Advancing our understanding of general psychopathology among young people: Optimising prevention targets and timing

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Abstract

Reconceptualising psychopathology in a hierarchical-dimensional framework has gained momentum in recent years. There is strong evidence for a single general psychopathology dimension that reflects the shared elements across mental and substance use disorders and captures their co-occurrence. Yet very little is known about what general psychopathology represents or whether it is a suitable intervention target. This thesis investigates the underlying structure, development, and prevention of general psychopathology among young people.

Chapter 2 is the first systematic review of empirically based models of psychopathology among young people aged 10-24 years. The review identified a wide range of risk factors associated with general psychopathology, as well as critical gaps and methodological shortcomings in existing research. Chapters 3-4 examine cross-sectional and longitudinal associations between psychopathology and four high-risk personality traits (anxiety sensitivity, negative thinking, impulsivity, and sensation seeking) highlighting the complex and dynamic interplay between personality and psychopathology. Chapter 5 explores the impact of a selective, personality targeted prevention program on general and specific dimensions of psychopathology providing some of the first evidence world-wide that growth in general psychopathology can be reduced through a brief, school-based intervention.

Together, these novel empirical studies make a highly significant contribution to our understanding of general psychopathology in adolescence and provide a critical foundation upon which prevention and intervention efforts can be personalised and optimised to reduce the considerable burden, harms and costs associated with mental and substance use disorders.

Thesis statement of originality

I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

This thesis has not been submitted for any other degree or purposes.

Samantha J. Lynch
23 February 2023

Author attribution statement

The work contained in the body of this thesis, except otherwise acknowledged, is the result of my own investigations.

I am the first and corresponding author of each publication, reflecting my substantial contribution to all aspects of these studies. Citations are provided on page xiii.

Chapter 2 is published in Clinical Psychology Review. All authors (SJL, MS, NN and CC) contributed to the design of the study which was conceived and led by SJL. SJL wrote the manuscript and CC, MS and NN provided advice, reviewed, and contributed to revisions of the manuscript. SJL conducted all searches. SJL screened 100% of the titles and abstracts, and CC, MS and NN screened 25%. SJL and MS reviewed 100% of the studies eligible for full text review. Quality assessments were completed by SJL (100%) and MS and CC (50%).

Chapter 3 is published in Development and Psychopathology. All authors (SJL, MS, MF, NN, MT and CC) contributed to the design of the study which was conceived and led by SJL. SJL designed and conducted all analyses and wrote the manuscript and CC, MS, MF, MT and NN provided advice, reviewed, and contributed to revisions of the manuscript.

Chapter 4 is under review with Journal of Psychopathology and Clinical Science (formerly Abnormal Psychology). All authors (SJL, MS, NN, MT and CC) contributed to the design of the study which was conceived and led by SJL. SJL designed and conducted all analyses and wrote the manuscript and CC, MS, MT and NN provided advice, reviewed, and contributed to revisions of the manuscript.

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Chapter 5 is under review with Journal of Consulting and Clinical Psychology. All authors (SJL, MS, NN, MT and CC) contributed to the design of the study which was conceived and led by SJL. SJL designed conducted all analyses and wrote the manuscript and CC, MS, MT and NN provided advice, reviewed, and contributed to revisions of the manuscript.

A description of my contribution to the studies from which data were analysed for this thesis is provided in Appendix A.

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As supervisors for the candidate upon which this thesis is based, we can confirm that the author attribution statement above is correct.

Cath Chapman   **Nicola C. Newton**   **Matthew Sunderland**

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For all the people who don't fit neatly into boxes.

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Publications associated with this thesis

Lynch, S. J., Sunderland, M., Newton, N. C., & Chapman, C. (2020). Transdiagnostic Risk and Protective Factors for Psychopathology in Young People: Systematic Review Protocol. *JMIR Research Protocols*, 9(8), e19779. https://doi.org/10.2196/19779

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Lynch, S. J., Sunderland, M., Forbes, M.K., Teesson, M., Newton, N. C.*, & Chapman, C.* (2023). Structure of psychopathology in adolescents and its association with high-risk personality traits. *Development and psychopathology*, 1–16. https://doi.org/10.1017/S0954579422001262

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Additional publications during candidature

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Chapter 1

General introduction

Mental and substance use disorders are common and have immense impacts on individuals, families, and communities. Overall, 50% of mental disorders emerge by age 14, and 75% emerge by age 25, making adolescence a critical period for the development, diagnosis and prevention of mental disorders (Kessler et al., 2005; Solmi et al., 2021). Once established, many mental disorders persist and result in significant disability, reductions in quality of life, and limit educational attainment and occupational opportunities (Fusar-Poli et al., 2021; McGorry et al., 2022; Patton et al., 2014; Plana-Ripoll et al., 2023). Globally, mental and substance use disorders are the leading cause of years lived with disability and, among young people, these disorders are the number one contributor to the total burden of disease (Costello et al., 2011; Erskine et al., 2015; Whiteford et al., 2015). Compared to the general population, young people with mental disorders have higher morbidity and mortality risk, resulting in a 10–20-year reduction in life expectancy (Chesney et al., 2014).

Approximately 10-20% of adolescents experience mental health problems, including anxiety, depressive and conduct related disorders (WHO, 2022). Worryingly, young people's mental health appears to be deteriorating around the world. According to epidemiological research in the USA, UK, Europe and Australia, young people are experiencing increases in anxiety, depression, suicide, and psychological distress (Keyes et al., 2019; Mojtabai et al., 2016; Slee et al., 2021; Twenge et al., 2018; Wiens et al., 2020). Moreover, this trend appears to have been exacerbated by the COVID-19 pandemic. For example, data from the United States of America indicated that the prevalence of anxiety and depressive disorders increased by 25% among young people (18-24 years) in the first year of the pandemic.

Mental and substance use disorders frequently co-occur, with epidemiological research consistently showing high rates of comorbidity among all mental disorders (Kessler, et al., 2011; Slade et al., 2015). Co-occurrence among mental and substance use disorder is especially common, with up to three-quarters of people with a substance use disorder likely to also have an anxiety, mood, or disruptive behaviour disorder (Kandel et al., 1999). Among young people, it is estimated that up to two-thirds of individuals with one mental disorder have at least one additional co-occurring disorder (Kessler et al., 2011; Leadbeater et al., 2012). Comorbidity increases the burden placed on individuals because it is associated with greater symptom severity and chronicity, as well as poorer treatment outcomes (Kessler et al., 2011).

The consequences of mental disorders extend far beyond the individual. Mental disorders account for 35% of the global economic burden, making them the largest contributor to gross domestic product (GDP) loss among non-communicable diseases, followed by cardiovascular disease (33%) and cancer (18%; Bloom et al., 2011). Bloom and colleagues (2011) estimated the global cost of mental disorders to be US$2.5 trillion in 2010 and expect this to rise to US$6 trillion by 2030 due to the early onset of psychopathology in young people and the long-term impact on productivity during adulthood.

Alarmingly, the mortality and morbidity associated with mental and substance use disorders has not decreased in over 30 years (GBD 2019 Mental Disorders Collaborators, 2022; Whiteford et al., 2015). Modelling has also revealed that treatment alone is insufficient to address the mental health burden, with improved access to and quality of treatment only able to alleviate 28% of the disease burden (Andrews et al., 2004). Given the limitations of existing treatments, reducing the impact of mental and substance use disorders requires significant investment in effective prevention and early intervention. However, progress has been slow thus far, with clinical research and practice hampered by the limitations of the prevailing approaches to classifying and conceptualising psychopathology.

1.1   Approaches to classifying and conceptualising psychopathology

1.1.1   Categorical approaches

Existing classification systems such as the Diagnostic and Statistical Manual of Mental Disorders (DSM; American Psychiatric Association, 2013) and the International Classification of Diseases

(ICD; World Health Organization, 2019) typically conceptualise psychopathology as distinct, categorical and dichotomous entities. In this framework, a disorder is usually determined to be either present or absent based on whether a certain number of diagnostic criteria are met. These systems describe a larger number of mental and substance use disorders, which have guided mental health research and provided the basis for assessment, prevention, and intervention efforts for decades. However, there are myriad limitations of existing categorical classification systems. First, research has consistently shown that psychopathology exists on a continuum that includes normal-range functioning (Carragher et al., 2015; Eaton et al., 2015; Markon, 2010; Markon et al., 2011). Dichotomous diagnoses can therefore lead to a loss of clinically relevant information, such as when an individual does not meet diagnostic criteria for any disorder despite experiencing significant impairment. Second, categorical diagnoses have demonstrated poor reliability (Markon et al., 2011), both over time (Bromet et al., 2011; Heslin et al., 2015; Shea et al., 2002) and between clinicians (Regier et al., 2013). Third, there is high heterogeneity within diagnoses such that there can be hundreds of different combinations of symptoms or ways to receive a given diagnosis (Allsopp et al., 2019; Clark et al., 1995; Hasler et al., 2004; Young et al., 2014; Zimmerman et al., 2015). For example, according to the DSM-V (American Psychiatric Association, 2013), a person only needs to meet five of nine criteria to be diagnosed with major depressive disorder, implying that there are 227 possible ways to receive this diagnosis (Fried & Nesse, 2015). This number rises to 16,400 when different symptom presentations within criteria are considered (e.g., increase vs. decrease in appetite). Individuals with the same diagnosis can therefore present with very different problems and have few overlapping symptoms, if any. Finally, the high rates of comorbidity described earlier suggest that some conditions have been unnecessarily and arbitrarily split into multiple diagnoses. Taken together, the empirical evidence to date indicates that a categorical conceptualisation of psychopathology does not adequately or accurately represent psychopathology. This has significant consequences for research and clinical practice.

The dimensional nature of psychopathology and high rates of comorbidity complicate research design, often leading to a loss of ecological validity (through case-control designs), insufficient power to detect associations or effects due to unaccounted similarities between conditions, and ultimately, hinder the discovery of modifiable intervention targets (Ofrat & Krueger, 2012). The limited validity, reliability, and apparent arbitrariness of categorical models of psychopathology potentially explains why we have yet to delineate a clear aetiology of mental disorders or see reductions in the associated burdens and harms. Overcoming these limitations stands to have a profound impact on people with mental health and substance use problems by providing a more

accurate representation of how people experience symptoms and conceptualise their own mental health. Similarly, advancements in the conceptualisation and classification of psychopathology would have greater clinical utility and lead to better prognostication, outcome monitoring and facilitate the development of efficient and effective interventions. The limitations of existing classification systems, and potential impacts of overcoming those limitations, have led to a surge of quantitative, structural research seeking to generate an empirically robust model of psychopathology.

1.1.2 Transdiagnostic approaches

Transdiagnostic approaches acknowledge that many disorders share common risk factors and correlates, have similar courses and outcomes, and respond to the same treatments (Barlow et al., 2014, 2017; Eaton et al., 2015; Stockings et al., 2016). In a transdiagnostic model of psychopathology, the overlap between disorders or covariation among symptom domains are captured by one or more latent dimensions. Early transdiagnostic research based on factor analytic studies of symptoms and behavioural issues in children identified two correlated dimensions: internalising and externalising (Achenbach, 1966; Achenbach & Edelbrock, 1978, 1984). Internalising latent dimensions are typically characterised by symptoms related to sadness, fear and anxiety and reflect covariation among anxiety and depressive disorders, as well as eating pathology and post-traumatic stress disorder. In contrast, externalising latent dimensions are usually characterised by symptoms relating to aggression and impulsivity, and reflect covariation among conduct, attention-deficit/hyperactivity disorder, and substance use problems. There is extensive empirical support for this two-correlated-factors model, with studies having demonstrated clinical utility and reliability across numerous populations, age groups and clinical and non-clinical samples (Blanco et al., 2015; Cosgrove et al., 2011; Kessler, Petukhova, et al., 2011; Krueger et al., 1998; Lahey et al., 2017; Olino et al., 2018; Slade & Watson, 2006). Furthermore, scores on internalising and externalising latent factors are better predictors of future psychopathology than discrete diagnoses (Kim & Eaton, 2015). Given the relatively poor reliability and stability of categorical psychopathology diagnoses (Markon et al., 2011), the predictive validity of latent dimensions of psychopathology is a significant improvement over traditional models of psychopathology.

Despite these improvements, the internalising-externalising model does not fully capture the breadth or depth of the complex relations among different forms of psychopathology. For example, certain disorders frequently co-occur with disorders across internalising and

externalising spectra (e.g., depression frequently co-occurs with both anxiety and substance use problems). This implies that there may be a broader, general dimension of psychopathology (Caspi et al., 2014; Lahey et al., 2012; Tackett et al., 2013). Indeed, internalising and externalising dimensions tend to be moderately correlated, roughly .50 according to meta-analytic estimates (Krueger & Markon, 2006). These examples of covariation and interrelation within and across latent dimensions suggests the need to identify a more comprehensive framework and investigate multiple levels of dysfunction.

1.1.3   Hierarchical-dimensional approaches

Hierarchical-dimensional approaches propose that the covariation among latent dimensions of psychopathology can be captured in or explained by broader, overarching dimensions. Thus, psychopathology is conceptualised in a hierarchical framework with latent dimensions further classified or grouped together according to the covariation between them. For example, internalising has often been found to split into two subordinate dimensions: distress and fear (Krueger & Markon, 2006). Similarly, there is evidence to suggest that externalising is comprised of substance use and conduct disorder dimensions (Castellanos-Ryan & Conrod, 2011). There is also considerable evidence that a variety of diagnoses, symptoms and symptom domains load onto a general psychopathology dimension, often referred to as the p factor[1] (Caspi et al., 2014; Caspi & Moffitt, 2018; Lahey et al., 2012, 2017; Tackett et al., 2013). The discovery of this general factor of psychopathology has sparked a huge and rapidly growing body of literature and prompted the recent shift towards hierarchical-dimensional approaches to conceptualising and studying psychopathology.

Support for hierarchical-dimensional models of psychopathology has been found in a variety of populations and study designs (Caspi et al., 2014; Laceulle, Vollebergh, & Ormel, 2015; Lahey et al., 2012; Murray, Eisner, & Ribeaud, 2016; Tackett, Lahey, et al., 2013) and evidence from this work has been synthesised into a comprehensive Hierarchical Taxonomy of Psychopathology (HiTOP) model. As shown in Figure 1.1 the HiTOP framework organises psychopathology into dimensions of increasing breadth and generality. At the foundation sit symptom components and maladaptive traits, which combine to form increasingly broader dimensions of psychopathology from syndromes, to subfactors, to spectra, to super-spectra and at the apex sits the p factor.

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[1] The term "general psychopathology" in this thesis is typically used instead of "p factor" as it is a more neutral and broader term that allows for alternative statistical instantiations and theoretical interpretations beyond specific models of psychopathology such as the bifactor model or the HiTOP framework.

