Friendship stress buffering in young people with childhood adversity

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Chapter 7

Executive Summary & General Discussion

Executive Summary

Globally, approximately 60% of children and adolescents are exposed to at least one form of childhood adversity (Madigan et al., 2023). Chronic and repeated exposure to such stressful and potentially traumatic experiences, particularly during sensitive developmental periods, dramatically elevates the risk of both experiencing and perpetrating victimization as well as developing various forms of psychopathology later in life (McLaughlin, 2016; Widom, 1989b; Widom et al., 2008). Theoretical models propose that adversity-induced neurocognitive adaptations aid different forms of victimization (Cicchetti & Valentino, 2006; Sroufe & Rutter, 1984) and increase psychopathology vulnerability through their impact on social functioning (Gerin et al., 2019; McCrory et al., 2022). For example, the neurocognitive social transactional model of psychiatric vulnerability (introduced in **Chapter 1**; McCrory et al. (2022)) suggests that these adaptations may lead to social thinning (i.e., fewer protective social relationships) and stress generation (i.e., a social environment characterized by more stressful interpersonal experiences), thus exacerbating risks for victimization and psychopathology.

Importantly, young people who are able to maintain high levels of perceived friendship support show reduced risks of victimization and psychopathology following childhood adversity (Huang et al., 2013; van Harmelen et al., 2016, 2021; T. Williams et al., 2005). However, the underlying mechanisms that may explain this friendship buffering effect remain poorly understood. The social stress buffering literature suggests that the presence and availability of one or more supportive social partners can attenuate perceptions, reactions, and physiological responses to acute stress (Gunnar, 2017), thereby lowering allostatic load and ultimately promoting better health outcomes (Doan & Evans, 2011; Hennessy et al., 2009).

Building on these frameworks, this dissertation aimed to identify psychological, cognitive, and neural stress-related pathways through which social support, particularly friendships, reduce the risks of victimization and psychopathology in young people with childhood adversity. To advance a more nuanced understanding of these mechanisms, insights are drawn from literature reviews, cross-sectional analyses, and longitudinal analyses, employing both behavioral and neuroimaging techniques.

The **first part** of this dissertation examined how maladaptive neurocognitive and social functioning following maltreatment experiences during childhood or adolescence can increase the risk of experiencing and perpetrating victimization later in life. **Chapter 2** (Scheuplein et al., 2023) reviewed the cycle of victimization literature, highlighting the link between child maltreatment and victimization within and outside the family environment. It also outlined three

social functioning mechanisms underlying this association and reflected on the potential buffering role of social support. Specifically, victimization within the family environment has been reviewed in the context of the intergenerational transmission of maltreatment hypothesis. This hypothesis encompasses two perspectives: the victim-to-perpetrator perspective, where victims of maltreatment are more likely to become maltreating parents (Widom, 1989b), and the victim-to-victim perspective, where children of parents with a history of maltreatment are more likely to become victims themselves, even if their parents are not direct perpetrators (Madigan et al., 2019). Victimization outside the family environment has been reviewed in the context of the violence breeds violence hypothesis, which posits that being maltreated as a child increases the risk of becoming a violent perpetrator later in life (Fitton et al., 2020). In line with latent vulnerability and adaptive calibration models (Del Giudice et al., 2011; McCrory et al., 2022; McCrory & Viding, 2015), three mechanisms were reviewed as potential contributors to impaired social functioning and the association between child maltreatment and victimization: heightened attentional bias to threat, diminished reward processing and feedback learning, and emotion dysregulation. For example, a heightened attentional bias to threat may facilitate adaptive behaviors in high-stress environments. However, in non-threatening contexts, this adaptation may increase the risk of maladaptive behaviors, such as over-attributing hostile intent to others, which may provoke aggressive or avoidance behavior, impair social functioning, and increase risks for victimization and psychopathology (Crick & Dodge, 1994; N. V. Miller & Johnston, 2019). The chapter concluded by highlighting the role of safe, stable, and nurturing social support as a protective factor capable of mitigating victimization and psychopathology risk through potentially influencing these neurocognitive risk mechanisms (Schofield et al., 2013; van Harmelen et al., 2016). However, it became evident that breaking the cycle of victimization and improving health outcomes requires greater translation of knowledge about how neurocognitive mechanisms are shaped by childhood adversity and influenced by social support.

