhood trauma. *J Am Acad Child Adolesc Psychiatry*, **34,** 1167-1173.

Jensen PS, Bhatara VS, Vitiello B, et al. (1999) Psychoactive medication prescribing practices for U.S. children: gaps between research and clinical practice. *J Am Acad Child and Adolesc Psychiatry*, **38 (5),** 557-565.

Kaufman J, Birmaher DB, Brent D, et al. (1997) Schedule for Affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime Version (K-SADS-PL): Initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry,* **36(7),** 980-988.

Kastelic EA, Labellarte MJ, Riddle MA (2000) Selective serotonin reuptake inhibitors for children and adolescents. *Curr Psychiatry Rep,* **2(2),** 117-123.

Kutcher S (1997) Practitioner review: The pharmacotherapy of adolescent depression. *J Child Psychol Psychiatry*, **38 (7),** 755-767.

Leonard HL, March J, Rickler KC, Allen AJ (1997) Pharmacology of the selective serotonin reuptake inhibitors in children and adolescents. *J Am Acad Child Adolesc Psychiatry,* **36(6),** 725-736.

Lepola UM, Wade AG, Leinonen EV, et al. (1998) A controlled, prospective, 1-year trial of citalopram in the treatment of panic disorder*. J Clin Psychiatry,* **59,** 528-534.

Looff D, Grimley P, Kuiler F, et al. (1995) Carbamazepine for posttraumatic stress disorder (letter). *J Am Acad Child Adolesc Psychiatry,* **34,** 703-704.

Marmar CR, Foy D, Kagan B, et al. (1994) An integrated approach for treating posttraumatic stress. In: Pynoos RS (ed.). *Posttraumatic Stress Disorder: A Clinical Review*, Lutherville, MD: Sidran Press, pp 99-132.

Marshall RD, Schneier FR, Fallon BA, et al. (1998) An open trial of paroxetine in patients with noncombat-related, chronic posttraumatic stress disorder. *J Clin Psychopharm,* **18(1),** 10-18.

Meek JK, Kablinger A (1998) Antidepressants and posttraumatic stress disorder. *J Louisiana State Medical Society,* **150(10),** 487-489.

Milne RJ, Goa KL (1991) Citalopram. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in depressive illness. *Drugs,* **41 (3),** 450-477.

Mukaddes NM, Abali O, Kaynak N (2003) Citalopram treatment of children and adolescents with obsessive-compulsive disorder: a preliminary report. *Psychiatry Clin Neurosci,* **57(4),** 405-8.

Nader KO, Kriegler JA, Blake DD, et al. (1996) Clinician Administered PTSD Scale for Children and Adolescents for (DSM-IV)(CAPS-CA), Current and Lifetime Diagnostic Version, and Instruction Manual. A National Center for PTSD and UCLA Trauma Psychiatry Program collaboration.

Namerow LB, Thomas P, Bostic JQ, et al. (2003) Use of citalopram in pervasive developmental disorders. *J Dev Behav Pediatr,* **24(2),** 104-8.

Pine DS (2001) Fluvoxamine for the treatment of anxiety disorders in children and adolescents. *NEJM,* **344 (17),** 1279-1285.

Tan JY, Levin GM (1999) Citalopram in the treatment of depression and other potential uses in psychiatry. *Pharmacotherapy*, **19,** 675-689.

Thomsen PH (1997) Child and adolescent obsessive-compulsive disorder treated with citalopram: findings from an open trial of 23 cases. *J Child Adolesc Psychopharmacol*, **7 (3),** 157-166.

Thomsen PH, Mikkelsen HU (1995) Course of obsessive-compulsive disorder in children and adolescents: a prospective follow-up study of 23 Danish cases. *J Am Acad Child Adolesc Psychiatry,* **34(11),** 1432-1440.

Thomsen PH (1997) Child and adolescent obsessive-compulsive disorder treated with citalopram: findings from an open trial of 23 cases. *J Child and Adolesc Psychopharmacol,* **7(3),**157-166.

van der Kolk BA, Dreyfuss D, Michaels M, et al (1994) Fluoxetine in posttraumatic stress disorder. *J Clin Psychiatry,* **55,** 517-522.

van der Kolk BA (1997) The psychobiology of posttraumatic stress disorder. *J Clin Psychiatry,* **58(9),** 16-24.

Wade AG, Lepola U, Koponen HJ, Pedersen N, Pedersen T (1997) The effect of citalopram in panic disorder. *Br J Psychiatry*, **170,** 549-553.

Wagner KD, Robb AS, Findling RL, et al. (2004) A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children and adolescents. *Am J Psychiatry*, **161(6),** 1079-83.

Ziervogel CF (2000) Selective serotonin re-uptake inhibitors for children and adolescents. *Eur Child Adolesc Psychiatry,* **9 (suppl 1),** I20-26.

TABLE 1: Trauma and PTSD Characteristics (N=8)

Patient	Trauma Type	Acute *<3months*	Chronic *≥3months*	Delayed *≥6months*	Duration of PTSD Symptoms (*months*)
1	Rape	No	Yes	No	4
2	Repeated sexual abuse	Yes	No	Yes	2
3	Witnessing domestic violence	No	Yes	Yes	24
4	Repeated physical and sexual abuse/rape	No	Yes	No	24
5	Repeated physical/ Sexual abuse/ 2 rapes	No	Yes	No	24
6	Shooting/ Gunshot wound/ Loss of baby	No	Yes	No	4
7	Witnessing death of friend	Yes	Yes	Yes	2
8	Witnessing mass genocide in Rwanda	No	Yes	Yes	48