Compared to DSM diagnoses, the dimensions in the HiTOP framework have been found to better account for neurobiological processes, functional improvement, patterns of heritability, effects of environmental risk factors, and differences in treatment response (Kotov et al., 2021). Furthermore, the hierarchical-dimensional framework resolves issues of comorbidity, poor reliability and heterogeneity associated with existing categorical diagnoses.

Figure 1.1 Hierarchical Taxonomy of Psychopathology (HiTOP) model
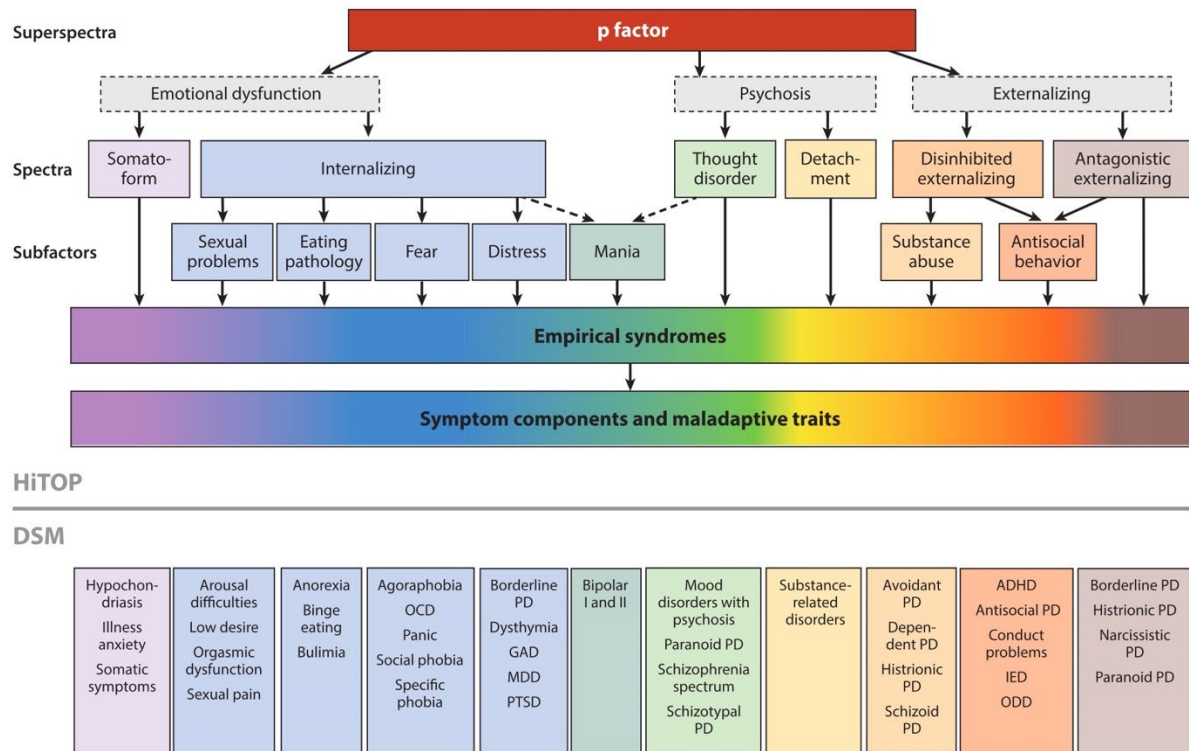
Note. DSM diagnoses are not included in the HiTOP model, but symptoms and signs that constitute them are in HiTOP. Dashed lines indicate dimensions included on a provisional basis. Emotional dysfunction, psychosis, and externalising superspectra are hypothesised but not formally part of HiTOP at present. Symptom components and maladaptive traits are listed in Kotov et al. (2017, figure 3). Abbreviations: ADHD, attention-deficit/hyperactivity disorder; DSM, Diagnostic and Statistical Manual of Mental Disorders; GAD, generalized anxiety disorder; HiTOP, Hierarchical Taxonomy of Psychopathology; IED, intermittent explosive disorder; MDD, major depressive disorder; OCD, obsessive–compulsive disorder; ODD, oppositional defiant disorder; PD, personality disorder; PTSD, posttraumatic stress disorder. Source: "The Hierarchical Taxonomy of Psychopathology (HiTOP): A Quantitative Nosology Based on Consensus of Evidence", Kotov et al., 2021, p. 87.

Despite the advantages of a hierarchical-dimensional approach, there are unresolved methodological issues that are important to acknowledge (Bonifay et al., 2017; Watts, Poore, & Waldman, 2019). Concerns have been raised about the most appropriate statistical model to best capture general psychopathology, with recent methodological research suggesting that the field may have prematurely drawn conclusions regarding the best model (Bonifay et al., 2017; Greene et al., 2019; Watts, Poore, & Waldman, 2019). Several recommendations have been proposed to address these concerns, including further consideration of alternative plausible structures (e.g., higher-order vs. bifactor models), and additional model reliability and replicability metrics to assist with adjudicating between structures (Forbes, Greene, et al., 2021; Rodriguez et al., 2016b). Resolving these issues is important as the interpretation of latent dimensions is informed by the underlying structure. For example, a general psychopathology factor derived from a bifactor model represents the shared variance across all indicators (e.g., symptoms), whereas a general psychopathology factor derived from a higher-order model represents the correlation among first-order factors (e.g., internalising and externalising). Previous research indicates that differences on statistical models can impact the strength and even direction of associations between latent factors and external criteria (Watts, Poore, & Waldman, 2019). Therefore, research seeking to better understand the meaning and utility of different dimensions of psychopathology must consider multiple models and adjudicate among them by using robust metrics of model fit, reliability and replicability.

Although much of the last decade research has been focused on delineating an empirical structure of psychopathology, there is now a need to address more substantive questions about what the different dimensions of psychopathology represent, and how this framework can be used to advance and optimise prevention and early intervention efforts. Hierarchical-dimensional models are a catalyst for a new era of research aiming to advance our understanding of risks and causal mechanisms; improve the accuracy and efficiency of assessment tools; and optimise prevention and early intervention efforts (Conway et al., 2019; Kotov et al., 2021; Ruggero et al., 2019). Such research will result in better screening and prognostic tools, refine intervention targets and lead to the development of new interventions, or optimisation of existing interventions, so that people can be matched with the most appropriate and effective intervention.

This thesis is primarily focused on understanding general psychopathology because of its potential as a preventive and early intervention target (Forbes et al., 2019). Implicit within hierarchical-dimensional models of psychopathology is the idea that all forms of psychopathology are connected via an underlying general dimension. However, it is not yet clear whether general

psychopathology represents meaningful psychological or biological processes. Identifying and understanding the factors that increase or decrease levels of general psychopathology holds potential to provide new avenues for reducing levels of general psychopathology, and accordingly prevent a wide range of mental disorders from developing. Chapter 2 provides a thorough review of the biological, psychological, and socioenvironmental factors associated with general psychopathology among young people. An important and formative finding from this review is the robust links between personality and broad dimensions of psychopathology.

1.2 Personality and psychopathology

There are structural and empirical parallels between personality and psychopathology (Brandes & Tackett, 2019; Tackett & Mullins-Sweatt, 2021; Widiger et al., 2019). For example, the Five Factor Model of personality describes broad personality dimensions (often referred to as the Big 5) in much the same way that psychopathology can be reflected in broad, hierarchically organised dimensions (Caspi et al., 2005; McCrae et al., 2016). The Big 5 personality factors are: conscientiousness, agreeableness, neuroticism, openness to experience, and extroversion. Conscientiousness is characterised by tendencies towards being organised, dependable and self-disciplined. Agreeableness reflects tendencies such as empathy, compassion, and cooperativeness. Neuroticism refers to a tendency towards experiencing negative affect (e.g., depression, anxiety, irritability, and anger). Openness is characterised by tendencies towards creativity, curiosity, and imagination. Finally, extroversion reflects qualities such as outgoingness, excitement seeking, assertiveness and positive energy. Each of these broad traits can be further broken down into narrower facets. For example, neuroticism is comprised of six facets: anxiety, depression, angry hostility, self-consciousness, impulsivity, and vulnerability. While there is considerable evidence demonstrating associations between each of the Big 5 traits and various life outcomes, including psychopathology, recent research suggests that facet level traits of the Big 5 domains have greater predictive power than the broad traits themselves (Revelle et al., 2021; Stewart et al., 2022; Wessels et al., 2021). Furthermore, there is evidence to suggest that personality and psychopathology may even fit together in a broader, comprehensive model of human thoughts, feelings and behaviours that range from normal to maladaptive. In considering how personality and psychopathology may be related within the context of hierarchical-dimensional models of psychopathology, and in the interest of leveraging such relations for optimising prevention and intervention efforts, one strong candidate is the four-factor model of vulnerability.

The four-factor model of vulnerability integrates prior research linking aspects of neuroticism and closely related inhibited and disinhibited personality traits to harmful substance use and comorbid psychopathology via distinct cognitive and motivational pathways (Castellanos-Ryan et al., 2016; Castellanos-Ryan & Conrod, 2012). The four traits are negative thinking (sometimes referred to as 'hopelessness'), anxiety sensitivity, impulsivity and sensation seeking. Negative thinking reflects a tendency to experience hopelessness and low positive affect. Anxiety sensitivity is the fear of anxiety-related sensations due to beliefs that such sensations could lead to harmful consequences. Impulsivity reflects a failure to inhibit behaviours that are likely to have negative consequences. Finally, sensation seeking reflects a willingness to take risks for the sake of novel experiences. Negative thinking, anxiety sensitivity and impulsivity all arguably represent nuanced features of broader neuroticism[2], whereas sensation seeking is more closely related to extroversion.

Each of the four traits are associated with higher levels of, and increased risk for, multiple forms of psychopathology, including substance use problems as well as other common mental disorders. Negative thinking and anxiety sensitivity are associated with mood and anxiety-related problems, as well as increased substance use problems (to manage or relieve symptoms of anxiety and depression). Impulsivity is associated with emotional and behavioural regulation issues, conduct-related problems, and greater risk for substance misuse due to enhancement, coping, and conformity motives. In contrast, individuals with greater levels of sensation seeking are more likely to develop substance use problems as a result of their increased susceptibility to the rewarding properties of alcohol and other substances. Sensation seeking appears to be more directly associated with substance use problems than to other externalising behaviours (Castellanos-Ryan & Conrod, 2011).

Prior research on the four-factor model of vulnerability and hierarchical-dimensional model of psychopathology has revealed patterns of association with transdiagnostic dimensions that are theoretically aligned (though there are some exceptions). For instance, negative thinking and anxiety sensitivity appear to be prospectively and concurrently associated with greater

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[2] Although the four-factor model considers impulsivity to be a disinhibited personality trait it is important to acknowledge that there are alternative conceptualisations. Notably, the Big 5 model of personality considers impulsivity to be a facet of neuroticism (which is conceptually more aligned with inhibited personality traits). Considering the existing empirical research on hierarchical-dimensional models of psychopathology has tended to focus on Big 5 traits, and that previous research has reported that negative thinking, anxiety sensitivity and impulsivity are correlated with neuroticism (r = 0.50, 0.23 and 0.41, respectively), it seems reasonable to consider that these three traits represent distinct aspects of neuroticism (Castellanos-Ryan et al., 2013). Accordingly, this conceptualisation is used in the current thesis.

internalising and general psychopathology (Carragher et al., 2016; Castellanos-Ryan et al., 2016) and either unrelated or inversely related to externalising (although one study reported a positive association between negative thinking and externalising, internalising symptoms were not included in the model [e.g., Castellanos-Ryan & Conrod, 2011]). Similarly, impulsivity and sensation seeking appear to be more closely associated with externalising-related dimensions, with impulsivity being more closely associated with conduct or general externalising and sensation seeking being more closely aligned with substance use and related harms. Additionally, one study found a negative correlation between sensation seeking and negative thinking (Carragher et al., 2016). Exploration of unique associations with subfactors of internalising and externalising, or even individual symptoms, may help to clarify some of the contradictory findings of previous research. Furthermore, as three of the traits arguably represent unique aspects of neuroticism, the four-factor model of vulnerability provides an important opportunity for advancing knowledge of the links between narrower aspects of personality and psychopathology.

1.3 Thesis aims and overview

Overall, this thesis aims to investigate the structure of psychopathology among adolescents and shed light on the development of general psychopathology, its interaction with vulnerable or high-risk personality traits, and its utility as a preventive intervention target. This thesis contains four studies designed to address five main research questions:

1. What is the underlying structure of psychopathology in young people?
2. What are the risk and protective factors for general and specific dimensions of psychopathology in young people?
3. How are high-risk personality traits associated with different levels of a hierarchical-dimensional model of psychopathology?
4. How do high-risk personality traits and general psychopathology influence each other during adolescence?
5. What impacts does a personality-targeted prevention program have on trajectories of general and specific dimensions of psychopathology?

The literature reviewed above provides the background for this thesis and highlights the opportunities for enhancing the effectiveness of prevention efforts by advancing our understanding of general psychopathology among adolescents. The following chapters address critical gaps in existing knowledge and apply sophisticated data analytic techniques to better

understand the underlying structure of psychopathology in adolescents.

Chapter 2 is the first systematic review of transdiagnostic risk and protective factors for general and specific dimensions of psychopathology among young people aged 10 to 24 years. A total of 41 studies were included in the review.

Chapters 3 and 4 present a novel and rigorous exploration of the underlying structure of psychopathology among a large adolescent sample, focusing on concurrent (Chapter 3) and prospective (Chapter 4) associations with four high-risk personality traits (anxiety sensitivity, negative thinking, impulsivity, and sensation seeking). These studies use data from two large randomised controlled trials (RCTs) of Australian adolescents (N = 8,654).

Chapter 3 evaluates different structural models of psychopathology (correlated factors, bifactor and higher-order models) among 8,654 adolescents (mean age 13 years) and examines associations with high-risk personality traits across multiple levels of a hierarchical-dimensional model of psychopathology. The best performing model identified in this chapter is then used in subsequent chapters.

Chapter 4 examines the co-development of general psychopathology and high-risk personality traits over three years (aged 13 to 16 years) among adolescents in the control conditions (N= 2,083). Latent curve models with structured residuals are used to identify prospective and reciprocal associations within individuals.

Chapter 5 presents the first study to examine the impact of *Preventure*, a selective, personality targeted prevention program, on the development of general and specific dimensions of psychopathology among adolescents over three years. Data from the Climate and Preventure RCT (N=2,190) were analysed using within-level Bayesian plausible values and mixed effects models accounting for school-level clustering. In addition to examining main intervention effects, additional exploratory analyses investigating effects within each high-risk personality group, and across high and low risk students are presented.

Finally, Chapter 6 synthesises findings from the previous chapters and discusses their theoretical and clinical implications.

Chapters 2 and 3 have undergone peer review and have been published in high-impact

international journals, and Chapters 4 and 5 are currently under review. These chapters are direct replications of the published or submitted manuscripts and have only been modified from the published versions to minimise duplication of definitions of key terms and background information, ensure consistency of referencing style, abbreviations, spelling, and numbering of figures, tables, and appendices.