Hence, the **second part** of this dissertation zoomed in more closely on the psychological, cognitive, and neural stress-related pathways that link friendship support to reduced psychopathology risk in young people with childhood adversity. **Chapter 3** (Scheuplein & van Harmelen, 2022) systematically reviewed whether friendships reduce neural stress responses in young people with childhood adversity. In line with the PRISMA guidelines (Page et al., 2021), this pre-registered systematic literature review included empirical studies published in English involving young people with an average age between 10 and 24 years who had experienced childhood adversity. Friendships had to be assessed within the same average age range and neural stress responses had to be measured using neuroimaging techniques. After screening 4,297 records and 66 full-text articles for eligibility, only two studies matched all eligibility criteria. Two more studies

were included after broadening the scope to allow stress responses from various neurobiological systems. Ultimately, only two of these four studies directly investigated whether friendships buffer neurobiological stress responses in young people with childhood adversity. In a sample of institutionalized young people, Tang et al. (2021) found that high-quality friendships at age 12 can buffer the indirect effect of maladaptive stress physiology on peer problems at age 16. In contrast, in a small and well-functioning sample of young people with childhood adversity, Fritz, Stretton, et al. (2020) found no association between friendship support at ages 14 or 17 and affective behavioral or neural responses to social rejection. Hence, these findings highlight the critical need for future research to examine whether friendships aid mental health and well-being through mitigating neurobiological stress responses in young people with childhood adversity.

Thus, to deepen the mechanistic understanding of friendship stress buffering, **Chapter 4** (König et al., 2023) examined whether perceived friendship quality was associated with better mental health and well-being as well as reduced neural stress responses in young people with childhood adversity. This study analyzed cross-sectional behavioral and neuroimaging data from the Resilience After Individual Stress Exposure (RAISE) study (Moreno-López et al., 2021), which involved 102 young people (aged 16-26 years) in the United Kingdom (UK) who retrospectively self-reported low to moderate levels of childhood adversity. While no support was found for social thinning following childhood adversity, high-quality friendships were strongly associated with better mental health and well-being. A representative subset of 62 young people underwent functional magnetic resonance imaging while completing the Montreal Imaging Stress Task (Dedovic et al., 2005), an acute psychosocial stress paradigm. Acute stress exposure increased state anxiety and elicited enhanced neural activity in five predefined frontolimbic brain regions: the left hippocampus, bilateral insula, left medial prefrontal cortex (anterior cingulate cortex), right nucleus accumbens, and bilateral thalamus. Dimension-specific analyses revealed a weak interaction between threat experiences and friendship quality predicting left hippocampal reactivity to stress. Specifically, left hippocampal reactivity to acute stress increased with more severe threat experiences in participants reporting lower friendship quality. However, this effect did not survive multiple comparison correction and requires replication in larger, ideally longitudinal samples.

Although the COVID-19 outbreak and the reallocation of clinical research facilities shortened the data collection period of the RAISE study and led to a smaller neuroimaging sample, this collective, multidimensional stressor offered a rare opportunity to longitudinally follow the same sample of 102 vulnerable young people as part of the Resilience after the COVID-19 Threat (REACT) study (A. J. Smith et al., 2021). **Chapter 5** (König et al., 2025) therefore investigated friendship buffering effects on mental health symptoms before and at three

timepoints during the COVID-19 pandemic. Specifically, remote behavioral assessments were analyzed from before the pandemic (baseline), the first UK lockdown, the phased reopening, and the second UK lockdown. Compared to pre-pandemic baseline levels, anxiety symptoms peaked during the first lockdown and returned to baseline levels thereafter. Depressive symptoms on the other hand continued to rise following the COVID-19 outbreak. Perceived friendship quality was elevated during both lockdown periods but return to baseline levels during reopening. Social thinning was observed during the COVID-19 pandemic in that more severe childhood adversity was associated with lower friendship quality. Across all assessment timepoints, greater friendship quality was consistently associated with lower anxiety and depressive symptoms and vice versa. Notably, high-quality friendship support before the pandemic buffered anxiety and depressive symptoms during the pandemic through reducing perceived stress.

Finally, **Chapter 6** (König et al., 2025) investigated whether friendship support engages cognitive patterns shaped by childhood adversity to lower stress and boost mental health. Inspired by the neurocognitive social transactional model of psychiatric vulnerability (McCrory et al., 2022), this chapter examined whether friendship support promotes mental health in young people with childhood adversity through influencing the specificity of positive autobiographical friendship memories, which may, in turn, reduce stress perceptions. This study analyzed both quantitative and qualitative cross-sectional behavioral data from the first 100 participants of the Towards Health and Resilience in Volatile Environments (THRIVE) study, an ongoing longitudinal study of young people aged 18-24 years in the Netherlands, all of whom retrospectively self-reported low to moderate levels of childhood adversity. The findings indicated that while more severe childhood adversity was associated with social thinning, individuals who were able to maintain high levels of perceived friendship support self-reported lower levels of perceived stress and fewer depressive symptoms. Contrary to initial predictions, the specificity of positive autobiographical friendship memories was not associated with friendship support. These results, alongside the longitudinal findings in the previous chapter, suggest that friendship support may protect mental health in young people with childhood adversity through reducing perceived stress, rather than by influencing autobiographical memory processing.

Together, this dissertation marks an essential step toward a more nuanced understanding of the psychological, cognitive, and neural stress-related pathways through which social support, particularly friendships, reduce victimization and psychopathology risk in young people with childhood adversity. Each review and empirical chapter contextualized its findings within the broader literature, while also acknowledging relevant limitations. The following general discussion synthesizes key findings, addresses general limitations, and proposes directions for future research.