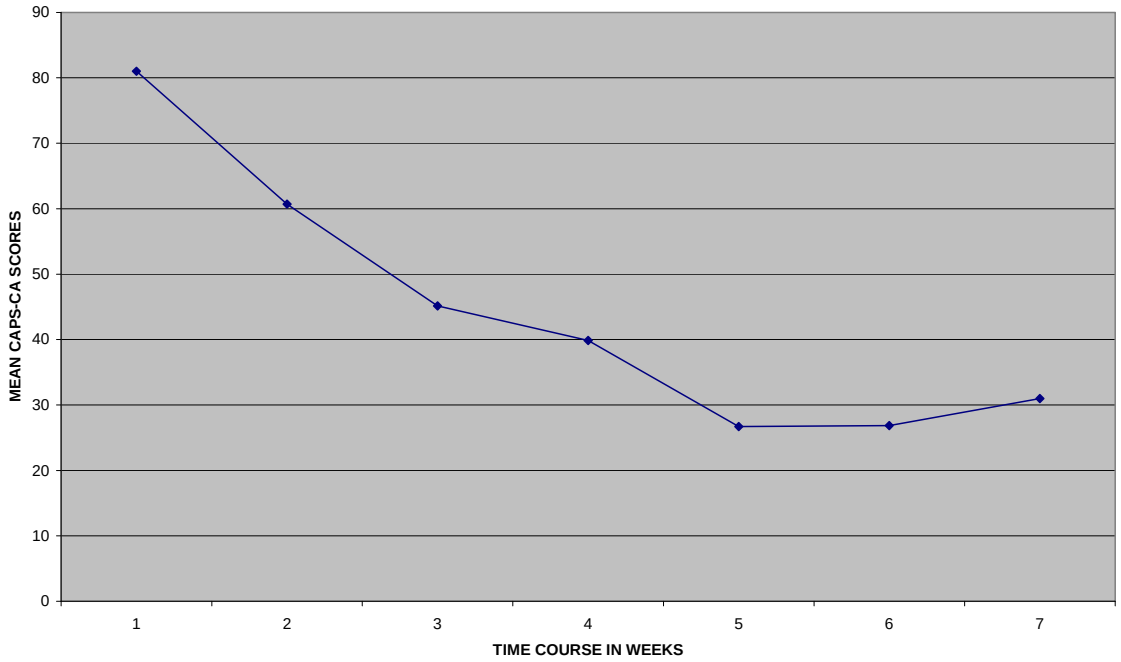
TABLE 2: Mean Total Scores (SD): CAPS-CA, ZUNG, CGI-S (N=7 Completers)

	Baseline	6 Weeks	12 Weeks
CAPS-CA	81 (14.9)	39.9 (20.4)	31 (17.2)
ZUNG	41.5 (4.9)	41.3 (7.3)	41.2 (6.1)
CGI-S	5.1 (0.7)	3.6 (0.8)	2.6 (0.8)

TABLE 3: CAPS-CA Symptom Cluster Scores (sum of frequency and severity scores, paired two sample t-tests for means [N=7])

	Mean Score		***p* value**
	Baseline	12 weeks	
Re-experiencing	27.0 (5.5)	8.1 (7.8)	0.001
Avoidance	27.7 (7.8)	11.8 (8.1)	0.0001
Hyperarousal	26.3 (6.9)	11.6 (5.8)	0.001

FIG. I: Mean CAPS-CA Scores versus Time Course in Weeks



Significant reduction in mean CAPS-CA total scores between week 0 and week 4 ($p<0.0002$)
Significant reduction in mean CAPS-CA total scores between week 4 and week 12 ($p<0.01$)

5. PHARMACOTHERAPY OF ADOLESCENT POSTTRAUMATIC STRESS DISORDER

Comparison of Response to Citalopram in Adolescents and Adults with Posttraumatic Stress Disorder

5.1 Study Summary

As has been highlighted, the SSRIs may play a role in treating the essential symptoms of posttraumatic stress disorder (re-experiencing, avoidance, numbing, hyperarousal) in both children and adolescents. As a follow-up to the pilot study described, this trial compared outcome in adolescents and adults with a DSM-IV diagnosis of PTSD.

Twenty-four children/adolescents and 14 adults assessed for PTSD severity at baseline were followed up on citalopram treatment (20-40mg/day) at 2-weekly intervals over 8 weeks. The Clinician-Administered PTSD Scale (CAPS) and the Clinical Global Improvement Scale (CGI) were used as outcome measures.

There were no significant differences in outcome measures between adolescents (n= 24) and adults (n=14), and both

groups had significant reductions in mean CAPS total scores, symptom cluster scores, and CGI ratings, at endpoint.

While the SSRIs have established efficacy and safety in the treatment of adult PTSD, literature on their use in child and adolescent PTSD is sparse. Controlled data is needed to support the clinical perception that SSRIs are agents of choice in the treatment of paediatric posttraumatic stress disorder. In the interim, these data do suggest continuity in treatment response across adult and adolescent PTSD populations.

5.2 Introduction

As the previous study demonstrated, appropriate pharmacological management of PTSD with SSRIs (also incorporating aspects of education and psychosocial support) may be potentially useful in adolescents in reducing core symptoms (e.g., flashbacks, nightmares, avoidance of reminders of the trauma, restricted range of emotions, and hyperarousal symptoms) (APA, 1994) and improving overall well-being and functioning (Davidson, 2000).

This study, a follow-up to the preliminary open-label study (Chapter 4), examined between-group differences in response to citalopram in adolescents and adults with DSM-IV posttraumatic stress disorder (APA, 1994). (Seedat et al., 2000; Seedat et al., 2001). It provides data on a larger sample of adolescents (three-fold the size of the original sample) as well as a comparative analysis of response to an SSRI in adolescent and adult PTSD.