Systematic Review of Transdiagnostic Risk and protective factors for general and specific dimensions of psychopathology

Preface

As outlined in Chapter 1, the last decade has seen a large body of research emerge investigating empirical models of psychopathology. These models account for comorbidity among mental disorders and facilitate the identification of risk and protective factors that are common across disorders (from those that are unique to certain disorders or symptom domains). This chapter presents findings from the first systematic review of the literature to identify common structures of psychopathology and transdiagnostic risk and protective factors for general and specific dimensions of psychopathology among young people (10-24 years).

This chapter addresses the first and second research question of this thesis: What is the underlying structure of psychopathology in young people? and What are the risk and protective factors for general and specific dimensions of psychopathology in young people?

This study was published as:

Lynch, S. J., Sunderland, M., Newton, N. C., & Chapman, C. (2021). A systematic review of transdiagnostic risk and protective factors for general and specific psychopathology in young people. *Clinical Psychology Review, 87, 102036.*

Figure 2.1 Screenshot of "A Systematic review of transdiagnostic risk and protective factors for general and specific psychopathology in young people" by Lynch et al. (2021) published in Clinical Psychology Review

Supplementary data and materials are available online, and a description has been included in Appendix E.

2.1 Abstract

A large body of research has emerged over the last decade examining empirical models of general and specific psychopathology, which take into account comorbidity among psychiatric disorders and enable investigation of risk and protective factors that are common across disorders. This systematic review presents findings from studies of empirical models of psychopathology and transdiagnostic risk and protective factors for psychopathology among young people (10 – 24 years). PsycInfo, Medline and EMBASE were searched from inception to November 2020, and 41 studies were identified that examined at least one risk or protective factor in relation to broad, empirically derived, psychopathology outcomes. Results revealed several biological (executive functioning deficits, earlier pubertal timing, genetic risk for ADHD and schizophrenia, reduced grey matter volume), socio-environmental (stressful life events, maternal depression) and psychological (low effortful control, high neuroticism, negative affectivity) transdiagnostic risk factors for broad psychopathology outcomes, including general psychopathology, internalising, and externalising. Methodological complexities are discussed and recommendations for future studies of empirical models of psychopathology are presented. These results contribute to a growing body of support for transdiagnostic approaches to prevention and intervention for psychiatric disorders and highlight several promising avenues for future research.

2.2 Introduction

Mental and substance use disorders often emerge between the ages of 13 and 24 years and are among the leading causes of burden of disease worldwide (Costello et al., 2011a; Kessler et al., 2011; Whiteford et al., 2013). It is estimated that up to two-thirds of young people who have one mental or substance use disorder, have at least one additional comorbid disorder (Kessler et al., 2011; Leadbeater et al., 2012). Comorbidity is associated with greater symptom severity and chronicity, and poorer treatment outcomes (Kessler et al., 2011). Comorbidity between mental disorders can undermine the validity of discrete diagnostic classifications and hinder or complicate aetiological research. Research that fails to account for additional disorders may demonstrate support for putative risk and protective factors of a given disorder that are in fact due to the compounding nature of psychopathology rather than a specific, direct association (Dalgleish et al., 2020). Thus, relying on case-control research designs that exclude cases with multiple diagnoses leads to a loss of ecological validity and may not reflect actual clinical populations where comorbidity is common (Ofrat & Krueger, 2012). Furthermore, focusing on specific disorders alone may result in a loss of power to detect associations between risk and protective factors and psychopathology due to unaccounted similarities between interrelated conditions. In light of the challenges and limitations associated with discrete diagnostic entities, alternative approaches for conceptualising psychopathology have emerged to better understand and study the nature of psychiatric comorbidity (Eaton, 2015). The resulting empirically based models of psychopathology provide an important framework for investigating, identifying, and delineating specific versus transdiagnostic risk and protective factors.

2.2.1 *Empirical models of psychopathology*

Empirical models of psychopathology apply statistical techniques, such as latent variable (e.g., factor analysis and latent class analysis) or network approaches, to generate coherent structures of interrelated psychiatric conditions and symptoms, rather than relying on clinical consensus to form discrete diagnoses from traditional classification systems. As a result, newer empirical models accommodate psychiatric comorbidity which in turn enhances ecological validity (Carragher et al., 2015; Ofrat & Krueger, 2012). Two fundamental conceptualisations of psychopathology and comorbidity have emerged from two alternative statistical approaches.

Latent variable approaches conceptualise psychopathology as a hierarchical-dimensional structure comprised of a few, broad transdiagnostic dimensions (Kotov et al., 2017). For example, early comorbidity research among children and adolescents revealed the presence of two higher-order groupings: internalising and externalising (Achenbach, 1966). Internalising captures comorbidity among mood and anxiety disorders, whereas externalising reflects comorbidity among substance use, antisocial, oppositional and impulse related disorders. There is also consistent evidence that internalising and externalising are positively correlated, and there is mounting support for a higher-order, general factor of psychopathology (Caspi et al., 2014; Kotov et al., 2017).The general factor of psychopathology (sometimes referred to as 'p-factor' or 'p') may reflect a shared vulnerability to mental disorders (Kotov et al., 2017). More specifically, dispositional negative emotionality, impulsive responsivity to emotion, low cognitive functioning and thought dysfunction are all leading interpretations of what the general factor of psychopathology may reflect (Smith et al., 2020). However, it has also been suggested the general factor of psychopathology may reflect an index of overall impairment.

A variety of statistical methods have been used in studies of latent variable structures of psychopathology, however there are three particularly common statistical models: the correlated factor, higher-order and bifactor models (Forbes, Greene, et al., 2021). Although, these three models are closely related, each offer a different substantive interpretation of the structure of psychopathology. For example, a bifactor model's general psychopathology directly reflects the shared variance among all indicators, whereas a higher-order model's general factor reflects the shared variance among first-order factors, such as internalising and externalising. Further in correlated factors and higher-order models, the narrow latent variables reflect shared variance among a set of indicators, whereas specific factors in a bifactor model are uncorrelated and reflect the variance unique to a factor (after the shared variance among indicators has been attributed to the general factor). The differences between statistical models presents a challenge when interpreting evidence relating to key constructs derived from different methods. For example, the strength and direction of the relationship between latent variables and external criteria has sometimes differed as a function of the statistical model used (Watts, Poore, & Waldman, 2019).

Network modelling approaches however propose that disorders are comprised of networks of causally related symptoms, and comorbidity is the result of some symptoms causing symptoms in other disorder networks resulting in a broad network of associations among disorders (Borsboom, 2017; Eaton, 2015). Transdiagnostic groupings identified through latent variable modelling and found in hierarchical-dimensional models, such as internalising and externalising, have also been

replicated in network models (Boschloo et al., 2016; McElroy et al., 2018). Both hierarchical (latent variable) dimensional and network models accommodate comorbidity (network models through the analysis of associations among pairs of symptoms and latent variable models through the analysis of shared and unique variance among symptoms and/or diagnoses) among mental disorders and facilitate the investigation of transdiagnostic (vs. disorder-specific) risk and protective factors that is not achievable with traditional classification systems (Forbes et al., 2019; Fried et al., 2017; Krueger & Markon, 2011).

2.2.2   *Transdiagnostic risk and protective factors*

Previous research on risk and protective factors for mental disorders among young people has heavily relied on studies focussing on associations with single disorders. Some previous reviews have defined transdiagnostic risk/protective factors as factors associated with four or more disorders (Harvey et al., 2004). However, as described above, relying on studies of specific disorders has lower ecological validity and may also have less power to detect associations (Ofrat & Krueger, 2012). Transdiagnostic psychopathology constructs, such as internalising, externalising, and general psychopathology factors offer an alternative approach. While three previous systematic reviews have examined risk and protective factors in relation to internalising and externalising dimensions among children and adolescents, to our knowledge, no previous systematic reviews have synthesised evidence from studies of other broadband dimensions or constructs such as thought disorder or general psychopathology (Crews et al., 2007; McMahon et al., 2003). Furthermore, these reviews have tended to focus on narrow risk factor groups, particularly trauma and stress. Crews and colleagues (2007) conducted a systematic review of meta-analyses looking at child, family, school, community and cultural factors correlated with either internalising behaviours, externalising behaviours, or both. The review reported that six risk factors and three protective factors were common to both internalising and externalising, however it is unclear from the review whether internalising and externalising were examined simultaneously in the studies included. As such, it is not possible to conclude whether the identified risk and protective factors were transdiagnostic across internalising and externalising disorders. McMahon and colleagues (2003) conducted a systematic review of studies examining the relationship between several domains of stressors and internalising and externalising psychopathology in children and adolescents. The review reported that most stressors, such as exposure to violence, poverty and parental divorce were transdiagnostic across internalising and externalising. A more recent systematic review and meta-analysis also found that stressful life events during adolescence increase risk for both internalising and externalising (March-Llanes et

al., 2017). However, it is unclear from these reviews whether the transdiagnostic nature of stressors holds across other domains of psychopathology, such as thought disorders, or whether these specific associations remain when multiple transdiagnostic psychopathology groupings are examined simultaneously. Additionally, while stressors may increase risk across disorders and are useful for identifying young people at risk of developing mental disorders, a broader synthesis is needed to identify modifiable factors (e.g., coping skills, emotion processing and regulation, maladaptive thinking styles and beliefs) that can be targeted through intervention (Forbes et al., 2019).

The advent of empirical models in recent decades has generated a sizeable body of literature on factors associated with transdiagnostic constructs in young people, particularly in relation to the internalising and externalising dimensions and more recently general psychopathology. However, to date, no systematic review has brought together the findings from this body of research. The present review addresses this gap via the synthesis and critical evaluation of studies with empirically based models of psychopathology to identify transdiagnostic risk and protective factors for psychopathology among young people. Insights drawn from this review may provide a foundation upon which interventions can be developed to reduce or prevent mental health problems earlier in life, and thus disrupt the cascade of psychopathology sequelae into adulthood.

2.3 Methods

2.3.1 *Search strategy and selection criteria*

This systematic review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement (Moher et al., 2015). The protocol was registered with PROSPERO (CRD42020161368) and was previously published (Lynch, Sunderland, Newton, & Chapman, 2020). Medline, EMBASE and PsycINFO databases were searched systematically for studies published from inception to November 2020 that examined empirically based models of psychopathology in young people and at least one potential transdiagnostic risk or protective factor. Search strings for each database can be found in the online supplementary material (Appendix A).

An initial search in December 2019 yielded a total of 2,676 studies, and 2,016 remained after removing duplicates. Searches were re-run in November 2020 (and limited to publication between 2019 to 'current'). A further 839 studies were returned, and 393 remained after deduplication.

Search results were imported into Covidence for screening (Veritas Health Innovation, 2020). After removal of duplicates, all titles and abstracts were screened by one reviewer (SJL). The other reviewers (CC, NCN, MS) screened 25% of the titles and abstracts, which were randomly selected. Full-text articles were screened by SJL and MS. Disagreements at each stage of screening were resolved through discussion between the two screening authors or by a third reviewer.

2.3.2   Inclusion and exclusion criteria

The eligibility criteria were developed using the Population Exposure Comparator Outcome (PECO) framework. Empirical studies were included if they met the following criteria:

1. Participants mean age was between 10 and 24 years, in accordance with the World Health Organisation definition of 'young person' (World Health Organization, 2014).

2. Examined any risk/protective factor variable, such as genetic, neurobiological, cognitive, social and environmental characteristics, and their association with an empirically based model of psychopathology.

3. Studies were not required to have a comparison group as the dimensional nature of psychopathology implicit within contemporary knowledge precludes the need for control groups.

4. Psychopathology outcomes derived from empirically based models of at least two broad groups of signs or symptoms, such as internalising, externalising, or thought disorder.

5. Written in English.

6. Peer-reviewed.

Articles were excluded if they did not report peer-reviewed, original empirical findings, such as reviews, opinion pieces and conferences abstracts.

2.3.3   Quality assessment

Study quality was assessed independently by two reviewers using checklists from the Joanna Briggs Institute (Moola et al., 2019). Cross-sectional studies were evaluated using the Checklist for Analytical Cross-Sectional Studies, and longitudinal studies were evaluated using the Checklist for Cohort Studies (Moola et al., 2019). Uncertainty around interpretation of items on either checklist or application to studies included in the review was resolved through discussion between authors. In order to compare the quality of studies, a percentage score was calculated using the method described by Hoppen & Chalder (2018). That is, the number of items rated

'yes' were summed and then divided by the number of maximum possible number of 'yes' ratings (and multiplied by 100). The maximum possible score was the total number of applicable items only as not all items were applicable to each study.

2.4 Results

2.4.1 Selection of studies

After screening titles and abstracts, 160 studies remained for inclusion, of which 119 were excluded following full-text review (see Figure 2.2). Inter-rater reliability was moderate for title and abstract screening (92% agreement; Cohen's κ = 0.60) and full-text screening (82% agreement; Cohen's κ = 0.59).

2.4.2 Characteristics of studies

A summary of the included studies is shown in Table 2.1. Of the 41 included studies, 26 were cross-sectional and 15 were longitudinal, and 54% were published in the last two years (n=22). The vast majority of studies were from the United States of America (USA), the remaining studies were from Australia, Europe (Romania, Sweden, Netherlands and Italy), the United Kingdom (UK) and South Korea.