General Discussion

Friendships play a pivotal role in buffering stress responses and safeguarding mental health in young people with childhood adversity. However, this seemingly straightforward conclusion requires careful contextualization to clarify its scope and limitations. This dissertation yielded key empirical insights into the interwoven relationships between childhood adversity, stress mechanisms, friendship support, and psychopathology (Figure 1).

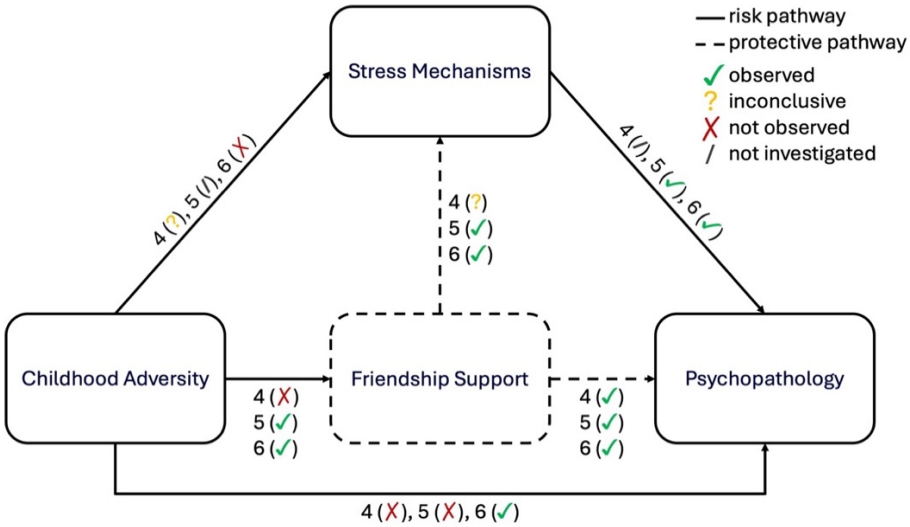

Figure 1. Key constructs and findings across empirical **Chapters 4, 5, and 6**. Arrows depict theory-based risk (solid) and protective (dashed) pathways. Constructs include childhood adversity (cumulative, threat-specific, deprivation-specific), stress mechanisms (neural, psychological), friendship support (availability, quality), and psychopathology (internalizing symptoms). Each pathway is annotated with the chapter number (4, 5, 6) and indicates if an effect consistent with the predicted pathway was observed (green tick), not observed (red cross), not investigated (gray slash), or yielded inconclusive findings (orange question mark).

To contextualize the empirical findings of this dissertation, it is useful to first consider the specific characteristics of the samples examined in **Chapters 4, 5, and 6**. Across the three empirical studies, data were analyzed from a total of 202 adolescents and young adults aged 16-26 years, each with a retrospectively self-reported history of childhood adversity within the family environment. Specifically, **Chapters 4 and 5** drew on data from a sample of 102 British young people (M_{age} = 22.24, 64% female), while **Chapter 6** presents findings from a sample of 100 Dutch young people (M_{age} = 21.23, 79% female). Although both sample sizes provided sufficient statistical power for the conducted analyses, the relatively small sample sizes highlight a common limitation in research involving

vulnerable populations, where recruitment and retention pose significant challenges (Bornstein et al., 2013). Based on established cut-off scores for the Childhood Trauma Questionnaire (Bernstein et al., 1994), both the British and Dutch sample can be characterized reporting low to moderate levels of childhood adversity. Additionally, both samples self-reported on average high level of perceived friendship support, indicating particularly well-functioning groups of vulnerable young people. Data collection for both samples took place remotely and in-person, which could have unwillingly led to the exclusion of individuals who were unable to access the internet to complete parts of the study.

On the one hand, some findings were consistently observed across the two independent samples of young people with childhood adversity, revealing broader patterns in line with previous research. First, young people who experienced more severe childhood adversity were at heightened risk of diminished access to or maintenance of supportive friendships (**Chapters 5, 6)**. In **Chapter 5**, the REACT study analyzed longitudinal data and demonstrated patterns of social thinning following the COVID-19 outbreak. This finding aligns with the stress sensitization hypothesis (Hammen, 2015; Hammen et al., 2000), which suggests that individuals with a history of childhood adversity are more sensitive to later stressors. As shown by Wade et al. (2019), this stress sensitization can affect externalizing behavior, thereby impairing social functioning. In **Chapter 6**, the THRIVE study analyzed cross-sectional data and found a moderate negative association between childhood adversity and friendship support. This finding aligns with prior cross-sectional studies reporting lower friendship support in young people with more severe childhood adversity (McLafferty et al., 2018; Nevard et al., 2021; Salzinger et al., 1993).