5.3 Methods

24 adolescents (aged 10 to 18 years) and 14 adults (aged 19 years upwards) with a current PTSD diagnosis (DSM-IV) (American Psychiatric Association, 1994) of at least moderate severity (as determined by a Clinical Global Impression Severity score of ≥ 4) (CGI-S) (Guy, 1976), were eligible for trial inclusion. Diagnostic specificity was ascertained by means of the Structured Clinical Interview for DSM-IV (SCID-1) (First et al., 1995) and the Clinician-Administered PTSD Scale-Diagnostic and Symptom Status versions (CAPS) (Blake et al., 1990; Blake et al., 1995) in adults; the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS) (Kaufman et al., 1997) and the Clinician Administered Posttraumatic Stress Disorder Scale-Child and Adolescent version (CAPS-CA) (Nader et al., 1996) in adolescents. The SCID-I (adults) and K-SADS (adolescents) also captured the onset and duration of PTSD symptoms. The presence of comorbidity was screened for using the SCID-1 (adults) and K-SADS (adolescents) (First et al., 1995; Kaufman et al., 1997).

The study was approved by the ethics committee of the University of Stellenbosch Medical School, Tygerberg.

Written informed consent for trial inclusion was obtained from all adult participants, and from the parents or legal guardians of adolescents (in addition, adolescents gave assent). Subjects were recruited via media advertisement between 1997 and 2000.

Subjects who met DSM-IV criteria for a psychotic disorder, bipolar disorder, organic disorder, and/or substance abuse/dependency in the preceding 6 months, were excluded. The presence of comorbid mood and anxiety disorders were not exclusions, provided that these disorders did not precede the primary PTSD diagnosis. Additionally, subjects who had previously been on citalopram treatment were excluded. There was a 2-week washout period for all subjects on benzodiazepines and/ or antidepressants (except for fluoxetine: 5-week washout). Concomitant pharmacotherapy or psychotherapy was not permitted during the trial, however, supportive counselling was provided by the treating clinician.

The primary outcome measures were: (1) mean change from baseline in PTSD symptoms as assessed by the CAPS (adults) (Blake et al., 1990; Blake et al., 1995) and CAPS-CA

(adolescents) (Nader et al., 1996) and (2) Clinical Global Impression (CGI) (Guy, 1976) change scores at endpoint.

CAPS (adults) and CAPS-CA (adolescents) interviews were used to establish both PTSD caseness and treatment outcome. Based on the adult CAPS, the CAPS-CA (used in children aged 8 upwards) measures the seventeen core PTSD symptoms (DSM-IV) grouped in categories of: (1) re-experiencing (items 1-5, maximum score 40), (2) avoidance/numbing (items 6-12, maximum score 56), and (3) hyperarousal (items 13-17, maximum score 40). CAPS and CAPS-CA interviews were administered by the treating clinician at 2 weekly intervals over 8 weeks.

CGI-improvement scores at endpoint distinguished responders from non-responders. A final CGI-I score of 1 or 2 (much or very much improved) defined "response", while a final CGI-I score of ≥ 3 (minimally improved or worse) defined "non-response". Citalopram was initiated at 20mg/daily, and up-titrated after 2 weeks to a maximum daily dose of 40mg, if tolerated. Adverse events were documented at all clinic visits.

5.4 Results

A comparison of the two groups with respect to demographic features, index trauma, multiplicity of trauma, and onset/duration of PTSD symptoms, is presented in Table 1.

5.4.1 Demographic characteristics

Seventeen adolescents (71%) entered completed 8 weeks of treatment. The sample comprised 16 girls and 8 boys. The adult group (n = 14) comprised 7 men and 7 women, with 11 completers (79%) by week 8. The sample as a whole comprised 8 "Caucasian" subjects, 5 "Black" subjects, and 25 subjects of "mixed" race. The mean age of adolescent subjects was 14.3 years ± 2.3 (range 10 to 18 years, median 14 years) while the mean age of adult subjects was 33.5 years ± 8.4 (range 20 to 52 years, median 33.5 years).

5.4.2 Trauma type

In the adolescent group, traumatic exposure included rape/other sexual assault (n = 14), witnessing of violence or death (n = 8), perpetration of violence (n = 1) [16 year-old boy who accidentally stabbed his 18 year-old brother to death in an argument], and violent physical assault (n = 1). Adult traumas constituted rape/other sexual assault (n=5), violent physical assault (n=5),

combat (n = 2), torture (n=1), and witness to extreme violence/physical harm (n=1).

5.4.3 PTSD symptoms

The mean duration of PTSD symptoms prior to treatment for adolescents was 10.96 months (± 10.95) (range: 2 to 48 months, median: 6 months), while the mean duration of PTSD symptoms for adults was 38.4 months (± 50.8) (range 3 months to 141 months, median 13 months). Only 6 of the 24 adolescents (25%) met criteria for acute PTSD (duration of PTSD symptoms < 3 months). In addition, 6 adolescents had a delayed onset of symptoms (≥ 6 months after the traumatic event). In the adult group, only 1 of 14 adults met criteria for 'acute PTSD'. Four had 'delayed onset' of symptoms.

On baseline assessment of symptom severity (Clinical Global Severity score) (CGS) (Guy, 1976), 6 adolescents (25%) vs. 8 adults (57%) were classified 'moderately ill' (CGS = 4), while 18 adolescents (75%) vs. 6 adults (43%) were classified 'markedly ill' (CGS = 5). Differences in baseline CGS scores did not reach statistical significance for the groups (χ^2 test).