Figure 2.2 PRISMA flow diagram depicting study selection process
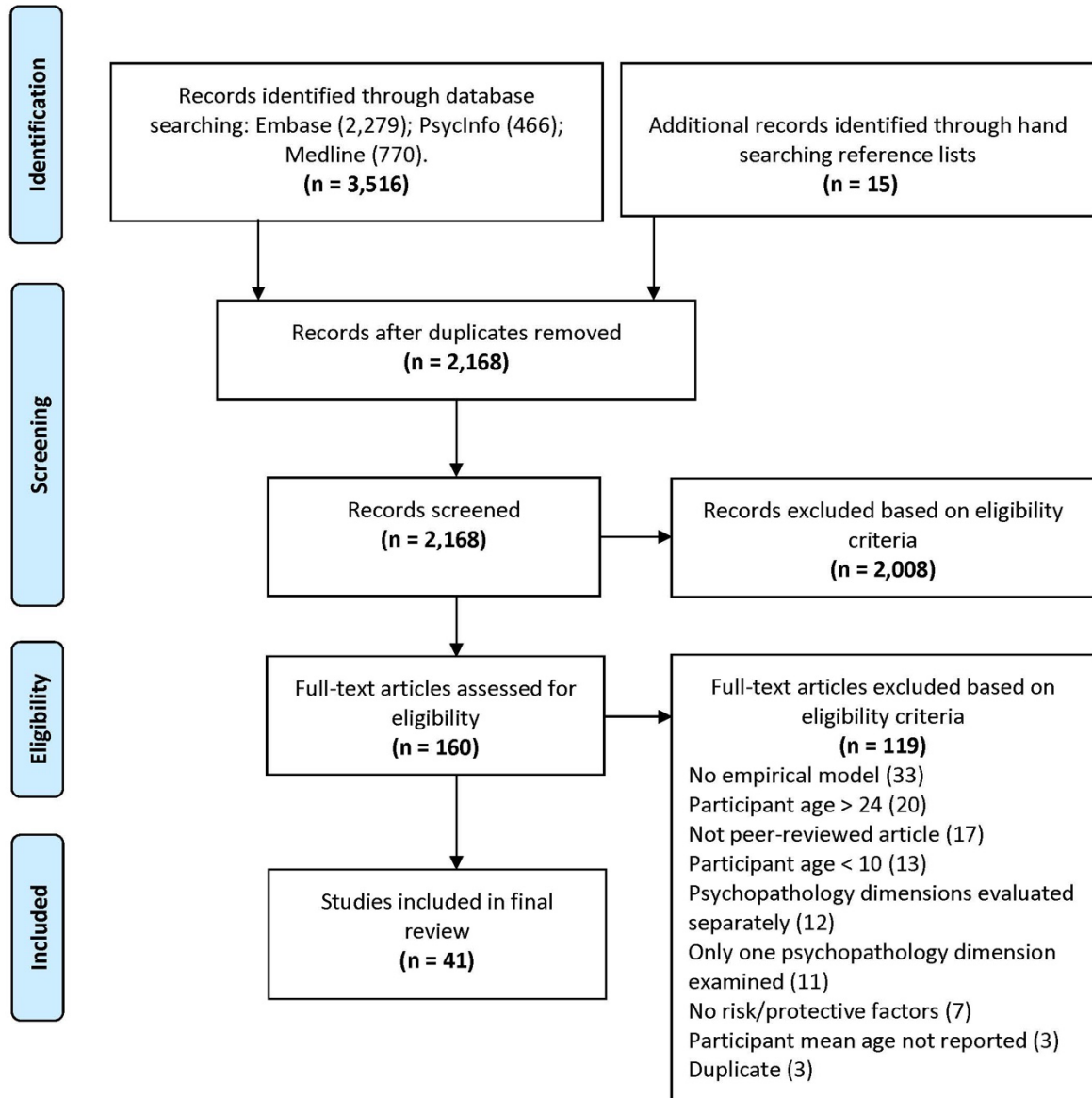
2.4.3 Overall quality

The overall quality of included studies was high with a mean rating of 90% across all studies. Cross-sectional studies demonstrated slightly higher quality with an average score of 93%, compared to 84% for longitudinal studies (See online supplementary material Appendix B and C for details). Lower quality ratings were largely due to studies not identifying confounding factors, and/or not stating strategies for dealing with confounds. Many longitudinal studies did not report follow up details, such as completion rate or reasons for loss to follow up, however generally strategies for addressing incomplete follow up were described in these studies. Agreement between independent raters was high (84%). Fleiss' kappa ($\kappa = 0.71$) indicated moderate agreement between raters, based on two raters with three response categories (Yes, No and Unclear).

2.4.4 Models of psychopathology

In total, 50 structural models of psychopathology from 41 studies were examined in the papers. A summary of the models is presented in Table 2.2, and more detailed information is provided in the online supplementary material (Appendix D). As shown in Table 2.2, latent variable models were the most common. The most commonly used method was a bifactor model (n=25, including one modified bifactor model), followed by confirmatory factor analysis (n=8). None of the included studies examined a network model of psychopathology. In terms of transdiagnostic psychopathology groupings, a 3-group model comprised of general psychopathology, internalising and externalising was the most common structure examined in the included studies. Five studies examined relationships with a general psychopathology latent variable only, and six studies focussed on internalising and externalising latent variables only. Over 60 different measures of psychopathology were used across the included studies, of which only 16 were used in more than one study. The two most common measures were the Youth Self Report and the Child Behavior Checklist (Achenbach & Rescorla, 2001).

2.4.5 Risk and protective factors

Of the 41 included studies, 31 analysed biological (average Quality Score (QS) = 90%), 15 analysed socio-environmental (average QS = 93%) and 19 analysed psychological (average QS = 91%) risk/protective factors. Included studies examined more than 130 unique risk and protective

factors. Transdiagnostic risk and protective factors supported by evidence from two or more studies (or where two or more studies found no association) are summarised in Table 2.3, and a visual summary is presented in Figure 2.3. A longer summary of findings from the included studies can be found in the online supplementary material (Appendix E), and detailed information about the findings, including effect sizes where available, can be found in Appendix F. What follows is a summary of findings relating to variables examined in more than one study, and notable trends within some sub-domains.

2.4.5.1 Biological risk and protective factors

Only birth weight, executive functioning, genetic variance, non-shared environment, genetic risk for schizophrenia and ADHD, and sex/gender were examined in more than one study (see online supplementary material Appendix E). Evidence from biological studies indicated that earlier pubertal timing, executive functioning deficits, connectivity between regions in the default mode network, heteromodal frontoparietal network, visual association cortex and somatosensory network, less cerebellar grey matter, reduced white matter integrity of the pontine pathways and lower rates myeline maturation in dorsal cingulum and uncinate fasciculus were associated with increased general psychopathology. The two studies that examined birth weight reported mixed findings. One study found that lower birth weight was associated with higher general psychopathology, while the other found no significant associations between general psychopathology, internalising, or externalising. Executive functioning deficits and early pubertal timing were also associated with greater levels of internalising and externalising. Regarding functional connectivity involving the dorsal anterior cingulate cortex (dACC) there were conflicting results. One study reported no significant associations with general psychopathology and resting-state functional connectivity of dACC and amygdala and with amygdala–medial frontal connectivity (van Hoof et al., 2019). In contrast, Kaczkurkin and colleagues (2018) found that general psychopathology was associated with reduced connectivity between dACC and bilateral caudate, right thalamus, supramarginal gyrus and right putamen, and increased connectivity between dACC and dorso-medial frontal cortex.

Findings from genetic studies indicated that variance in general psychopathology, internalising, externalising, thought disorder, and depression and anxiety related latent variables were in part explained by genetic influences, and non-shared environmental influences were unique to specific disorder dimensions. Additive genetic influences (i.e., heritable genetic factors) on negative emotionality and daring were positively associated with general psychopathology, while additive

genetic influences on prosociality were negatively associated with general psychopathology. Additive genetic influences on prosociality and daring were also related to externalising, such that prosociality reduced and daring increased externalising scores. There was also evidence that earlier onset of menarche was associated with greater externalising, distress, and fear.

Regarding sex/gender, it was typically reported that males/boys were higher on general psychopathology and externalising, whereas females/girls were higher on internalising, however three studies found no significant associations with sex/gender. Furthermore, there were some inconsistencies among the significant findings. For example, Hamlat and colleagues (2019) reported that girls were higher on both externalising and internalising, and boys were higher on general psychopathology in a bifactor model, whereas in a correlated factors model using the same sample there were no gender differences for externalising. These results differ from other studies reporting on bifactor models, which found that males/boys were higher on externalising (Carragher et al., 2016; Wade et al., 2018).

2.4.5.2 *Socio-environmental risk and protective factors*

As shown in Table 2.3, *stressful life events* were positively associated with general psychopathology and externalising in two studies, one of which found that the association was moderated by *collective efficacy*, which is a measure of environment reflecting a neighbourhood broadly characterised by social cohesion, shared values among neighbours and a willingness to improve safety and order (Liu et al., 2017; Snyder et al., 2019). A similar trend emerged in the remaining childhood trauma and stress factors, such that most were typically related to general psychopathology and externalising (see online supplementary material Appendix E). Only *childhood abuse and neglect* was associated with internalising and externalising, however this study did not examine general psychopathology (Wilson et al., 2015). Interestingly, *exposure to violence* was associated with externalising, but not internalising or general psychopathology (Liu et al., 2017).

Family and home environment factors were also reported to increase transdiagnostic risk for psychopathology in young people. *Institutional rearing* was examined in one sample across two studies, which reported that history of institutional rearing predicted greater levels of general psychopathology at ages 12 and 16, and greater levels of externalising at age 12 (Wade et al., 2018, 2019). Children who remained institutionalised demonstrated sustained high levels of general psychopathology from ages 8 to 16 years, whereas children who were placed in foster care

demonstrated significant declines in externalising and modest declines in general psychopathology.

Paternal substance use disorder increased the likelihood of being in an internalising vulnerability latent class (Olino et al., 2019), and *family tobacco environment* was associated with increased general psychopathology (T. M. Jones et al., 2019). S*ibling substance use* increased the likelihood of being in multiple classes (comorbid Alcohol Use Disorder-Anxiety Disorder-Major Depressive Disorder (AUD-ANX-MDD), Alcohol Use Disorder only (AUD), comorbid Substance Use Disorder-Conduct Disorder class (SUD-CD)), such that different classes were associated with different substances used by siblings (McCutcheon et al., 2013), for example sibling alcohol problems were associated with an increased likelihood of being in the AUD-ANX-MDD class, whereas sibling marijuana or other drug use was associated with increased likelihood of being in the AUD class.

In general, *parental psychopathology* increased likelihood of being placed in a poor mental health class, though one study found no relationship with general psychopathology (Deutz et al., 2020; Jones et al., 2019; McCutcheon et al., 2013; Olino et al., 2019). *Paternal history of Major Depressive Disorder (MDD)* was associated with increased risk for internalising and externalising (Olino et al., 2019), and *maternal history of MDD* was associated with increased general psychopathology and internalising, and increased likelihood of being placed in an AUD-MDD-ANX class (Deutz et al., 2020; Jones et al., 2019; McCutcheon et al., 2013; Olino et al., 2019).

Three socio-environmental protective factors were identified, however only two of these were found to act transdiagnostically. *Parental warmth* was associated with reduced risk for moderate to high mental health difficulty trajectories (Vella et al., 2019). In contrast, *positive family environment* was negatively associated with an anxiety indicator but was not associated with general psychopathology. *Collective efficacy*, acted as a protective factor for general psychopathology and externalising among African-American young people living in economically disadvantaged areas (Liu et al., 2017). The study also reported that *collective efficacy* moderated the effects of *stressful life events* and *racial discrimination* on general psychopathology and externalising.

Lifestyle and peer and friendship problems also appeared to increase risk transdiagnostically. Findings from a growth mixture model revealed that *sociability* was associated with a reduced likelihood of being placed in a poorer mental health trajectory (Vella et al., 2019). *Adolescent social involvement* was reported to moderate the relationship between childhood behavioural

inhibition and young adult anxiety. *Delinquent / anti-social peer behaviour* was associated with internalising and externalising like latent factors longitudinally (T. M. Jones et al., 2019; Lee & Bukowski, 2012). However only one study examined a general factor variable and did not find evidence for an association between general psychopathology and *delinquent peers. Poor sleep, risky sexual behaviour* (multiple sexual partners and not using condom at least once) and *academic performance* were all related to general psychopathology (or comorbid psychopathology like classes). While controlling for general psychopathology, *poor sleep and academic problems* were also associated with increased levels of internalising, and *risky sexual behaviours* was associated increased levels of externalising (Sunderland et al., 2020). *Substance use* was associated with increased levels of internalising and externalising (Silveira et al., 2019).

2.4.5.3 Psychological risk and protective factors

Personality and temperament factors were the most widely studied psychological variables, many of which were found to be associated with general and specific factors of psychopathology across multiple studies and methods of modelling psychopathology, as shown in Table 2.3. Levin-Aspenson and colleagues (2019) examined *neuroticism, extroversion* and *openness* among two sub samples of the National Comorbidity Survey in the United States in relation to a bass-ackwards derived model of psychopathology. Among adolescents (15-19 years) and young adults (20-29 years), *extroversion* was negatively correlated with general psychopathology, internalising, fear and distress components. The relationship was strongest at lower levels of the hierarchical model (i.e., internalising and fear), compared to higher levels (i.e., general psychopathology). *Neuroticism* was positively correlated with all psychopathology dimensions (general psychopathology, internalising, externalising, fear and distress factors and thought disorder). Associations with *neuroticism* were strongest with a general psychopathology factor compared to other dimensions, and stronger for internalising (vs. externalising) among both samples. Similar cross-sectional results were reported by Mann and colleagues (2020), who also found that increases in *neuroticism* were associated with increases in general psychopathology, externalising and an Attention Deficit Hyperactivity Disorder (ADHD) specific factor, but not internalising. Furthermore, increases in *extroversion* were associated with increases in general psychopathology and externalising overtime. It was also found that *conscientiousness* and *agreeableness* were related to initial levels of general psychopathology and specific factors, but not changes in psychopathology over time. No association was found between *openness* and psychopathology among either sample.

Additional temperament factors were also found to be related to broad psychopathology outcomes. *High negative affectivity* was related to higher levels of general psychopathology in three studies (using both bifactor and latent class analysis), and internalising in one study (Deutz et al., 2020; Hankin et al., 2017; Wang et al., 2020). *High behavioural inhibition* in early childhood was positively associated with internalising in two studies (Frenkel et al., 2015; Wang et al., 2020). *High rumination* was positively associated with general psychopathology and internalising in two studies (Schweizer et al., 2020; Snyder et al., 2019). However, as shown in Table 2.4, one study reported a negative association with externalising (ß = -0.47), while the other reported a positive association (ß = 0.42). *Low effortful control* was associated with higher general psychopathology across three studies, and externalising across four studies, however only two studies reported significant associations with internalising (one using a bifactor model, and the other a correlated factors model), however inspection of effects sizes revealed that this association was weaker in longitudinal studies (see Table 2.4; Deutz et al., 2020; Hankin et al., 2017; Shields et al., 2019).

Four studies (average QS = 95%) reported mixed findings for associations between *attachment style* and general psychopathology. Two of these studies found no significant association between general psychopathology, internalising or externalising and attachment style (Deutz et al., 2020; van Hoof et al., 2019), while another study found that *lower levels of attachment* were associated with high levels of internalising at age 10 (Lee & Bukowski, 2012). A fourth study found that *attachment style* moderated the relationship between gambling and internalising and externalising (Terrone et al., 2018).

2.4.5.4 Longitudinal vs. cross-sectional studies

Findings from longitudinal studies identified several important risk factors for general psychopathology. A summary of effect sizes for replicated findings grouped by design and type of effect size is provided Table 2.4. High behavioural inhibition, high negative affectivity and executive functioning deficits were reported to be predictive of (or longitudinally associated with) general psychopathology (Deutz et al., 2020; Frenkel et al., 2015; Hatoum et al., 2018; Jones et al., 2019; Wade et al., 2019; Wang et al., 2020). Cross-sectional studies examining genetic, biological or historical influences found that genetic risk for ADHD and schizophrenia, stressful life events and earlier pubertal timing were also associated with increased general psychopathology (Brikell et al., 2020; Hamlat et al., 2019; Jones et al., 2018; Liu et al., 2017; Platt et al., 2017; Riglin et al., 2020; Snyder et al., 2019).