Second, vulnerable young people with higher levels of perceived friendship support reported improved psychosocial functioning (**Chapters 4, 5, 6**). In **Chapter 4**, the RAISE study analyzed cross-sectional data and found a moderate positive association between friendship quality and psychosocial functioning. Furthermore, **Chapter 5**, which prospectively examined the same sample of vulnerable young people, found that higher friendship quality also predicted reduced internalizing symptoms, particularly anxiety and depressive symptoms, during the COVID-19 pandemic. Similarly, in **Chapter 6**, greater friendship support was moderately associated with fewer depressive symptoms. These robust friendship buffering findings replicate previous cross-sectional and longitudinal research highlighting the critical role of social support, especially friendship support, in promoting mental health and well-being in young people with childhood adversity (Fritz, de Graaff, et al., 2018; Lagdon et al., 2021; Salazar et al., 2011; van Harmelen et al., 2016, 2021).

Third, vulnerable young people with greater friendship support reported lower levels of perceived stress (**Chapters 5, 6**). In **Chapter 5**, pre-pandemic friendship quality longitudinally buffered anxiety and depressive symptoms through reducing perceived stress during the COVID-19 pandemic. In **Chapter 6**, greater friendship support was cross-sectionally associated with lower levels of perceived stress, which, in turn, were linked to fewer depressive symptoms. Critically, these findings align with and extend the social stress buffering literature (Gunnar, 2017; Gunnar & Hostinar, 2015), emphasizing the pivotal role of friendship support in mitigating stress responses in vulnerable young people (C.-Y. S. Lee & Goldstein, 2016; Shahar et al., 2009) and, thereby, reducing psychopathology risk (Achterberg et al., 2021; Gotlib et al., 2020).

On the other hand, some findings appeared more specific to individual studies. First, despite robust evidence linking childhood adversity to various forms of youth psychopathology (Clark et al., 2010; Francis et al., 2023; Kessler et al., 2010; McLaughlin, 2016), this association was not observed in one of the two samples investigated (**Chapters 4, 5**). Specifically, the British sample analyzed in **Chapters 4 and 5** showed no association between childhood adversity and psychopathology, either cross-sectionally or longitudinally. The absence of such a relationship may reflect a relatively well-functioning sample of young people who reported only low to moderate levels of childhood adversity and, on average, high levels of perceived friendship quality.

Second, it remains unclear whether friendship support buffers neural stress responses in young people with childhood adversity (**Chapters 3, 4**). As highlighted in the systematic review presented in **Chapter 3**, only two studies have previously investigated the stress buffering role of friendship support at the neurobiological level in this population. Tang et al. (2021) found that low levels of friendship quality were associated with blunted sympathetic nervous system reactivity to social rejection feedback at age 12, linking early institutionalization experiences with greater peer problems at age 16. In contrast, Fritz, Stretton, et al. (2020) found that friendship support at ages 14 or 17 was not associated with neural responses to social rejection feedback at age 18 in a sample of young people with childhood adversity. Similarly, **Chapter 4**, does not provide conclusive evidence of whether friendship support buffers frontolimbic responses to experimentally induced acute psychosocial stress. Although high-quality friendships were associated with reduced left hippocampal reactivity to acute stress in young people with threat experiences, this interaction effect did not survive correction for multiple comparisons. While this uncorrected, dimension-specific finding aligns with previous research linking childhood adversity, particularly threat exposure, to structural and functional alterations in the hippocampus, which are known risk factors for later-life psychopathology (Y. Chen et al., 2008; Cohodes et al., 2021; McLaughlin et al., 2014), future research

in needed to replicate and extend these findings in larger, ideally longitudinal samples.

Third, although not a primary focus of **Chapter 6**, young people with more severe childhood adversity did not report higher levels of perceived stress. On average, this Dutch sample reported low to moderate levels of perceived stress in the four weeks prior to assessment, suggesting the presence of protective factors, such as friendship support. However, it is possible that in the absence of such protective factors, more severe childhood adversity, or exposure to acute stress (e.g., a global pandemic), vulnerable young people may report higher levels of perceived stress, as demonstrated in previous studies (Bourassa et al., 2023; Gotlib et al., 2020; McLaughlin, Conron, et al., 2010).

Friendships Matter

Friendships play a vital role in the lives of young people, particularly when it comes to mitigating psychopathology risk following childhood adversity (**all Chapters**). Simultaneously, critical knowledge gaps remain in the understanding of stress-related mechanisms that underpin these protective effects (**Chapter 3**), insights that are essential for the development of targeted prevention and intervention strategies.

Chapters 4, 5, and 6 provide robust empirical evidence affirming *that* friendships matter by demonstrating consistent positive associations between friendship support and mental health in young people with childhood adversity. While prior research had already established this link (A. S. Masten et al., 2003; Powers et al., 2009; van Harmelen et al., 2016, 2021), replicating this powerful insight in two independent, hard-to-recruit samples of young people with childhood adversity holds considerable value. It emphasizes that investing time in the formation and maintenance of friendships can help mitigate the disproportionately high risk of experiencing mental health problems faced by those with a history of childhood adversity. This is particularly relevant for individuals with multiple adversities, who, as noted in **Chapter 1**, are 3.7 times more likely to develop anxiety and 4.7 times more likely to experience depression (K. Hughes et al., 2017). Reducing the prevalence of adversity-related mental health conditions could also alleviate the broader societal and economic burdens these issues impose (Bellis et al., 2019), benefitting not only vulnerable individuals but also society at large.