5.4.4 Comorbidity

Half of all adolescents (n=12) met criteria for a current diagnosis of major depressive disorder (MDD) (mild/ moderate severity). In the adult group, 6 (36%) met criteria for either current major depressive disorder or dysthymic disorder, of post-traumatic onset. There was no statistically significant difference between adolescents and adults in comorbidity with depression (χ^2). Additionally, 1 adolescent met criteria for panic disorder (current diagnosis) and separation anxiety disorder (lifetime diagnosis). Lifetime diagnoses among adults included alcohol abuse and dependence (n=2), bulimia nervosa (n=1), attention deficit/hyperactivity disorder (n=1), and eating disorder not otherwise specified (n=1).

5.4.5 Early withdrawal

The mean daily dose of citalopram was 27.9 mg (± 9.95) in the adult group and 20.0 mg (± 3.53) in the adolescent group. Medication compliance was high in both groups. In the adolescent group, 5 subjects were lost to follow-up and 2 were withdrawn due to adverse events (withdrawal at 2 weeks due to nose bleeds, withdrawal at 4 weeks due to skin

rash). In the adult group, 3 subjects were lost to follow-up while none were withdrawn on account of adverse events.

5.4.6 Reported adverse events

Citalopram (20mg) was well tolerated overall. Most reported adverse events were mild and self-remitting. Amongst adolescents, treatment-emergent effects included drowsiness (n =10), headache (n = 7), nausea (n = 7), and increased sweating (n=5), while yawning, insomnia, dizziness, tremor, and increased appetite, were less commonly reported. One adolescent experienced akathisia (of moderate severity) which resolved without any intervention at three weeks. Two adolescents were withdrawn due to adverse events. One developed a skin rash in the first week of commencing citalopram, which resolved within 10 days of discontinuation. The other was withdrawn at 2 weeks (at the request of his parents) following three nosebleeds on day 10, and another episode two weeks after medication discontinuation. These nosebleeds were mild, did not require medical intervention, and in retrospect may not have been study drug-related.

Adult subjects most commonly reported drowsiness (n=5), nausea (n=4), headaches (n=2), dry mouth (n=2), and

diarrhoea (n=2). Less commonly reported events included increased sweating, blurred vision, and constipation. No episodes of self-harm of suicidal were reported.

5.4.7 Prior treatment for PTSD

Amongst adolescents, previous treatments included tricyclic antidepressant medication (amitriptyline and imipramine x 1 month) (n=2) and supportive therapy (n = 7). Previous treatments in adults included SSRIs (sertraline and fluoxetine x 6 months) (n = 2) and tricyclic antidepressants (amitriptyline x 3 months) (n= 2).

5.4.8 Response characteristics

Of the 17 adolescent completers, 16 (94%) were ‘responders’ on CGI-improvement scores at endpoint (week 8): 5 completers were ‘much improved’ (CGI=2) and 9 completers were ‘very much improved’ (CGI=1). Of the 3 ‘non-responders’, one was ‘minimally improved’ at endpoint, while two were ‘minimally worse’ (CGI= 5). Of the 11 adult completers, 9 adults (82%) were classed as ‘responders’: 6 completers were ‘much improved’ (CGI= 2) and 3 completers were ‘very much improved’ (CGI= 1). The two ‘non-responders’ were ‘minimally improved’ (CGI = 3) at endpoint. There were no significant differences in either

group between CGI responder status and (i) immediate/delayed onset PTSD (χ^2 test), (ii) single/multiple trauma, (χ^2 test), (iii) duration of symptoms (Mann-Whitney U test), and (iv) gender (χ^2 test). There was also no significant association between CGI responder status and comorbid depression for either group (Fisher's exact test). Furthermore, in both groups, there were no significant differences between completers and non-completers in CGI responder status and the abovementioned variables: gender, PTSD onset, PTSD duration, and comorbidity with depression.

For individual groups, paired t-tests demonstrated significant differences between baseline and endpoint CAPS total scores, baseline and endpoint CGI-severity scores, and baseline and endpoint symptom cluster scores (re-experiencing, avoidance/ numbing, and hyperarousal), for completers (Table 2). In the intent-to-treat analysis with the last observation carried forward (LOCF), the difference between baseline and endpoint (week 8) CAPS re-experiencing scores and baseline and endpoint CGI-severity scores was not statistically significant.

In the adolescent group (n=24), there was a mean reduction of 42.9 points (54 %) in CAPS total scores between baseline and endpoint (t= 9.88, $p < 0.001$). In the adult group (n=14), there was a mean reduction of 30.9 points (39 %) in CAPS total scores between baseline and endpoint (t = 6.4, $p < 0.001$). There were no significant differences in CAPS total scores (student t-test) and CGI responder status (CGI cut-off score of 1 or 2 defined ‘response’) between the two groups at any of the time points (week 0, 2, 4, 6, and 8) (Fig. 1) (χ^2 tests). However, the difference between the groups in improvement on hyperarousal cluster symptoms was significant (t=3.87, p <.001), with adolescents demonstrating greater improvement at week 8.

Efficacy analyses (CAPS total score and CGI severity score) using a general linear models (GLM) analysis of variance with group as a main effect and time as a repeated measure did not reveal significant time effects or group x time interactions.

5.5 Discussion

Although there were no significant differences in overall treatment response or time-to-response between the groups, both adolescents and adults had significant reductions in mean CAPS total scores and CGI scores at endpoint (week 8), with adolescents demonstrating greater reduction in mean CAPS total scores. With respect to PTSD symptom clusters, adolescents had significantly greater improvement in hyperarousal symptoms, but not re-experiencing and avoidance symptoms, compared with adults at week 8 (Table 2). Duration of PTSD symptoms and mode of onset of PTSD (immediate vs. delayed) did not impact on treatment outcome for either group. There are few studies that have examined the relationship between the delayed-onset subtype of PTSD and treatment-response (Hermann and Eryavec, 1994; Solomon et al., 1995; Buckley et al., 1996; Ehlers et al., 1998).