There was also evidence for risk factors for internalising and externalising psychopathology supported by longitudinal studies and cross-sectional studies where biological or historical influences were examined. Behavioural inhibition was found to have a stronger, more consistent association with internalising than externalising (Frenkel et al., 2015; T. M. Jones et al., 2019; Wang et al., 2020). High negative affectivity was reported to be uniquely associated with internalising and consistently not associated with externalising (Deutz et al., 2020; Hankin et al., 2017; Wang et al., 2020). Stressful life-events were found to have a small to non-significant association with internalising, and small to medium association with externalising (Liu et al., 2017; Snyder et al., 2019). Pubertal timing associated with both internalising and externalising (Hamlat et al., 2019; Platt et al., 2017).

Comparison of effect sizes reported by longitudinal and cross-sectional studies generally revealed effects to be weaker longitudinally (i.e., generally small to medium effect size) than cross-sectionally. For example, high negative affectivity was found to have a small or not significant longitudinal association (ß = 0.07) and large cross-sectional association with internalising (ß = 0.81). Similarly, effortful control was associated with greater levels of general psychopathology and externalising in one longitudinal study (Deutz et al., 2020) and two cross-sectional studies (Hankin et al., 2017; Shields et al., 2019). An association with internalising was only found cross-sectionally, and in one instance the association was non-significant. As shown in Table 2.4, the effect sizes were larger in the cross-sectional studies.

Table 2.1 Characteristics of included studies

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Brikell et al., 2020)	Sweden	C	6,603 A-TAC sub-sample, 6,854 SCARED sub-sample (9 or 12 years, 50% male)	Genetic risk for ADHD, sex/gender	PRS for ADHD using GWAS summary statistics	A-TAC, SMFQ, SCARED	SR	<u>Correlated factors A-TAC:</u> IA, H/I, ASD, LD, ODD, CD, DEP, ANX <u>Correlated factors SCARED:</u> IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP <u>Bifactor A-TAC:</u> general psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, ANX <u>Bifactor SCARED:</u> general psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP	86%
(Buzzell et al., 2020)	Romania	L	124 (40 institutionalised, 40 foster care, 44 never institutionalised; assessed at 12 and 16 years; 45% male	Cognitive control, mediofrontal theta oscillations	Go/No-Go task, EEG	MHBQ	PR, TR	<u>Bifactor:</u> general psychopathology, internalising, externalising	60%
(Carragher et al., 2016)	Australia	C	2,175 (mean age = 13.3 years, 57.4% male)	Sex/gender, anxiety sensitivity, impulsivity, negative thinking sensation seeking	SURPS	SDQ, BSI, RAPI, Hallucinatory experiences	SR	<u>Modified bifactor (correlated factors):</u> general psychopathology, internalising, externalising and thought disorder	71%
(Deutz et al., 2020)	USA	L	1,073 (assessed at age 14; 51.2% male)	Birth weight, attachment, temperament, cognitive ability, EF, self-control, positive maternal caregiving, harsh control, maternal depression, home environment	Refer to Deutz 2020 for measurement details	CBCL, YSR	SR, PR	<u>Bifactor:</u> general psychopathology, internalising, externalising	100%
(Elliott, Romer, Knodt, & Hariri, 2018b)	USA	C	605 (university students, mean age = 20.23, 44% male)	Connectome wide intrinsic functional connectivity	fMRI	e-MINI, SCID-I	SR	<u>Bifactor:</u> general psychopathology	100%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Frenkel et al., 2015)	USA	L	116 (18-21 years, 43.7% male,	Adolescent social involvement LCA: 1. high social involvement and large network size 2. low social involvement and small network size Childhood BI (assessed 14 months through 7 years) latent class analysis: 1. Stable High BI 2. Stable Low BI	H-SAS, NRI POS, TBAQ, CCTI-SS	SCID-I, ASR, LSAS	SR	<u>LCA</u>: healthy, internalising (primarily anxiety), externalising (primarily substance use)	90%
(Hamlat et al., 2019)	USA	C	567 (9-17 years, mean age = 13.58 years, 44.5% male)	Pubertal timing	PDS	CDI, MASC, CBCL, YSR, EATQ-R, SNAP-IV	SR, PR	<u>Bifactor</u>: general psychopathology, internalising, externalising <u>CFA (correlated factors)</u>: internalising, externalising	100%
(Hankin et al., 2017)	USA	C	571 youth parent pairs (youth age 9.3-17.5 years, mean age = 13.58, 45% male)	Effortful control, negative affectivity, positive affectivity	EATQ-R; PANAS-C	CDI, MASC, CBCL, YSR, EATQ-R, SNAP-IV	SR, PR	general psychopathology, internalising, externalising	71%
(Harden et al., 2019)	USA	C	1,913 twins and multiples (7.8-20.1 years, mean age = 13.1 years; 51% male, 35% MZ, 65% DZ; 1,007 pairs)	Overall EF, visuospatial reasoning, verbal ability, general intelligence, genetic correlation, non-Shared environment correlation	WASI-II, Zygosity classified using LCA of twins', parents', and research assistants' ratings of physical similarity and ease of being mistaken for one another, Animal Strong, Stop Signal and Mickey tasks, Trail Making, Local-Global and Plus-Minus tasks, Digit Span Backward, Symmetry Span and Listening Recall	CBCL, CPRS, BFI-N	SR, PR	<u>Bifactor</u>: general psychopathology, internalising, externalising, attention problems	100%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
					tasks, 2-Back, Keeping Tack and Running Memory for Letters tasks				
(Hatoum et al., 2018)	USA	L	885 same sex twins (16.5-20.1 years, mean age 17.3 years, 49% male)	Common EF, updating specific, shifting specific	Computerised executive functioning task battery (9 tasks)	CBCL, TRF	PR, TR	Parallel process LGM: internalising, externalising	60%
(Jones et al., 2018)	Australia	C	2,863 (mean age = 16.5 years)	Genetic risk for neuroticism and schizophrenia	PRS for schizophrenia, MDD, neuroticism and bipolar disorder using GWAS summary statistics	PLIKS-Q, CAPE, MFQ, DAWBA	SR	Bifactor: general psychopathology, anxiety, psychotic experiences, depression, negative (symptoms of psychosis) factors CFA (correlated factors): anxiety, psychotic experiences, depression, negative (symptoms of psychosis) factors	86%
(Jones et al., 2019)	USA	L	765 (13-14 years, 51% male, recruited through schools)	Family history of psychopathology, family tobacco environment, positive family environment, peer antisocial behaviour, peer substance use, behavioural disinhibition	Refer to Jones 2019 for measurement details	TRF, past month alcohol, cigarette & marijuana use	SR, PR, TR	CFA (one factor): general psychopathology	75%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Jung, Lee, Park, & Hong, 2019)	South Korea	C	913 (high school students in South Korea)	Sex/gender, Peer conflict, academic problems, family conflict, violence, number of school counsellors, number of counselling sessions in school, number of counselling sessions out-of-school, school dropout rate, number of students per teacher, counselling rate, percent of population aged 15-19, suicide rate for teenagers aged 15-19, availability of mental health services, ratio of public assistance recipients, social welfare facilities, percentage of education budget to total budget, percentage of welfare budget to total budget	AMPQ-II, school and community characteristics obtained from government information services	AMPQ-II	SR	<u>Multilevel LPA:</u> group 1 – high scores on all mental health domains, group 2 – high scores on internalising/emotional domains, low scores on externalising/behavioural domains, group 3 – low scores on all mental health domains	75%
(Kaczkurkin et al., 2018)	USA	C	1042 (11-23 years, mean age =16.12 years; 45% males)	Functional connectivity of the dorsal ACC and regions associated with general psychopathology, cerebral blood flow	fMRI, arterial spin labeled (ASL) MRI	GOASSESS	SR, PR	<u>Bifactor:</u> general psychopathology, anxious-misery, psychosis, behavioral (externalizing), fear	100%
(Kaczkurkin et al., 2019)	USA	C	1,394 (mean age = 14.98, 48% male)	Gray matter volume, cortical thickness	fMRI	GOASSESS	SR, PR	<u>Bifactor:</u> general psychopathology, anxious-misery, psychosis, behavioral (externalizing), fear	100%
(Lahey, Van Hulle, Singh, Waldman, & Rathouz, 2011)	USA	C	1571 twin pairs (9-17 years)	Genetic variance, non-shared environment	Biometric modelling	CAPS	SR, PR	<u>Bifactor:</u> general psychopathology, internalising, externalising	100%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Lee & Bukowski, 2012)	South Korea	L	2,844 (10-13 years, 54% male)	Sex/gender, level of attachment, parental knowledge of whereabouts, delinquent peers, externalising (initial level), internalising (initial level), parental violence	Refer to Lee 2012 for measurement details	YSR, JHDS, SDQ + others	SR	<u>Parallel process LGM</u>: internalising, Externalising	90%
(Levin-Aspenson, Khoo, & Kotelnikova, 2019)	USA	C	1,798 (20-29 years old, young adult sub-sample); 806 (15-19 years old, adolescent sub-sample)	Extroversion, neuroticism, openness	GL-NEO-S	UMCIDI	SR	<u>Bass-ackwards young adults</u>: general psychopathology, internalising, externalising, fear, distress and thought disorder <u>Bass-ackwards adolescents</u>: general psychopathology, internalising, externalising, fear and distress	71%
(Liu et al., 2017)	USA	C	592 (13-19 years, mean age = 15.9 years, 49% male, 100% African American, raised in high-poverty neighbourhood)	Exposure to violence, racial discrimination, stressful life events, collective efficacy	EVI-Q, SRE, TSI, TCES	YSR	SR	<u>Bifactor</u>: general psychopathology, internalising, externalising	100%
(Mann, Atherton, DeYoung, Krueger, & Robins, 2020)	USA	L	646 (50% female, Mexican origin, assessed annually from age 12 to 17 years)	Agreeableness, neuroticism, openness/intellect, extroversion, conscientiousness	TIPI	DISC-IV	SR	<u>Parallel process LGM</u>: general psychopathology, internalising, externalising, ADHD	90%
(McCutcheon et al., 2013)	USA	C	831 (offspring of male-male twin pairs who served in the military during the Vietnam era, mean age = 22.7 years, 51.5% male)	Sex/gender, genetic x environment risk, childhood physical/sexual abuse, mother inconsistent with rules, maternal depression, sibling substance use	Refer to McCutcheon 2013 for measurement details	SSAGA	SR	<u>LCA</u>: AUD, AUD-ANX-MDD & SUD-CD classes	100%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Olino et al., 2019)	USA	L	567 (14-18 years at wave 1, mean age = 16.6 years, excluded participants with lifetime history of psychosis or bipolar spectrum disorders, and adolescents with a history of MDD and/or dysthymia)	Sex/gender, parental education, paternal history of MDD, paternal SUD, early/childhood psychopathology	Refer to Olino 2019 for measurement details	K-SADS, LIFE, SCID-I	SR	LCA: thriving functioning, average functioning, externalising vulnerability and family stress, internalising vulnerability	100%
(Platt et al., 2017)	USA	C	4,925 (13-17 years, 100% female)	Onset of menarche	Self-reported age at first period	CIDI-A	SR	EFA (correlated factors): Distress, fear, externalising and eating pathology	100%
(Riglin et al., 2020)	UK	L	5,518 (assessed at birth, age 7/8 and 13 years)	Genetic risk for schizophrenia, ADHD, autism spectrum disorder and depression	PRS from weighted mean number of disorder risk alleles in approximate linkage equilibrium	DAWBA	PR	Bifactor: general psychopathology, emotional problems, behavioural problems, neurodevelopmental problems	50%
(Romer et al., 2018)	USA	C	1246 (mean age = 19.69, 42% male)	White matter integrity of pontine pathways, cerebellar gray matter volume	fMRI	e-MINI, MASQ-SD, STAI-T, CESD, SRP-SF, SRD, AUDIT, RDUS	SR	Bifactor: general psychopathology	100%
(Schweizer et al., 2020)	USA	C	571 youth parent pairs (youth age 9.3-17.5 years, mean age = 13.58, 45% male)	Common cognitive risk, self-criticism, rumination (brooding), dysfunctional attitudes, negative inferential style, and dependency	CDAS, ACSQ, CRSQ-RS, CDEQ	CDI, MASC, CBCL, YSR, EATQ-R, SNAP-IV	SR, PR	Bifactor: general psychopathology, internalising, externalising	100%
(Shanmugan et al., 2016)	USA	C	1,129 (mean age = 15.5 years, 46% male)	Executive system activation	fMRI, T1, and B0 images, fractal version of n-back task	GOASSESS	SR, PR	Bifactor: general psychopathology, anxious-misery, psychosis, behavioral (externalizing), fear	100%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Shields et al., 2019)	USA	C	895 (aged 8 – 18 years, mean age = 11.54, 48% male)	Effortful control, EF	EATQ-R, TMCQ, digit span forward, digit span backward, Go/No-Go, Trail-Making Test Part B, Iowa Gambling Task or Hungry Donkey	CBCL, C-DISC	PR	Bifactor: general psychopathology, internalising, externalising CFA (correlated factors): internalising, externalising	100%
(Silveira et al., 2019)	USA	C	6,127 (aged 15-17 years)	Tobacco, alcohol and drug use	Past 12-month tobacco, alcohol and drug use, refer to Silveira 2019 for details	GAIN-SS	SR	LCA (entered as covariates): internalising, externalising	86%
(Snyder et al., 2019)	USA	C	292 (13-22 years, mean age = 16.2 years, 44% male)	Common EF, stressful life events, rumination	ALEQ-R, CRSQ-RS, Anti-cascade, Stroop, Stop Signal, Keep Track, Letter Memory, Spatial 2-back, Category Switch, Color-Shape, Letter-Number	CDI, PSWQ-C, MASC, CBCL, YSR, SDQ, SNAP-IV	SR	Bifactor: general psychopathology, internalising, externalising	86%
(Sunderland et al., 2020)	Australia	C	2,002 (aged 14-17 years, mean age = 15.5 years, 51.4% male)	Suicide attempt, suicidal ideation, self-harm, self-esteem, poor sleep (weekend/weeknight), multiple sexual partners, condom use	self-reports of health and behavioural factors, ASQ	DISC-IV, substance use items, psychotic-like experiences items	SR	CFA (higher order): general psychopathology, internalising, externalising and psychotic-like experiences	100%
(Tackett et al., 2013)	USA	C	1,569 twin pairs (ages 9-17; monozygotic twin pairs (n = 316 female pairs; n = 283 male pairs), same-sex dizygotic twin pairs (n = 256 female pairs; n = 258 male pairs), and opposite-sex dizygotic twin pairs (n = 456 pairs))	Genetic influences, disposition (negative emotionality, prosociality (empathy and remorse), and daring (sensation seeking and risk taking))	Biometric modelling, CADS	CAPS	SR, PR	Bifactor: general psychopathology, internalising, externalising	100%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Terrone et al., 2018)	Italy	C	91 (17-22 years, mean age = 17.77 years, 67% male, recruited through schools in Rome)	Attachment style	TRQ	YSR	SR	CFA (correlated factors): internalising, externalising	88%
(Vanes et al., 2020)	UK	L	293 (aged 14-24 years, selected to ensure sex, age and ethnicity distribution representative of London and Cambridgeshire)	Myeline maturation	magnetisation transfer imaging	R-CMAS, MFQ, SPQ, r-LOI, ABQ, RSE, WB	SR	Bifactor: general psychopathology	75%
(van Hoof et al., 2019)	Netherlands	C	74 (12-20 years, mean age = 15.42, 14.90% male)	Resting state functional connectivity (whole brain and region of interest), unresolved-disorganised attachment	fMRI, AAI	YSR, CBCL, RCADS, TSCC, CDI, A-DES	SR, PR	PCA: general psychopathology	100%
(Vella et al., 2019)	Australia	L	3,717 (12-13 years at wave 5, mean age at wave 5 = 12.41, 51.75% male, representative sample of Australian children)	Sex/gender, household income, parental warmth, sociability, sports participation	Primary parent report, STS	SDQ	SR, PR	Growth mixture modelling: mental health trajectory from 4 to 12 years of age: low difficulty, improvers, decliners, early decliners/late improvers, early improvers/late decliners, high difficulty	88%
(Wade et al., 2018)	Romania	L	220 (119 ever institutionalised, 50% male, assessed at ages 6, 12 & 16 years)	Sex/gender, history of institutional rearing (foster care, institutionalised, never institutionalised)	Institutional rearing groups randomly assigned as part of an RCT, a matched sample of never-institutionalised children were recruited for comparison	MHBQ	PR, TR	Bifactor: general psychopathology, internalising, externalising	100%