To optimally support young people with childhood adversity, who are known to be at greater risk for social thinning (**Chapters 5, 6**; McCrory et al. (2019), (2022)), future research should focus on identifying behaviors that promote the initiation and maintenance of supportive friendships (Oswald et al., 2004). Additionally, it is essential to explore how these skills can be safely harnessed in

an increasingly digital world, where vulnerable youth face serious risks, such as exposure to cyberbullying or the normalization of self-harm behavior (Daine et al., 2013).

Chapter 5 provides rare longitudinal insights into *how* friendships matter by identifying a psychological pathway through which friendships provide stress-buffering mental health benefits for young people with childhood adversity. Specifically, this prospective longitudinal study demonstrated that pre-pandemic levels of perceived friendship quality mitigated anxiety and depressive symptoms during the COVID-19 pandemic through reducing levels of perceived stress. Although **Chapter 6**, based on cross-sectional data, could not examine such a longitudinal friendship stress buffering pathway, it nonetheless confirmed the buffering role of friendships, showing that higher perceived friendship quality was associated with lower levels of perceived stress and fewer depressive symptoms.

These results integrate well with prior research highlighting the relationship between elevated levels of subjectively appraised stress (i.e., perceived stress) and greater physiological stress responses, including heightened circulating levels of pro-inflammatory biomarkers (e.g., interleukin-6 (IL-6) or C-reactive protein (CRP)) (Knight et al., 2021), accelerated biological aging (Bourassa et al., 2023; Epel et al., 2004), along with poor physical and mental health outcomes that accompany these allostatic states (Christensen et al., 2019; Guidi et al., 2021; McEwen, 2005). In the context of childhood adversity, persistent and severe exposure to and perception of stress is believed to disrupt neuroendocrine and immune system regulation, contributing to the onset and maintenance of treatment-resistant psychopathology (Ioannidis et al., 2020; G. Miller et al., 2009; Mondelli et al., 2015). For example, a prospective longitudinal study demonstrated that early exposure to adverse experiences (prior to age 8) predicted elevated levels of IL-6 and CRP at age 10 as well as increased levels of CRP at age 15 (Slopen et al., 2013). Furthermore, structural equation modeling by Knight et al. (2021) demonstrated that perceived stress was associated with flattened diurnal cortisol slopes (indicating HPA axis dysregulation), which, in turn, were associated with heightened systemic inflammation in U.S. adults with traumatic life experiences. Prolonged systemic inflammatory responses have been linked to glucocorticoid resistance, diminishing the anti-inflammatory effects of glucocorticoids and further elevating levels of peripheral pro-inflammatory biomarkers (Barnes, 1998; Barnes & Adcock, 2009). Through permeating the vascular blood-brain barrier, pro-inflammatory biomarkers are thought to exert disruptive effects on brain development and functioning, thereby increasing psychopathology risk (Danese & Baldwin, 2017; A. H. Miller & Raison, 2016).

Conversely, social relationships, including friendships, may help counteract or buffer these effects. Meta-analytic findings across 47 studies have shown that

social support and social integration were robustly associated with lower levels of inflammatory markers, such as IL-6 and CRP (Uchino et al., 2018). Furthermore, longitudinal research with breast cancer survivors revealed that lower perceived social support before treatment predicted higher IL-6 levels, greater pain, and more depressive symptoms post-treatment, compared to those with greater levels of perceived social support pre-treatment (S. Hughes et al., 2014). These findings illustrate the need for resilience research to adopt a complexity theory approach that captures the dynamic interplay between multiple psychological, social, and neurobiological systems over time, ideally through prospective longitudinal study designs (Ioannidis et al., 2020).

To advance the understanding of *how* and *why* friendships matter for young people with childhood adversity, future research should also address several conceptual limitations of the studies presented in this dissertation. First, each empirical chapter (**Chapters 4, 5, 6**) utilized a single friendship support index that measured the subjectively self-reported perception of support, leaving it unclear which specific aspects of friendship support are most critical for providing protective, stress-buffering benefits. Friendships typically involve characteristics like mutuality, reciprocity, trust, and a sense of obligation (Bukowski et al., 1998; Dunbar, 2018; Hartup & Stevens, 1997). Additionally, the principal of homophily suggests that social networks, including friendships, often form based on similarities across dimensions, such as age, gender, language, place of origin, educational history, hobbies and interests, sense of humor, and worldview (Dunbar, 2018; McPherson et al., 2001). Thus, the pathway towards mental health may vary depending on the characteristics or shared dimensions that define a friendship. For example, friendships based on a shared sense of humor are more likely to involve laughter, which has been shown to increase endorphin secretion, reduce endocrine release, lower levels of perceived stress, and activate brain regions associated with reward processing, such as the thalamus or caudate nucleus (Manninen et al., 2017; Mora-Ripoll, 2011; Yim, 2016). Consequently, by stimulating laughter, friendships may reduce psychological and neurobiological stress responses, thereby promoting mental health.