The high prevalence of co-occurring MDD and dysthymia in our sample (36% of adults, 50% of adolescents) is supported across several studies that suggest that PTSD and MDD in trauma victims may be influenced by overlapping or common vulnerabilities (Kessler et al., 1995; Breslau et al., 2000). While in this study the presence of comorbid depression did not significantly affect treatment outcome

in either group, it is widely known that comorbidity negatively impacts on prognosis and course of illness. There has been little investigation of the treatment of comorbid PTSD and MDD or dysthymia; however, many of the agents that have demonstrated efficacy in the treatment of PTSD are also antidepressant agents (Brady et al., 2000).

These findings suggest similar effects for citalopram on core PTSD symptoms in both adolescent and adult subjects. Given the many other differences (demographic characteristics, duration of PTSD symptoms) between the groups, the similarity in treatment response may be indicative of ‘continuity’ in the underlying neurobiology of the disorder in different cohorts. Both groups were treated with a comparable mean daily dose of citalopram, consistent with SSRI dosing schedules employed across paediatric and adult anxiety disorders. The reasons for response to similar dosing schedules across this age spectrum might be two-fold: (i) although developmental differences in children and adolescents are known to impact on the pharmacokinetics of SSRIs, these differences become less marked around puberty and, (ii) serotonergic neurotransmission and serum concentrations of serotonin metabolites do not alter significantly with childhood

development which could account for lack of significant pharmacodynamic differences (Vitiello and Jensen, 1995; Tosyali and Greenhill, 1998; Murphy et al., 2000).

Tolerability of citalopram was also similar for the groups, and commonly occurring adverse effects (gastrointestinal, central nervous system) were generally mild and short-lived. Behavioural activation (motor restlessness) was seen in one child, but did not result in medication discontinuation. The emergence of epistaxis in another child did result in medication discontinuation. While SSRI-associated haemostatic dysfunction (mechanism: reduction of serotonin leading to disturbances in platelet function) appears to be a rare adverse effect (Berk and Jacobson, 1998), bruising and epistaxis have been described in children 1 week to 3 months after starting SSRI treatment (Lake et al., 2000). Overall, adverse effects in adolescents in this study were consistent with those reported in other paediatric SSRI studies.

The findings are encouraging, however, interpretation is limited by a small sample size, absence of placebo-controlled/ double-blind design, and lack of assessment measures beyond core PTSD symptoms (i.e., no measures of

depression, disability). Another shortcoming was the lack of an independent evaluator to administer outcome measures.

5.6 Conclusion

In conclusion, while evidence for efficacy of the SSRIs in adult PTSD is fairly robust, it is largely a clinical perception that SSRIs (e.g., citalopram) are safe and efficacious in paediatric populations (DeVane and Sallee, 1996; AACAP, 1998). The current off-label prescribing of the SSRIs for child and adolescent PTSD needs the support of blinded, systematic, placebo-controlled, efficacy and safety studies. In the interim, the current preliminary data do suggest continuity in treatment response to citalopram across adult and child/adolescent PTSD patients.

5.7 References

Allen AJ, Leonard H, Swedo S (1995) Current knowledge of medications for the treatment of childhood anxiety disorders. *J Am Acad Child Adolesc Psychiatry*, **34,** 976-986.

American Academy of Child and Adolescent Psychiatry (AACAP) (1998) Practice parameters for the assessment and treatment of adolescents with posttraumatic stress disorder. *J Am Acad Child Adolesc Psychiatry,* **37 (suppl 10),** 4S-26S.

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders (4th ed) (DSM-IV). Washington, DC: APA.

Berk M, Jacobson BF (1998) Selective serotonin reuptake inhibitor-induced disturbances of haemostasis: Mechanisms and therapeutic implications. *CNS Drugs*, **10 (6),** 441-446.

Blake DD, Weathers FW, Nagy LM (1990) A clinician rating scale for assessing current and lifetime PTSD: the CAPS-1. *Behaviour Therapist,* **13**, 187-188.

Blake DD, Weathers FW, Nagy LM, et al. (1995) The development of a Clinician Administered PTSD Scale. *Journal of Traumatic Stress,* **8,** 75-90.

Brady KT, Killeen TK, Brewerton T, Lucerini S (2000) Comorbidity of psychiatric disorders and posttraumatic stress disorder. *J Clin Psychiatry*, **61(suppl 7),** 22-32.

Breslau N, Davis GC, Peterson EL, Schultz LR (2000) A second look at comorbidity in victims of trauma: the posttraumatic stress disorder-major depression connection. *Biol Psychiatry*, 48:902-909.

Buckley TC, Blanchard EB, Hickling EJ (1996) A prospective examination of delayed onset PTSD secondary to motor vehicle accidents. *J Abnorm Psychol,* **105 (4),** 617-625.

Davidson JRT (2000) Pharmacotherapy of posttraumatic stress disorder: treatment options, long-term follow-up, and predictors of outcome. *J Clin Psychiatry,* **61 (suppl 5),** 52-56.

DeVane CL, Sallee FR (1996) Serotonin selective reuptake inhibitors in child and adolescent psychopharmacology, a review of published experience. *J Clin Psychiatry*, **57,** 55-66.

Ehlers A, Mayou RA, Bryant B (1998) Psychological predictors of chronic posttraumatic stress disorder after motor vehicle accidents. *J Abnorm Psychol*, **107 (3),** 508-519.

First MB, Spitzer MB. Gibbon RL,Williams JBW (1995) Structured Clinical Interview for DSM-IV Axis I disorders-Clinician Version. Biometrics Research Department, New York State Psychiatric Institute, 722 West 168th Street, New York, New York 10032.

Guy W (1976) ECDEU Assessment Manual for Psychopharmacology, 2nd ed (DHEW Publication ABM 76-388). Washington DC: US Government Printing Office.