Study	Country	Design	Sample	Risk/Protective Factors	Risk/Protective Factors Measures	Measures of Psychopathology	Respondent	Model: Outcome Variables Examined	Quality Score
(Wade et al., 2019)	Romania	L	188 (children in foster/institutional care, assessed at ages 6, 12 & 16 years)	Common executive functioning, early/childhood psychopathology, history of institutional rearing (foster care, institutionalised, never institutionalised)	CANT, MHBQ	MHBQ	PR, TR	Bifactor: general psychopathology, internalising, externalising	100%
(Wang et al., 2020)	USA	L	515 (14 years, 50% male)	Behavioural inhibition, inhibitory control, negative affect, aggression and internalising PRS	observational measures at age 2 and 3, CBQ, RACS, PRS	CBCL, TRF	PR, TR	LCA: low problems, internalising problems only, externalising problems only, co-occurring problems Bifactor: general psychopathology, internalising, externalising	88%
(Wilson et al., 2015)	USA	L	177 (14-22 years at wave 6, mean age = 17.72, 100% female, 100% African American, sought services from outpatient mental health clinics in low-income areas in Chicago)	Childhood abuse and neglect	Self-reports, reports from maternal caregiver, LTVH, CEQ	YSR, AIDS-RBA	SR	Parallel process LGM: internalising, externalising	100%
(Xia et al., 2018)	USA	C	999 (8-22 years, mean age = 15.76, 45%)	Brain region functional connectivity	fMRI	GOASSESS	SR, PR	Sparse canonical correlation analysis: mood, psychosis, fear, externalising behaviour	100%

Notes. **Abbreviations:** C = cross-sectional design, L = longitudinal design, RCT = Randomised Controlled Trial; **Respondent:** SR = self-report, PR = parent/caregiver-report, TR = teacher-report; **Models:** CFA = Confirmatory Factor Analysis, EFA = Exploratory Factor Analysis, LCA = Latent Class Analysis, PCA = Principial Component Analysis; **Risk Factors:** BI = Behavioural inhibition, EF = Executive functioning; **Outcome variables:** AUD = Alcohol Use Disorder Class, AUD-ANX-MDD = Alcohol Use Disorder, Anxiety Disorder and Major Depression Disorder Class, SUD-CD = Substance Use Disorder and Conduct Disorder Class, IA = inattention, H/I = hyperactivity/impulsivity, ASD = autism spectrum disorder, LD = learning difficulties, ODD = oppositional defiant disorder, CD = conduct disorder, DEP = depression, ANX = anxiety, PD = panic disorder, GAD = generalised anxiety disorder, SAD = separation anxiety, SA = school anxiety, SP = social phobia; **Risk/Protective Factors Measures:** AAI = Adult Attachment Interview, ACSQ = Adolescent Cognitive Style Questionnaires, ASQ = Adolescent Self-esteem Questionnaire, ALEQ-R = Adolescent Life Events Questionnaire Revised , CANT = Cambridge

Automated Neuropsychological Test Battery, CCTI-SS = Colorado Children's Temperament Inventory Shyness/Sociability subscale, CDAS = Children's Dysfunctional Attitudes Scale, CEQ = Childhood Experiences Questionnaire, CDEQ = Children's Depressive Experiences Questionnaire, CRSQ-RS = Child Response Styles Questionnaire-Rumination subscale, CSHQ = Child Sleep Habits Questionnaire, EEG = Electroencephalogram, EVI-Q = Exposure to Violence Interview – Questionnaire version, fMRI = functional magnetic resonance imaging, GL-NEO-S = Goldberg lexical neuroticism, extroversion, and openness scales, GWAS = Genome Wide Association Study, H-SAS = Hetero-Social Activities Scale Social Involvement subscale, LTVH = Lifetime Trauma and Victimization History, NRI = Networks Relationships Inventory, PANAS-C = Positive and Negative Affect Scale for Children, PDS = Pubertal Development Scale, POS = Play Observation Scale, PRS = Polygenic Risk Score, RACS = Relationship Affect Coding System, SRE = Schedule of Racist Events, STS = Short Temperament Scale, SURPS = Substance Use Risk Profiles Scale, TBAQ = Toddler Behaviour Assessment Questionnaire, TCES = The Collective Efficacy Scale, TIPI = Ten Item Personality Inventory, TMCQ = Temperament in Middle Childhood Questionnaire, TRQ = The Relationship Questionnaire, TSI = The Stress Index, WASI-II = Wechsler Abbreviated Scale of Intelligence-II; **Measures of Psychopathology:** A-DES = Adolescent Dissociative Experiences Scale, A-TAC = Autism-Tics, ADHD, and Other Comorbidities inventory, ABQ = Antisocial Behaviour Questionnaire, AIDS-RBA = AIDS-Risk Behavior Assessment (substance use & sexual risk behaviours), AMPQ-II = Adolescents Mental Health and Problem Behavior Screening Questionnaire-II, ASR = Adult Self Report questionnaire, AUDIT = Alcohol Use Disorders Identification Test, BFI-N = Neuroticism subscale of Big Five Inventory, BSI = Brief Symptom Inventory, C-DISC = Computer Assisted Diagnostic Interview Schedule for Children, CAPE = Community Assessment of Psychic Experiences, CAPS = Child and Adolescent Psychopathology Scale, CBCL = Child Behavior Checklist, CDI = Children's Depression Inventory, CESD = Center for Epidemiological Studies on Depression scale, CIDI-A = Composite International Diagnostic Interview - Adolescent Version, CIDI-UM = Composite International Diagnostic Interview - University of Michigan version, CPRS = Conners 3 parent rating scales, DAWBA = Development and Well-being Assessment, DIS = Diagnostic Interview Schedule, DISC = Diagnostic Interview Schedule for Children, DISC-IV = Diagnostic Interview Schedule for Children, e-MINI = Mini International Neuropsychiatric Interview - electronic version, EATQ-R = Early Adolescent Temperament Questionnaire, GAIN-SS = Global Appraisal of Individual Needs - Short Screener, GOASSESS = modified version of K-SADS, JHDS = John's Hopkins Depression Scale, K-SADS = Schedule for Affective Disorders and Schizophrenia for School Age Children, LIFE = Longitudinal Interval Follow-Up Evaluation, LSAS = Liebowitz Social Anxiety Scale, MASC = Manifest Anxiety Scale for Children, MASQ-SF = Mood and Anxiety Symptom Questionnaire—Short Form, MFQ = Mood and Feelings Questionnaire, MHBQ = MacArthur Health and Behavior Questionnaire, PLIKS-Q = Psychosis-Like Symptom Questionnaire, PSWQ-C = Penn State Worry Questionnaire for Children, R-CMAS = Revised Children's Manifest Anxiety Scale, r-LOI = Revised Leyton Obsessional Inventory, RAPI = Rutgers Alcohol Problem Index, RCADS = Revised Child Anxiety and Depression Scale, RDUS = Recreational Drug Use Scale, RSE = Rosenberg Self-Esteem Scale, SCARED = Screen for Child Anxiety Related Emotional Disorders, SCID-I = Structured Clinical Interview for DSM-IV Axis 1 Disorders, SCID-I: MAS = Structured Clinical Interview for DSM-IV Axis 1 Disorders: Mood, Anxiety and Substance Use modules, SDQ = Strengths and Difficulties Questionnaire, SMFQ = Short Mood and Feelings Questionnaire, SNAP-IV = Swanson, Nolan, and Pelham scale, SPQ = Schizotypal Personality Questionnaire, SRD = Self Report of Delinquency Scale, SRP-SF = Self Report of Psychopathy Short Form Scale, SSAGA = Semi-Structured Assessment for the Genetics of Alcoholism, STAI-T = State-Trait Anxiety Inventory—Trait, TRF = Teacher's Rating Form, TSCC = Trauma Symptom Checklist for Children, WB = Warwick-Edinburgh Mental Well-Being Scale, YSR = Youth Self Report

Table 2.2 Summary of empirical models of psychopathology from included studies

Statistics Family	Modelling approach	Description	Outcome Variables	Number of Models
Factor analytic	Bifactor	A bifactor model is comprised of a general factor (e.g., general psychopathology) that reflects shared variance among all indicators (i.e. observed variables), and two or more uncorrelated specific factors (e.g. internalising, externalising) that explain the remaining shared variance among selected indicators not accounted for by the general factor (Gibbons & Hedeker, 1992; Holzinger & Swineford, 1937; Markon, 2019).	General psychopathology	3
			General psychopathology, anxiety, psychotic experiences, depression, negative (symptoms of psychosis) factors	1
			General psychopathology, emotional problems, behavioural problems, neurodevelopmental problems	1
			General psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, ANX	1
			General psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP	1
			General psychopathology, internalising, externalising	14
			General psychopathology, internalising, externalising, attention problems	2
			General psychopathology, anxious-misery, psychosis, behavioural (externalising), fear	1
	Modified bifactor (correlated factors)	As above, except in this model the specific factors are allowed to correlate (see Carragher et al., 2016 for details).	General psychopathology, internalising, externalising and thought disorder	1
	Bifactor subtotal			**25**
	CFA (correlated factors)	Uses confirmatory factor analysis (CFA) to generate a model comprised of two or more latent variables (e.g., internalising, externalising) that reflect the shared variance among selected indicators. The latent factors are allowed to correlate; however, a general or underlying factor is not extracted. Details of the model, such as number of factors, and which indicators relate to which factors are prespecified by researcher (Brown, 2014; Thurstone, 1944).	Internalising, externalising	3
			Anxiety, psychotic experiences, depression, negative (symptoms of psychosis) dimensions	1
			IA, H/I, ASD, LD, ODD, CD, DEP, ANX	1
			IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP	1
	CFA (one factor)	Uses CFA to extract a single latent factor that explains the shared variance across all observed variables (Brown, 2014).	General psychopathology	1
	CFA (higher order)	Similar to CFA with correlated factors, however a higher-order latent variable (e.g., general psychopathology) is also extracted which reflects the shared variance among lower-order latent variables (e.g., internalising, externalising and thought disorder).	General psychopathology, internalising, externalising and psychotic-like experiences	1
	CFA Subtotal			**8**

Statistics Family	Modelling approach	Description	Outcome Variables	Number of Models
	EFA (correlated factors)	Similar to CFA with correlated factors, except in exploratory factor analysis (EFA) does not require details of a model to be prespecified, such as the number of factors or which indicators should be loaded onto which factors (Brown, 2014; Fabrigar, Wegener, MacCallum, & Strahan, 1999).	Distress, fear, externalising and eating pathology	1
Factor analytic subtotal				**34**
Growth curve analysis	Growth Mixture Modelling	Models change in latent classes overtime and allows for variation in trajectories within classes as well as estimating mean growth curves for each class (T. Jung & Wickrama, 2008; Muthén, 2006).	Mental health trajectory from 4 to 12 years of age: low difficulty, improvers, decliners, early decliners/late improvers, early improvers/late decliners, high difficulty	1
	Parallel Process Latent Growth Model	Models the change in latent factors over time, such as internalising and externalising. Latent variables in growth models are the initial status internalising and externalising (known as the intercepts) and change in internalising and externalising (known as the slopes; Duncan & Duncan, 2004; Preacher, Wichman, MacCallum, & Briggs, 2008).	General psychopathology, internalising, externalising, ADHD	1
			Internalising, externalising	3
Growth curve subtotal				**5**
Class-based	Latent class analysis	Latent class analysis (LCA) identifies groups of cases where individuals are most similar to each other and distinct from individuals in other groups. These groups are known as 'latent classes' and are categorical, rather than dimensional (Collins & Lanza, 2009). LCA is typically applied to categorical variables, however the term LCA is also sometimes used to describe models based on both categorical and continuous variables.	AUD, AUD-ANX-MDD & SUD-CD classes	1
			Healthy, internalising (primarily anxiety), externalising (primarily substance use)	1
			Internalising, externalising	1
			Low problems, internalising problems only, externalising problems only, co-occurring problems	2
	Latent profile analysis	Similar to LCA in that it identifies discrete groups of individuals, except analysis is applied to continuous variables (Collins & Lanza, 2009).	Thriving functioning, average functioning, externalising vulnerability and family stress, internalising vulnerability	1
	Multilevel latent profile analysis	Similar to latent profile analysis, except that it accommodates hierarchical data sets where individuals are nested within groups, such as schools (Henry & Muthen, 2010)	Group 1 - high scores on all mental health domains, Group 2 - high scores on internalising/emotional domains, low scores on externalising/behavioural domains, Group 3 - low scores on all mental health domains	1
Class-based subtotal				**7**
Principal component	Bass-ackwards	Similar to PCA, however correlations between component scores across levels (i.e. sequence) of extraction are calculated and used to generate a hierarchical structure (Goldberg, 2006). Sometimes referred to as sequential principal components.	General psychopathology, internalising, externalising, fear, distress and thought disorder	1
			General psychopathology, internalising, externalising, fear, and distress	1