However, while similarity within friendships can bolster their protective effects, individuals with childhood adversity are at heightened risk of forming friendships that may be more harmful than beneficial to their mental health. For example, Raposa et al. (2015) conducted a prospective longitudinal study following individuals from birth to age 25 and found that those who experienced adversity by age 5 were more likely to have a best friend at age 20 who struggles with psychopathology. This, in turn, increasing their own risk of depressive symptoms over the subsequent two to five years. Hence, future research should carefully examine which specific qualities make friendships effective buffers and which aspects may render them risk factors for vulnerable youth.

Second, the research presented in this dissertation examined the buffering role of friendship support in isolation, without accounting for potential interrelations with other protective factors. The drawback of this approach becomes apparent when considering the findings by Fritz, Fried, et al. (2018), who applied network modeling to examine the interrelations between protective factors in 14-year-olds with and without childhood adversity. Their research revealed that expressive suppression (i.e., the ability to intentionally inhibit or suppress outward emotional expression) had a distinct relationship with friendship support across these groups. Specifically, low expressive suppression was associated with low friendship support in the childhood adversity group but with high friendship support in the group without childhood adversity. Regarding the group of young people with childhood adversity, this finding puts forward three possible interpretations, as outlined by the authors: (1) ineffective emotional communication leads to friendship withdrawal, (2) friendship withdrawal contributes to ineffective emotional communication, or (3) these two factors influence each other reciprocally over time (Fritz, Fried, et al., 2018). This suggests that protective factors can sometimes interfere with, rather than strengthen, one another. Future translational research employing advanced modeling techniques is needed to uncover such potentially dysfunctional interrelations. Identifying these dynamics could help make interventions more targeted and effective, for example, by teaching young people with childhood adversity appropriate emotional communication skills, which may, in turn, foster more supportive friendships.

Evolving Perspectives on Childhood Adversity

Childhood adversity is a common and powerful risk factor for negative health outcomes in later life, including internalizing and externalizing psychopathology (Grummitt et al., 2021; Madigan et al., 2023). For example, as outlined in **Chapter 1**, young people with childhood adversity are three to four times more likely to develop internalizing psychopathology, such as anxiety or depression, compared to their peers without such experiences (K. Hughes et al., 2017). Relatedly, **Chapter 2** highlights that the children of parents who experienced child maltreatment are two to three times more likely to experience maltreatment themselves, compared to those with non-maltreated parents (Madigan et al., 2019). This intergenerational cycle of victimization may, in turn, contribute to the development of externalizing psychopathology, such as aggressive behavior (Richey et al., 2016), potentially through affecting a range of psychological, cognitive, and neural stress-related pathways critical for adaptive social functioning (Alink et al., 2019).

To adequately predict individualized health risks associated with childhood adversity, identify the mechanisms underlying these associations, and develop effective interventions to prevent or mitigate its detrimental consequences, it is

essential to rethink how childhood adversity is conceptualized, operationalized, and measured (Danese, 2020; Danese & Lewis, 2022). Conceptualization involves defining what constitutes childhood adversity, while operationalization translates these theory-based definitions into specific, measurable components. Measurement then employs reliable and valid tools to quantify childhood adversity based on the chosen operational framework.

As outlined in **Chapter 1** and central to all empirical studies presented in **Chapters 4, 5, and 6**, childhood adversity is *conceptualized* as the chronic or repeated exposure to stressful and potentially traumatic experiences during childhood or adolescence (before age 18) that represent a deviation from the "expectable" environment, such as abuse, neglect, bullying, or exposure to war (Cicchetti & Valentino, 2006; McLaughlin, 2016; Nelson & Gabard-Durnam, 2020). These often co-occurring experiences require young people to adapt their psychological, social, and neurobiological functioning, and the strategies they employ may increase the risk for later-life victimization and psychopathology (Brown et al., 2019; Clark et al., 2010; Danese & McEwen, 2012; Lupien et al., 2009; Widom et al., 2008).