Hermann N, Eryavec G (1994) Delayed onset post-traumatic stress disorder in World War II veterans. *Can J Psychiatry,* **39 (7),** 439-441.

Kaufman J, Birmaher DB, Brent D, et al. (1997) Schedule for Affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime Version (K-SADS-PL): Initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry,* **36(7),** 980-988.

Kessler RC, Sonnega A, Bromet E, Nelson CB (1995) Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry,* **52,** 1048-1060.

Lake MB, Birmaher B, Wassick S, et al. (2000) Bleeding and selective serotonin reuptake inhibitors in childhood and adolescence. *J Child Adolesc Psychopharmacology,* **10 (1),** 35-38.

Murphy TK, Bengston MA, Tan JY, et al. (2000) Selective serotonin reuptake inhibitors in the treatment of paediatric anxiety disorders: a review. *Int Clin Psychopharmacol*, **15 (suppl 2),** S47-63.

Nader KO, Kriegler JA, Blake DD, et al. (1996) Clinician Administered PTSD Scale for Children and Adolescents for (DSM-IV)(CAPS-CA), Current and Lifetime Diagnostic Version,

and Instruction Manual. A National Center for PTSD and UCLA Trauma Psychiatry Program collaboration.

Seedat S, Stein DJ, Emsley RA (2000) Open trial of citalopram in adults with post-traumatic stress disorder. *Int J Neuropsychopharmacology*, **3,** 135-140.

Seedat S, Lockhat R, Kaminer D, Zungu-Dirwayi MZ (2001) An open trial of citalopram in adolescents with post-traumatic stress disorder. *Int Clin Psychopharmacol* **16,** 21-26.

Solomon Z, Singer Y, Blumenfeld A (1995) Clinical characteristics of delayed and immediate-onset combat-induced post-traumatic stress disorder. *Mil Med*, **160 (9),** 425-430.

Tosyali MC, Greenhill LL (1998) Child and adolescent psychopharmacology: important developmental issues. *Pediat Clin N Am,* **45***,* 1021-1035.

Vitiello B, Jensen PS (1995) Developmental perspectives in pediatric psychopharmacology. *Psychopharmacol Bull,* **31,** 75-81.

TABLE 1: Demographic Variables and Characteristics of PTSD in Adolescents and Adults

	TOTAL SAMPLE (n = 38)	**ADOLESCENTS** (n = 24)	**ADULTS** (n = 14)
Female (%)	53 %	54 %	50 % [ns]
Mean age in years (SD)	21.34 (10.80)	14.25 (2.31)	33.50 (8.38)
Mixed race (%)	66 %	83 %	36 %
Mean duration of PTSD symptoms in months (SD)	21.05 (34.07)	10.96 (10.95)	38.36 (50.80)[ns]
Delayed onset of PTSD symptoms (%)	29 %	25 %	36 % [ns]
Multiple exposure to trauma ≥ 3 (%)	39 %	33 %	50 % [ns]
Index trauma (n)			
Rape	16	12	4
Witnessing violence or death	9	8	1
Other sexual trauma	3	2	1
Physical assault	6	1	5
Torture	1	0	1
Combat trauma	2	0	2
Perpetration of violence	1	1	0

[ns] no statistically significant difference between groups

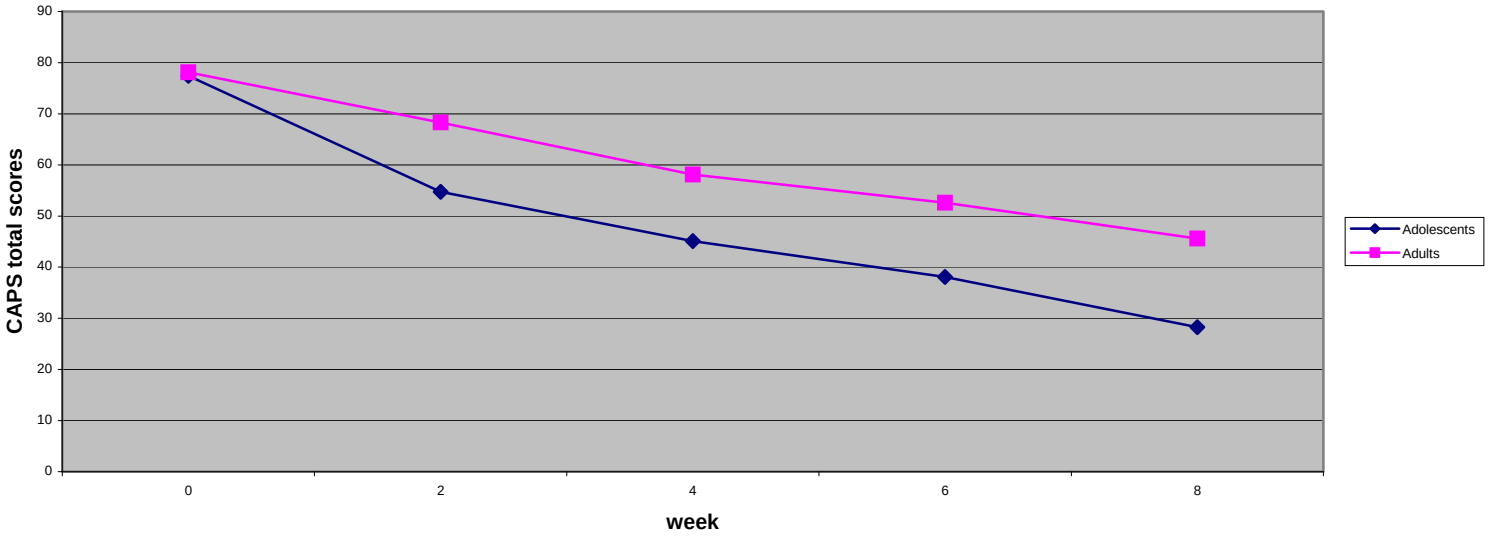
TABLE 2: Comparative Efficacy of Citalopram in Adolescents and Adults