Statistics Family	Modelling approach	Description	Outcome Variables	Number of Models
	Principal Component Analysis	Generates a series of uncorrelated components that reflect the maximum amount of variance from each observed variable, including error variance and unique variance. The first factor extracted accounts for the most amount of variance shared amongst included variables, each subsequent factor is the next largest factor after accounting for / removing the influence of the preceding factors. As such, the sequence that components are extracted reflects a decreasing order of importance in terms of how much variance is accounted for. Differs from factor analytic approaches which focus on the analysis of covariance, rather than all variance (Abdi & Williams, 2010; Everitt & Dunn, 2001; Tabachnick, 2014)	General psychopathology	1
Principal component subtotal				**3**
Machine Learning	Sparse canonical correlation analysis	Sparse canonical correlation analysis aims to reduce multidimensional data (e.g., neuroimaging or genomic data and psychopathology symptoms) to a smaller set of projected variables (i.e., canonical correlation vectors) that reflect the maximum correlation between two sets of multidimensional variables (Hardoon & Shawe-Taylor, 2011; Witten, Tibshirani, & Hastie, 2009).	Mood, psychosis, fear, externalising behaviour	1
Total number of models from included studies				**50**

Notes. IA = inattention, H/I = hyperactivity/impulsivity, ASD = autism spectrum disorder, LD = learning difficulties, ODD = oppositional defiant disorder, CD = conduct disorder,

DEP = depression, ANX = anxiety, PD = panic disorder, GAD = generalised anxiety disorder, SAD = separation anxiety, SA = school anxiety, SP = social phobia

Table 2.3 Summary of replicated transdiagnostic risk and protective factors by psychopathology outcome and modelling approach

	Psychopathology outcome			Modelling Approach				
	General psychopathology	**Internalising**	**Externalising**	**Bifactor**	**CFA (Correlated factors)**	**Growth model**	**LC/PA**	**Bass-ackwards**
Biological								
Genetic risk for ADHD	+++			✓				
Genetic risk for schizophrenia	++			✓				
Being female	+/- - -	+++	+ +/- - -/~	✓	✓			
Being male	+++/- -	++/- - -	++/-	✓	✓			
Earlier pubertal timing/onset of menarche	++	++	++	✓	✓			
Executive functioning deficits	+++	++/-	++/- -	✓	✓	✓		
Reduced gray matter volume	++			✓	✓			
Socio-environmental								
Maternal depression	++	+	-	✓			✓	
Stressful life events	++	+/-	++	✓				
Psychological								
Low extroversion	++/-	++/-	+/-			✓		✓
High negative affectivity	+++	++/-	- - -	✓			✓	
High neuroticism	+++	+++	+++	✓		✓		✓
High behavioural inhibition	++	++/-	+/- -	✓	✓		✓	
Low effortful control	+++	+/-	+++	✓	✓			
High rumination	+++	++/- -	++/~	✓				
Openness	- - -	- - -	- - -			✓		✓

Notes. '+' = evidence, but no replication, '++' = some replication (two samples), '+++' = consistent replication (3 or more samples), '~' = mixed evidence for direction of association, '-' = no association (one sample), '- -' = no association (two samples), '- - -' = no association (3 or more samples), ✓ = modelling approach used, CFA = confirmatory factor analysis, LC/PA = latent class or latent profile analysis

Figure 2.3 Sankey diagram visualising relationship between transdiagnostic risk and protective factors supported by evidence from two or more studies and psycho- pathology outcomes. The thickness of lines indicates the number of studies supporting the association
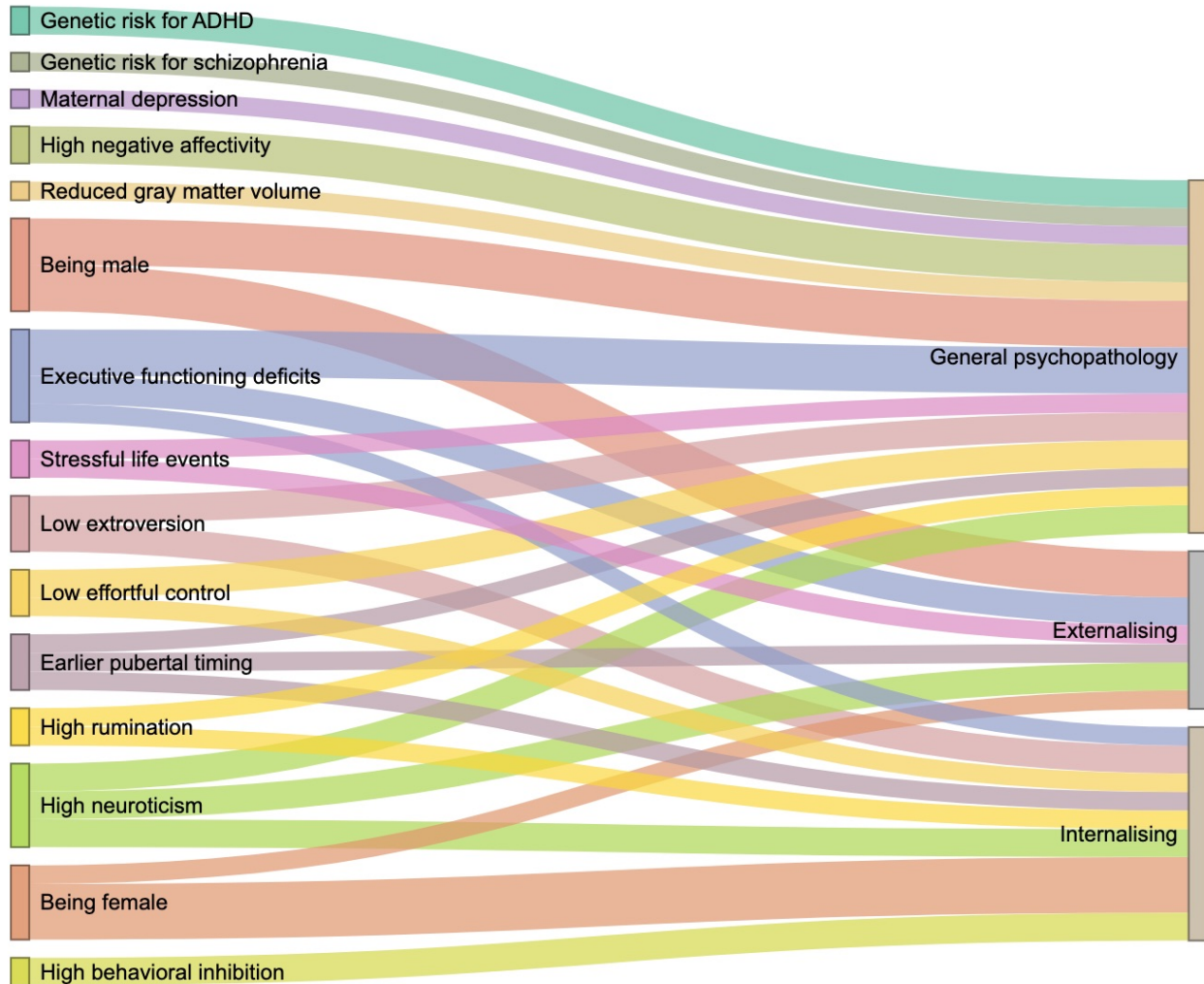
2.5 Discussion

A dizzying constellation of biological, psychological, and socio-environmental factors emerged from the reviewed studies that appear to be transdiagnostically relevant among young people aged between 10 and 24 years. Among these, 14 factors were replicated in two or more samples and generally replicated across multiple models of psychopathology. The results of the review highlight a number of factors that may serve as salient markers of risk or targets for transdiagnostic prevention and intervention efforts and revealed promising avenues for future investigation to better understand the many varied transdiagnostic risk and protective factors for psychopathology among young people.

2.5.1 Transdiagnostic risk and protective factors

2.5.1.1 Risk factors for internalising psychopathology

The review identified seven risk factors for the development of internalising psychopathology among young people. These included three biological factors (being female, earlier pubertal timing (including early onset of menarche) and executive functioning deficits), one socio-environmental factor (maternal depression), and four psychological factors (high neuroticism, low extroversion, high behavioural inhibition and high negative affectivity). Four additional risk factors for internalising that demonstrated some replication were also identified but require further investigation to clarify inconsistent results. Low effortful control and stressful life events were only associated with increased internalising in some studies, while other studies found no relationship. Both significant and non-significant associations were identified using bifactor models of psychopathology, which suggests that there may have been inconsistencies in study design, such as measurement, indicators or specification of the internalising variable across studies. Furthermore, high rumination was positively associated with internalising in two studies, and negatively in one study. As such, further research is needed to determine whether low effortful control, stressful life events and rumination are reliable risk factors for internalising psychopathology.

2.5.1.2 Risk factors for externalising psychopathology

There were six risk factors found to increase risk for the development of externalising psychopathology among young people in the present review. Three biological factors (executive functioning deficits, earlier pubertal timing, being male), one socio-environmental factor (stressful

life events), two psychological factors (high neuroticism and low effortful control). Additionally, although being male was fairly consistently found to be associated with increased externalising, there were also three studies that did not find any gender differences, and one study that reported being female increased risk for externalising (all studies with non-significant results used a bifactor model).

2.5.1.3 Risk factors for general psychopathology

Eleven risk factors for general psychopathology were identified. Four biological factors (executive functioning deficits, genetic risk for ADHD, genetic risk for schizophrenia, earlier pubertal timing), two socio-environmental (stressful life events and maternal depression) and five psychological factors (high negative affectivity, high neuroticism, low effortful control, high rumination and low extroversion). Although being male was typically associated with greater levels of general psychopathology, there were studies that also found no association with sex/gender.

Findings from twin studies indicated that variance in general psychopathology appears to be partly genetic in nature, while environmental influences tended to explain more variance among individual disorders. This is consistent with the 'generalist genes, specialist environments' hypothesis, which posits that co-occurring characteristics, such as internalising and externalising, tend to be influenced by common sets of genes, while the differences in internalising and externalising, are explained by environmental influences (Kovas & Plomin, 2007). However, there was also some evidence for genetic influences on more specific sub-factors (e.g., social phobia, hyperactivity/impulsivity, neurodevelopmental, and negative (symptoms of psychosis) specific factors), via genetic risk for schizophrenia and ADHD, which suggests that some genes may have more specific influences. There was also evidence for genetic and non-shared environmental influences on the association between psychopathology and other risk factors, including executive functioning and some psychological factors (e.g., prosociality and intelligence). In summary, the evidence indicates that genetic factors may increase risk for psychopathology transdiagnostically, however specific genetic markers and mechanisms have not yet been identified.

2.5.1.4 General summary of transdiagnostic risk and protective factors

Evidence from the present review indicates that high negative affectivity, low effortful control, and executive functioning deficits are well supported transdiagnostic markers of risk for psychopathology among young people. Rumination, neuroticism and extroversion also appear to be

important markers, however further longitudinal research is needed to determine whether they are true risk factors. Altogether, this is consistent with other recent reviews which have found evidence that the related over-arching constructs of self-regulation and emotion regulation may contribute to the development of a broad range of psychiatric disorders (Aldao et al., 2016; Nigg, 2017; Santens et al., 2020; Sloan et al., 2017).

Similarly, results from studies of childhood trauma and stress in the present review generally found consistent relationships with a variety of broad psychopathology outcomes, which is consistent with previous research which has indicated that stressors are associated with increased risk for both internalising and externalising psychopathology in adolescence (March-Llanes et al., 2017; McMahon et al., 2003). However, there were some inconsistent findings for the relationship between internalising and childhood stress and trauma in the present review. While the inconsistencies may be due to differences in methodology, it is also possible the consistent relationship between childhood stress and trauma and general psychopathology may indicate that previous reported associations with internalising were due to an unmeasured shared variability across internalising and externalising dimensions.

Despite consistencies with previous reviews, a number of limitations and methodological concerns were also identified that should be taken into account when interpreting the results and addressed in future research. There were also some areas of research that have so far been relatively underexplored that warrant investigation in future research.

2.5.2 *Methodological considerations*

It is important to stress that findings from this review must be interpreted with caution due to a number of methodological complexities and uncertainties. First, the studies varied considerably in terms of measures/indicators of psychopathology, statistical approaches and the outcomes examined. Many studies modelled general psychopathology, internalising and externalising as latent variables. However, the inconsistency of indicators and measures included in models across studies means that the extracted factors likely reflect different forms of psychopathology (Watts, Poore, & Waldman, 2019).While this may explain some of the inconsistent findings in the present review, it also suggests that factors that were replicated across multiple studies and models are likely very robust contributing factors for psychopathology. Overall, however, the diversity in the measures of psychopathology included across studies makes it difficult to draw unifying conclusions.

Second, over half of the studies used a bifactor model, which tend to show superior goodness of fit over other models because they are more flexible and accommodate complexities, such as random noise (Watts, Poore, & Waldman, 2019). However, model fit indices are increasingly considered an insufficient indicator of structural validity, and a number of additional tests are now recommended in adjudicating between structural models (Forbes, Greene, et al., 2021). In particular, there are increasing calls for the interpretability of models to be considered more carefully as well as the inclusion of more theoretically, rather than statistically, driven models. For example, higher-order latent variable models tend to show superior reliability and interpretability over bifactor models, particularly in relation to specific factors such as internalising, externalising and thought disorder (Lees et al., 2021; Sunderland et al., 2020). The convergence on a particular modelling approach, such as the bifactor model, may be premature given that there are multiple plausible models and explanations for the onset and maintenance of individual and co-occurring mental disorders (van Bork et al., 2017). Network models of psychopathology in particular have been gaining momentum in the literature over the last decade, but as yet no studies have examined risk or protective factors using a network approach among young people. This presents an important opportunity to better understand the influence of risk and protective factors on the development of mental disorders at the symptom level and would complement existing knowledge from factor analytic studies.

Third, it also worth noting that the majority of studies were based on cross-sectional data from the USA, thus making it difficult to determine causality and generalisability. Furthermore, most of the studies were from non-clinical samples which are more likely to have low-to-moderate levels of psychopathology. As such, it is possible that some studies may have detected 'false negatives' due to low levels of psychopathology.

Finally, the inclusion criteria applied in this review adopted the World Health Organisations definition of a young person and specified that participants mean age needed to between 10 and 24 years (World Health Organization, 2014). This unfortunately meant that studies from some new well-known cohorts, such as the Adolescent Brain Cognitive Development (ABCD) Study where the mean age is below 10 years, could not be included (e.g., Lees et al., 2020; Michelini et al., 2019). However, findings from relevant studies of the ABCD cohort generally corroborated findings from studies in the present review. For example, Lees and colleagues (2020) reported a number of common and dissociable patterns of functional connectivity relating to the frontoparietal, default mode and salience networks, which aligns with other studies of functional connectivity which did meet the criteria for inclusion in the present review (Elliott et al., 2018; Kaczkurkin et al., 2018; Xia et al., 2018).