Two predominant approaches to *operationalize* childhood adversity are the cumulative risk and dimensional models of adversity. The quantitative, cumulative risk approach aggregates the number of distinct adverse experiences into a single cumulative risk or adverse childhood experiences (ACEs) score (Evans et al., 2013; Felitti et al., 1998). This approach has gained wide acceptance in public policy and clinical practice due to its straightforward calculation, interpretability, and predictive power for group-level health outcomes (Lacey & Minnis, 2020). However, it has faced criticism for its limited accuracy in predicting individual health risks, variability in prediction accuracy based on the reporter, and its failure to account for critical features of adversity, such as type, severity, chronicity, and developmental timing (Baldwin et al., 2021; Choi et al., 2023; McLaughlin & Sheridan, 2016). These limitations are thought to hinder its ability to identify specific mechanistic risk pathways that could inform targeted intervention. Alternatively, the qualitative, dimensional approach aims to specify mechanistic pathways linking core dimensions of adversity (threat/harshness, deprivation, and unpredictability) to later-life health outcomes (Berman et al., 2022; McLaughlin et al., 2014, 2021). While this more sophisticated approach enables the assessment of how mechanistic pathways vary with features of exposure, including frequency and severity, challenges remain to be addressed regarding the conceptualization, operationalization, and measurement of these dimensions (Berman et al., 2022; McLaughlin et al., 2021).

Recognizing the value of both approaches (McLaughlin et al., 2021; K. E. Smith & Pollak, 2021), **Chapters 4 and 5** utilized these frameworks to assess friendship

buffering of neural and psychological stress responses in British young people with childhood adversity. To integrate both approaches, a principal component analysis was applied to a range of retrospectively self-reported childhood adversity measures (see Brieant et al. (2024) for an in-depth overview of leveraging multivariate approaches to operationalize childhood adversity). In line with dimensional models of adversity (McLaughlin & Sheridan, 2016), this dimensionality reduction technique identified two components resembling threat and deprivation experiences, which were subsequently used to compute dimensional scores. These scores were also combined into a cumulative childhood adversity index, weighted by their explained variance, with higher scores indicating more severe adversity.

One objective of **Chapter 4** was to investigate whether greater friendship quality was associated with reduced frontolimbic reactivity to acute stress. Results indicated that high-quality friendships were linked to reduced left hippocampal reactivity to acute stress in young people with childhood threat experiences. While this interaction effect did not survive correction for multiple comparisons, it underscores the value of assessing the severity of different adversity dimensions for specifying the neural mechanisms potentially underlying psychopathology risk (Cohodes et al., 2021; McLaughlin, Weissman, et al., 2019; Puetz et al., 2020). In **Chapter 5**, the focus shifted toward investigating the buffering effects of friendships on mental health symptoms before and during the COVID-19 pandemic. While no specific hypotheses were proposed regarding different dimensions of childhood adversity, uncorrected exploratory analyses – reported in the supplementary materials – revealed noteworthy findings. Cumulative childhood adversity and deprivation-specific, but not threat-specific, experiences were negatively associated with friendship quality, with more severe adversity linked to lower perceived friendship support. In contrast, threat-specific, but not cumulative or deprivation-specific, experiences were positively associated with anxiety and depressive symptoms, with more severe threat exposure linked to increased symptomatology. Together, these uncorrected findings highlight the value of integrating both cumulative and dimensional approaches when investigating health and developmental consequences following childhood adversity.

Little consensus exists regarding how to ideally *measure* childhood adversity, partly due to variation in measurement approaches across studies. For practical reasons, such as costs and time efficiency, most empirical research (incl. **Chapters 4, 5, 6**) relies on retrospective self-reports to capture individuals' subjective appraisals and memories of past experiences. Evidence from meta-analyses and cohort studies suggests that subjective, self-reported perceptions of childhood adversity are more strongly associated with psychopathology risk than objective, court-substantiated experiences (Danese & Widom, 2020; Francis et

al., 2023). Furthermore, meta-analytic findings from Baldwin et al. (2019) indicate that prospective and retrospective measures of childhood adversity identify largely distinct groups of individuals, each with differential risk pathways to psychopathology.

To address some of these challenges, researchers have recommended tools that differentiate between dimensions of environmental experiences, account for participants' developmental stage, and incorporate input from multiple reporters, both prospectively and retrospectively (Berman et al., 2022; E. S. Young et al., 2020). These research-oriented recommendations are particularly valuable for guiding novel data collection efforts and interpreting previously collected data. The empirical studies presented in this dissertation (**Chapters 4, 5, 6**) employed multiple measures of childhood adversity and psychosocial functioning, enabling a more accurate and reliable capture of the complexity and multidimensionality of these constructs.

A crucial next step is the development of robust and culturally sensitive tools to accurately identify vulnerable young people at greatest risk of psychopathology and, therefore, most in need of intervention (Danese, 2020). This would mark a critical advancement in screening practices, reduce barriers to care, and advance the identification of specific mechanistic risk pathways linking childhood adversity and psychopathology, alongside protective factors that buffer against psychopathology risk. A concrete example of how such a clinically useful tool could be operationalized is provided by S. J. Lewis et al. (2019), who utilized data from a population-representative UK cohort study of young people to investigate psychosocial and clinical risk factors for psychopathology following adversity exposure. One key, preliminary finding highlights the potential of leveraging these factors to robustly improve individualized risk stratification, representing an important step toward understanding and accounting for individual differences in response to adverse experiences.