RATING SCALE	BASELINE	WEEK 8	WEEK 8 Within–group differences (paired t-tests)		WEEK 8 Between-group differences (independent t-tests)	
	Mean (s.d.)	**Mean (s.d.)**	**t**	***p***	**df**	***p***
CAPS Total						
Adolescents	79.8 (15.3)	36.8 (26.1)	9.9	<.001*		
Adults	79.9 (15.6)	48.9 (23.6)	6.4	<.001*	29.6	.165
CAPS *Re-experiencing*						
Adolescents	26.5 (5.9)	9.7 (8.8)	9.1	<.001*		
Adults	19.6 (7.1)	12.9 (8.0)	3.2	<.007*	29.4	.259
CAPS ***Avoidance***						
Adolescents	27.9 (6.8)	15.9 (11.6)	6.1	<.001*		
Adults	29.9 (7.2)	14.9 (9.9)	8.1	<.001*	30.8	.792
CAPS ***Hyperarousal***						
Adolescents	25.4 (6.1)	10.9 (7.7)	10.1	<.001*		
Adults	30.4 (5.9)	21.3 (8.2)	4.3	.001*	26.1	.001*
CGI-Severity						
Adolescents	4.9 (.65)	3.0 (1.1)	8.2	<.001*		
Adults	4.4 (.51)	2.6 (.74)	8.3	<.001*	32.0	.845

Intent- to-treat analysis with LOCF
Adolescents: n = 24 Adults: n = 14

**Represents significant differences within/ between samples*

FIG. 1: CLINICIAN ADMINISTERED PTSD SCALE (CAPS) TOTAL SCORES (MEAN) AT BASELINE (WEEK 0) AND WEEKS 2, 4, 6, AND 8 FOR ADOLESCENTS AND ADULTS



No significant differences between groups at any of the time points

6. Conclusion & Directions for Future Research

6.1 Summary

The work presented here adds to existing evidence that adolescent PTSD is a common and chronic condition and that even in its subclinical form (partial PTSD), is associated with considerable morbidity. Adolescents with subclinical syndromes are as likely to demonstrate clinical impairment and distress as those with full-blown syndromes. The studies described in Parts 1 and II, although not conceptualised and designed to be directly comparative, nevertheless provide several convergent and replicable findings. In comparing the South African school and clinic samples, perhaps most striking were the highly similar gender patterns of trauma exposure and full and partial PTSD that emerged. Male-female differences in the rates of trauma and PTSD (*greater preponderance of PTSD in women despite the greater propensity for trauma [especially assaultive types] in men*) that have so consistently been replicated in adult studies, did not hold true in these two adolescent samples. The results suggest that adolescent girls may be no more vulnerable than adolescent boys to the occurrence of major life traumas, with the exception of sexual assault. Nor were girls more likely to report

multiple events or more likely to be affected by the cumulative effects of multiple events than males.

A second noteworthy finding, consistent across both samples, was that despite gender equivalence in the rates of full and partial PTSD syndromes, girls with full/partial PTSD were more likely to rate PTSD symptoms as occurring “most of the time” or “all of the time” than boys. Arguably the higher symptom burden in girls may to some extent account for the gender difference in functional impairment, with girls experiencing more interference from PTSD symptoms in family and social activities (but not in school activities), compared with boys. This suggests that, in assessing for gender differences in impairment in full and partial PTSD, it is also important to evaluate the impact of PTSD symptom frequency/ intensity on interference and distress.

Partial PTSD, a concept that is not as yet accepted by the DSM-IV (APA, 2000), remains an under-researched nosological category, particularly in children and adolescents. In the DSM-IV, an inherent aspect of the definition of PTSD is the mandatory requirement of the clinical significance criterion, namely the presence of “clinically significant

distress or impairment in social, occupational, or other important areas of functioning". This criterion is considered helpful for clinicians and researchers in establishing a threshold for diagnosis in those situations where PTSD symptoms on their own may not be pathological (APA, 2000). However, many of the symptoms of PTSD (e.g., recurrent and intrusive distressing recollections, recurrent and intrusive dreams) are themselves pervasive and intrinsically distressing to children and adolescents, and almost invariably associated with some level of impairment. Focusing on impairment alone in this age group(where there is usually a reliance on parents and caregivers for information), may not be an entirely adequate means of making a valid distinction between full and subthreshold disorder (Spitzer and Wakefield, 1999). From a clinical viewpoint, it would seem reasonable to identify adolescents who satisfy the impairment/distress criterion, because they are the ones who are most likely to require intervention at some level. At this stage, much remains to be learnt about this form of PTSD: Is partial PTSD a distinct entity, is it PTSD that has not yet fully evolved, or is it perhaps PTSD that has gone into remission? Replication of these findings in longitudinal studies may help to answer these questions and to

facilitate a better categorisation of PTSD phenomenology. It will be important to delineate whether subsyndromal forms in adolescents have the same biological underpinnings as full PTSD, through validation against neurobiological markers (e.g., cortisol) (Mylle and Maes, 2004). Of note, such a recent study in adults found that patients with persistent subsyndromal PTSD and marked hyperarousal had significantly elevated serum leptin levels (Liao et al., 2004). Thus, leptin, a peptide hormone released from adipose tissue that regulates food intake and controls weight, may be a neuroendocrine marker for this form of PTSD in adults, but it remains to be seen whether this also holds true for adolescents.

The high prevalence of multiple or compounded trauma exposure while not surprising, is concerning. It underscores the importance of routine and early detection of psychopathology in traumatised adolescents through informed, evidence-based assessment. In under-resourced settings, this is often difficult as many adolescents do not have access to mental health services. Moreover, many instances of adolescent injurious violence exposure remain hidden. The situation is aggravated by evidence from other countries which suggests that victimisation in adolescents

does not necessarily prompt use of health and trauma care services and that, in some instances, victimisation may actually be associated with a lower odds of subsequent mental health usage (Guterman et al., 2002). Nevertheless, routine enquiry of trauma in adolescents who present to general health care services may be the only way to enable timely referral and receipt of ameliorative treatment.

As has been demonstrated here, the SSRIs may relieve intrusive, avoidance, and hyperarousal symptoms in adolescents, as well as treat comorbid conditions (e.g., depression) associated with serotonergic dysregulation. In fact, it has been suggested that SSRIs may more effectively reduce avoidant/numbing symptoms than other agents (Friedman et al., 1995). This fits well with the observation in both school and clinic samples of higher rates of avoidance symptoms among boys and girls, compared with symptoms from the other two symptom clusters.

Recently there has much controversy about the use of the SSRIs to treat child and adolescent depression. Pooled analyses of 24 short-term placebo-controlled trials (4 to 16 weeks) of nine antidepressant drugs (SSRIs and others) in children and adolescents with MDD, obsessive-compulsive

disorder, and other psychiatric disorders (involving more than 4,400 patients) revealed a greater risk of suicidality during the first few months of treatment, with an average risk of 4% for those on drug versus 2% for those on placebo (APA, 2004). No suicides occurred in these trials. Amidst conflicting data (and the issuing of a black-box warning by the FDA on all antidepressants distributed within the United States), there is indisputable evidence of the efficacy of these agents in treating adolescent depression, including suicidality. These data may also not be generalisable to the treatment of PTSD, and the consequences of not treating moderate to severe disorder in youth may pose a far greater risk to their normal development and future functioning. Nevertheless, physicians prescribing SSRIs and other antidepressant agents should be keenly aware of the presence of suicidality in their child and adolescent patients prior to and especially during the early treatment phase. The preliminary data presented here on the use of citalopram as a first-line treatment for adolescent PTSD suggests that it is safe (i.e., there were no instances of self-harm of suicidal ideation reported) and effective, and underscores the need to conduct research to clarify the potential value and risks of these agents for this disorder.

In addition to the need for well-controlled clinical trials of the SSRIs and other agents for child and adolescent PTSD, research on the effects of early interventions and treatments are sorely needed. To this end, longitudinal studies that identify adolescents who are at risk for developing PTSD and related symptoms by examining risk modifier variables (e.g., severity and duration of trauma, primacy of exposure, age [older vs. younger adolescents], gender, other life events, psychiatric morbidity, parental PTSD), taking into account developmental differences and social contextual factors (March, 2003), will likely provide information that is useful for initial and later treatment interventions.

6.2 References

American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders-Text Revision (DSM-IV-TR), 4th ed. *American Psychiatric Press*: Washington, DC

American Psychiatric Association (2004) SSRIs: Beware of rush to judgment. *Psychiatric News*, **39(19),** 3.

Friedman MJ, Southwick SM (1995) Towards pharmacotherapy for post-traumatic stress disorder. In: Friedman MJ, Charney DS, Deutch AY (eds.). *Neurobiological and Clinical Consequences of Stress: From Normal Adaptation to PTSD*. Philadelphia (PA): Lippincott-Raven Publishers, 465-481.

Guterman NB, Hahm HC, Cameron M (2002) Adolescent victimization and subsequent use of mental health counseling services. *J Adolesc Health,* **30(5),** 336-45.

Liao SC, Lee MB, Lee YJ, Huang TS (2004) Hyperleptinemia in subjects with persistent partial posttraumatic stress disorder after a major earthquake. *Psychosom Med,* **66(1),** 23-8.

March JS (2003) Acute stress disorder in youth: A multivariate prediction model. *Biol Psychiatry*, **53,** 809-816.

Mylle J, Maes M (2004) Partial posttraumatic stress disorder revisited. *Journal of Affective Disorders,* **78,** 37-48.

Spitzer RL, Wakefield JC (1999) DSM-IV diagnostic criterion for clinical significance: does it help solve the false positives problem? *Am J Psychiatry,* **156(12),** 1856-64.

7. Acknowledgements

Part I

The Kenyan component of this survey was supported by the Chiromo Lane Medical Center while the South African component was supported by the MRC Unit on Anxiety and Stress Disorders. I am grateful to Drs. C Nyamai, F Njenga (Chiromo Lane Medical Center, Nairobi, Kenya) and B Vythilingum (MRC Unit on Anxiety and Stress Disorders, Tygerberg) for their assistance as co-investigators and Mrs CJ Hugo, Ms D Albers and Mr J Daniels from the MHIC (Mental Health Information Center of South Africa) for their assistance with data collection and management.

This work was supported by funding from the Medical Research Council (MRC) Unit on Anxiety and Stress Disorders, University of Stellenbosch, Tygerberg.

Parts II and III

I wish to thank Dr Carl Ziervogel, Dr Tessa Middleton, Mrs Wendy Rossouw, Ms Jennifer Walker and Mr Rafiq Lockhat for assistance with patient assessments and Ms Sharain Suliman, Ms Deborah Kaminer and Mrs Nompumelelo Zungu-Dirwayi for assistance with data management.

Dr Theunis J v W Kotze (statistician) provided statistical assistance (Part II).

Funding from the MRC Unit on Anxiety and Stress Disorders and the Lundbeck Institute of Psychiatry (Denmark) supported this work.