Towards Generalizability and Cultural Sensitivity

Selecting robust, accurate, and reliable measures remains a scientific challenge and necessity to ensure that findings generalize to real-world experiences. Self-report measures are known to be susceptible to recall and social desirability biases (Fadnes et al., 2009; Jordan & Troth, 2020; Latkin et al., 2017), while standardized laboratory-based paradigms are often criticized for lacking ecological validity (S. S. Dickerson & Kemeny, 2004). The prospective longitudinal study presented in **Chapter 5** leveraged a real-world stressor (i.e., COVID-19 pandemic) to examine friendship stress buffering, providing unique insights into how young people with childhood adversity adapt during acute, real-life stress exposure. To build on these findings, future research could integrate experience sampling methodology (ESM) to assess friendship support and stress

responses both inside and outside the laboratory. For example, Vaessen et al. (2023) examined neural stress responses during the Montreal Imaging Stress Task (MIST) alongside daily-life stress and affect using ESM. Consistent with the findings presented in **Chapter 4**, the MIST elicited limbic reactivity, which was associated with higher overall daily stress ratings, supporting its ecological validity in assessing stress responses (Vaessen et al., 2023). Regarding friendship support, the perceived quality of support may not always align with the actual support received (Haber et al., 2007). While research suggests that perceived, rather than actual received, support is a stronger predictor of mental health outcomes (McDowell & Serovich, 2007), future research could benefit from assessing received support in real-life situations, taking into account the context and need for support (Melrose et al., 2015).

Large, longitudinal, publicly available data sets, such as the Adolescent Brain Cognitive Development (ABCD) Study (Casey et al., 2018) or the Environmental Risk (E-Risk) Longitudinal Twin Study (Fisher et al., 2015), offer powerful resources to replicate and expand the empirical findings presented in this dissertation at both the individual and group levels (Kievit et al., 2022). Specifically, these substantially larger samples increase statistical power, thereby expand analytical flexibility to investigate the complex interplay between different features of adverse experiences (Brieant et al., 2024), a range of stress-regulatory systems (Ungar et al., 2023), multiple protective factors (Fritz, Fried, et al., 2018), and the dimensional nature of psychopathology (Lahey et al., 2012; Parkes et al., 2021).

Furthermore, leveraging rich secondary data sets can substantially improve the capacity to systematically study cross-cultural effects and diverse demographics, allowing for more nuanced insights into the sociocultural and policy-driven lived experiences of young people (Nketia et al., 2021; Saragosa-Harris et al., 2022). Whether the empirical findings presented in this dissertation (**Chapters 4, 5, 6**) – derived from predominantly female, white, and well-educated samples of young people living in the UK and the Netherlands – can be generalized to populations with vastly different sociocultural and contextual characteristics remains an open question.

Increasingly, there have been calls for the adoption of culturally and contextually sensitive approaches to improve the replicability and generalizability of research on risk and resilience following trauma exposure (Fried et al., 2018; Ungar et al., 2023). This is particularly timely given the anticipated demographic shifts in the Global South and the diverse experiences of adversity they entail. For example, by 2050, over one-third of the world's young people aged 15 to 24 years are projected to live in Africa (United Nations Department of Economic and Social Affairs, Population Division, 2022; D. Walsh & Morales, 2023). Meanwhile, in 2024,

prevalence estimates in sub-Saharan Africa suggest that approximately 72% of females and 82% of males aged 18-24 years have experienced at least one form of childhood adversity (Amene et al., 2024), rates that are more than three times higher than the 22.6% average prevalence estimated across 28 European countries (K. Hughes et al., 2021). To address the global burden of adversity and ensure that interventions are equitable, effective, and globally relevant, future research must therefore prioritize understanding the protective factors and mechanisms underlying risk and resilience within diverse samples (Ghai, 2021).

Concluding Remarks

In a world where childhood adversity remains a pervasive public health emergency with profound and long-lasting health and developmental consequences, understanding and leveraging the protective power of friendships presents a promising pathway toward building resilience in vulnerable youth. This dissertation set out to investigate the stress-related mechanisms through which social support, particularly friendships, buffer against victimization and psychopathology risk in young people with childhood adversity. Across five chapters, insights are presented from literature reviews (**Chapters 2, 3**), cross-sectional analyses (**Chapters 4, 6**), and longitudinal analyses (**Chapter 5**), demonstrating that childhood adversity is a potent risk factor for social thinning, victimization, and both internalizing and externalizing psychopathology. Conversely, friendship support emerged as a critical protective factor capable of reducing perceived stress and subsequently lowering internalizing symptoms. To more effectively inform targeted, equitable, and sustainable preventative interventions for young people with childhood adversity, future interdisciplinary research should adopt a complexity theory approach, capturing the intricate and dynamic interplay between psychological, social, and neurobiological systems over time, ideally through large, prospective longitudinal studies with diverse samples.