2.5.3 Future directions

Within the context of the methodological concerns surrounding bifactor models, it is recommended that future research explore multiple models of psychopathology by examining reliability metrics and relationships with external variables across multiple models. Furthermore, exploration of multiple models may help resolve some of the inconsistent findings identified in the review, such as the uncertain relationship between childhood trauma and stress and internalising psychopathology. Among the factors investigated by studies in the present review, there were some gaps and underexplored factors that warrant further investigation. In particular, very few studies explicitly examined protective factors, and none were examined in more than one study. Public health prevention policies and interventions could significantly benefit from the identification of reliable transdiagnostic protective factors. Neurobiological factors were also relatively underexplored in the present review. Advances in understanding the complexity of neurobiological mechanisms underlying the development of psychopathology on young people has important aetiological implications.

Future research should also aim to delineate the mechanisms through which key risk factors identified in the present review, particularly neuroticism, negative affectivity, effortful control and executive functioning, contribute to increased risk for psychopathology. Further, there has been very little research to date that integrates biological, psychological and socio-environmental factors. A multidisciplinary approach that explores multiple factors contributing to the development of psychopathology among young people may help identify transdiagnostic mechanisms and processes and foster the development of comprehensive aetiological models of psychopathology. In turn, this may lead to the identification of more salient targets for prevention and intervention.

2.5.4   Conclusions

To our knowledge, this is the first systematic review of empirical models of psychopathology and risk and protective factors in young people. Results from the review revealed several key risk factors for psychopathology, in particular executive functioning deficits, stressful life events, high neuroticism, negative affectivity and behavioural inhibition, and low effortful control. These findings have important implications for prevention and intervention. Improving emotion regulation and self-regulation and reducing environmental conditions that foster stressful life events may be particularly salient targets for the prevention and intervention of general and specific dimensions of psychopathology. In addition, this review identified a number of methodological concerns that should be addressed in future research. Specifically, there is a fundamental need for more longitudinal, multidisciplinary, causally driven methods and a clear need for a more consistent approach to modelling of psychopathology. Ultimately, a stronger foundation of knowledge for how best to model psychopathology will drive the identification of robust relationships between transdiagnostic risk and protective factors and mental and substance use disorders to inform our understanding of developmental psychopathology and facilitate empirically supported approaches to prevention and intervention.

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Chapter 3

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Structure of psychopathology and its association with high-risk personality traits

Preface

The results of the systematic review reported in Chapter 2 highlighted certain aspects of personality (e.g., neuroticism and negative affectivity) that may increase risk for general psychopathology among young people, and the need for a more consistent approach to modelling psychopathology. Primary concerns relate to the reliance on traditional goodness-of-fit statistics to adjudicate between alternative models (e.g., higher-order or correlated factors), and that, as described in Chapter 1, the lion's share of previous research has focussed on broad personality traits, rather than more nuanced aspects of personality, such as facets level traits. Recent studies have advocated for more meaningful tests of validity and model adjudication, including the use of additional, emerging, tests of reliability as well as the potential for establishing external validity and clinical utility. Addressing these issues, Chapter 3 presents a rigorous empirical investigation of multiple competing models and considers additional model reliability and replicability metrics in the adjudication process. Following this evaluation, associations with four high-risk personality traits—three of which align with different aspects of neuroticism—are examined across multiple levels of a hierarchical-dimensional model of psychopathology.

This chapter addresses the first and third questions of this thesis: *What is the underlying structure of psychopathology in young people?* and *How are high-risk personality traits associated with different levels of a hierarchical-dimensional model of psychopathology?*

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Figure 3.1 Screenshot of the article "Structure of psychopathology in adolescents and its association with high-risk personality traits" by Lynch et al. (2023) published in Development and Psychopathology

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Regular Article

Structure of psychopathology in adolescents and its association with high-risk personality traits

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Supplementary materials are available in Appendix F, and online (https://osf.io/cq2rz) along with the analysis code and output files.

3.1 Abstract

The present study examined high-risk personality traits and associations with psychopathology across multiple levels of a hierarchical-dimensional model of psychopathology in a large adolescent, general population sample. Confirmatory factor analyses were run using data from two randomised controlled trials of Australian adolescents (N = 8,654, mean age = 13.01 years, 52% female). A higher-order model—comprised of general psychopathology, fear, distress, alcohol use/harms, and conduct/inattention dimensions—was selected based on model fit, reliability, and replicability. Indirect-effects models were estimated to examine the unique associations between high-risk personality traits (anxiety sensitivity, negative thinking, impulsivity, and sensation seeking) and general and specific dimensions and symptoms of psychopathology. All personality traits were positively associated with general psychopathology. After accounting for general psychopathology, anxiety sensitivity was positively associated with fear; negative thinking was positively associated with distress; impulsivity was positively associated with conduct/inattention; and sensation seeking was positively associated with alcohol use/harms and conduct/inattention, and negatively associated with fear. Several significant associations between personality traits and individual symptoms remained after accounting for general and specific psychopathology (e.g., there were significant direct effects for negative thinking and symptoms of distress, including "unhappy", "depressed", and "worthless", over and above distress and general psychopathology). These findings contribute to our understanding of the underlying structure of psychopathology among adolescents and have implications for the development of personality-based prevention and early intervention programs.

3.2 Introduction

Personality is a well-established risk factor for psychopathology, with evidence for links with a variety of mental and substance use disorders (den Akker et al., 2013; Kotov et al., 2010; Tackett, 2006; Watson et al., 2005, 2019; Widiger et al., 2019). However, there are high rates of comorbidity among disorders, making it difficult to identify reliable links between personality traits and mental disorders. Recent advances in the study of the underlying structure of psychopathology supports a data-driven, hierarchical-dimensional model of psychopathology which accounts for comorbidity among disorders and enables the study of relations with external variables at various levels of specificity. Yet, only a small number of studies have examined the associations between personality traits and psychopathology within this framework among adolescents to date (Lynch et al., 2021; Chapter 2). Further, past research has primarily focused on associations between normal-range trait domains (e.g., 'the Big 5' or five factor model traits) and distinct disorders (Sellbom et al., 2020). Examining established high-risk personality traits (e.g., lower-order facets of neuroticism or sub-dimensions of disinhibition) may be informative in terms of refining our understanding of the underlying structure of psychopathology and for advancing knowledge of personality related risk for psychopathology. Focusing on these associations in a hierarchical-dimensional model of psychopathology, for example, may be particularly useful for clarifying the role personality may play in the development of general and specific forms of psychopathology, from individual symptoms up to broad transdiagnostic dimensions.

3.2.1 *Hierarchical-dimensional models of psychopathology*

Psychopathology has historically been conceptualised in terms of discrete diagnostic categories. However, categorical approaches to conceptualising psychopathology tend to have poor reliability and low specificity, as evidenced by the high rates of comorbidity between disorders and heterogeneity within disorders (Kotov et al., 2017; Ofrat & Krueger, 2012). In response to these issues, there has been a renaissance of empirical studies examining the underlying structure of psychopathology. This work has generated a wealth of evidence for conceptualising psychopathology in a hierarchical-dimensional framework, such as the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017, 2021). At the apex of hierarchical-dimensional models sits a general factor of psychopathology, which captures shared variance among mental and substance use disorders. Beneath the general factor sit more specific factors that reflect shared variance among closely related disorders, such as internalising and externalising dimensions. Internalising captures comorbidity among, for example, phobias, eating, obsessive-compulsive, and

mood and anxiety-related disorders, whereas externalising reflects shared variance among, for example, substance use, conduct, antisocial and impulse related disorders. There is also evidence that these dimensions may be partitioned into even narrower dimensions (Krueger et al., 2021; Watson et al., 2022). For example, internalising includes sub-dimensions of fear and distress, and externalising includes sub-dimensions of substance use and antisocial behaviour.

3.2.2 *Personality and psychopathology*

Previous research has consistently shown that there are strong associations between certain personality traits and certain forms of psychopathology (Brandes et al., 2019; Castellanos-Ryan & Conrod, 2012; Haltigan et al., 2018; Kotov et al., 2010; Widiger et al., 2019). For example, neuroticism has been established as an important risk factor for internalising and general psychopathology dimensions (Brandes et al., 2019; Castellanos-Ryan et al., 2016; Etkin et al., 2021; Kotov et al., 2010). Similarly, antagonism and impulsivity traits are both associated with externalising and substance misuse problems (Castellanos-Ryan et al., 2016; Etkin et al., 2022; Kotov et al., 2010; Lynam & Miller, 2019). However, currently very little is known about associations at the subfactor (e.g., fear and distress) and symptom levels of hierarchical-dimensional models of psychopathology (Brandes & Tackett, 2019; Kotov et al., 2010). Similarly, although personality can also be conceptualised hierarchically, most research thus far has focused on broad personality traits, rather than the underlying facets or aspects of these traits (Brandes & Tackett, 2019; Tackett, 2006; Watts, Poore, Lilienfeld, et al., 2019). Amid renewed calls for research on the integration of and differentiation between personality and psychopathology (Hopwood et al., 2022; Wright & Hopwood, 2022), exploration of associations between narrower components of personality and subfactor and symptom levels of psychopathology could help clarify the structure of lower levels of a hierarchical model of psychopathology or point to shared or distinguishable elements of personality and psychopathology.

The four-factor model of vulnerability integrates and distils previous research linking neuroticism as well as inhibited and disinhibited personality traits to substance misuse and comorbid psychopathology via distinct cognitive and motivational pathways (Castellanos-Ryan et al., 2016; Castellanos-Ryan & Conrod, 2012). Although this model was initially conceptualised as a model of personality-based risk for substance use, there is considerable evidence that the traits are also associated with higher levels of and increased risk for other forms of psychopathology (Carragher et al., 2016; Castellanos-Ryan et al., 2016). In contrast to comprehensive models of personality, such as the Big Five, the four-factor model of vulnerability is comprised of four particularly compelling

personality-based risk factors for substance use problems, and psychopathology more broadly (Castellanos-Ryan & Conrod, 2012). Inhibited/neurotic traits of *negative thinking* (tendency to experience hopelessness and low positive affect) and *anxiety sensitivity* (fear of anxiety-related sensations due to beliefs that such sensations could lead to harmful consequences) are associated with mood and anxiety related problems, as well as increased substance use problems (to manage or relieve symptoms of anxiety/depression). Disinhibition is partitioned into two sub-domains: *impulsivity*, which broadly reflects a failure to inhibit behaviours likely to result in negative consequences, and *sensation seeking*, which reflects a willingness to take risks for the sake of novel experiences. Individuals high in impulsivity have difficulties with emotion and behavioural regulation, tend to experience more conduct related problems and are at increased risk for substance misuse through enhancement, coping and conformity motives. Whereas individuals high in sensation seeking are more likely to develop substance use problems due to a heightened susceptibility to the rewarding properties of alcohol and other substances. Sensation seeking appears to be more directly related to substance misuse problems than other externalising related problems (Castellanos-Ryan & Conrod, 2011).

Prior research on the four-factor model of vulnerability and hierarchical-dimensional model of psychopathology have revealed theoretically aligned patterns of association with transdiagnostic dimensions (though there are some exceptions). For example, *negative thinking* and *anxiety sensitivity* appear to be prospectively and concurrently associated with greater internalising and general psychopathology (Carragher et al., 2016; Castellanos-Ryan et al., 2016), and either unrelated or inversely related to externalising (although one study reported a positive association between negative thinking and externalising, but internalising symptoms were not included in the model, e.g., Castellanos-Ryan & Conrod, 2011). Similarly, impulsivity and sensation seeking appear to be more closely related to externalising related dimensions, with impulsivity more closely related to conduct/general externalising and sensation seeking more closely aligned with substance misuse and related harms. One study also reported a negative association between sensation seeking and negative thinking (Carragher et al., 2016). Exploration of unique associations with subdimensions of internalising and externalising, or indeed individual symptoms, may help clarify some of the inconsistent findings from previous studies. To our knowledge, no studies have examined associations between these high-risk personality traits and lower levels of a hierarchical-dimensional model of psychopathology.

3.2.3   Methodological considerations

Despite strong empirical support for hierarchical-dimensional models of psychopathology, there are some outstanding conceptual and methodological issues. Critically, there is currently no clear consensus on which statistical model is most appropriate for studying the structure of psychopathology. Correlated-factors, bifactor and higher-order models appear most frequently in the literature (Forbes, Greene, et al., 2021; Lahey et al., 2021). These models are closely related yet offer different interpretations of the underlying structure of psychopathology. For example, a higher-order model's general factor reflects the shared variance among the lower-order specific factors, whereas a bifactor model's general factor directly reflects shared variance among all indicators. Further, in correlated factors and higher-order models, the specific factors reflect shared variance among a set of observed variables, whereas in a bifactor model the specific factors are uncorrelated and reflect variance unique to the factor (after the shared variance among indicators is accounted for by the general factor). When these models are directly compared using traditional goodness-of-fit statistics, the bifactor model typically outperforms the others (e.g., Greene et al., 2019). However, there are increasing concerns about relying on goodness-of-fit statistics to adjudicate between models, as bifactor models tend to overfit data which can result in inflated goodness-of-fit statistics and consequently lead to the premature dismissal of other plausible structures (Bonifay et al., 2017). As such, there have been calls to consider additional metrics for model reliability and replicability when studying the underlying structure of psychopathology (Forbes, Greene, et al., 2021; Rodriguez et al., 2016b). Although very few studies have reported on these additional metrics to date, two previous studies have found a higher-order model to outperform a bifactor model of psychopathology in young people (Lees et al., 2021; Sunderland et al., 2020).

Another important methodological issue that requires further attention is the unit of measurement used for observed variables. Much of the past research on hierarchical-dimensional models has been based on diagnostic level indicators (Forbes, Sunderland, et al., 2021). This may inadvertently constrain models to the framework of the prevailing diagnostic taxonomies. Symptom-level approaches are theorised to be better able to capture the underlying structure of psychopathology because they are not bound by the constraints of existing diagnostic categories. Further, symptom-level approaches may be more sensitive to detecting emerging forms of psychopathology (e.g., cases where symptoms are present, but the individual does not yet meet full diagnostic criteria; Forbes, Sunderland, et al., 2021). Given that many mental disorders first emerge during adolescence (Costello, Copeland, & Angold, 2011; Kessler et al., 2011), it is likely that symptom-level analyses may be more appropriate for studying psychopathology in adolescents. Another advantage of

symptom-level analysis is that it enables the identification of important symptoms with unique links to risk or vulnerability factors. These symptoms may highlight potential aetiological mechanisms and therefore could be salient intervention targets. In summary, symptom-level analyses are important both for advancing our understanding of the underlying causes of mental and substance use disorders and ultimately, for facilitating the identification of better intervention targets.

3.2.4 The present study

The aim of the present research was to conduct a more thorough exploration of the structure of psychopathology and associations with high-risk personality traits among adolescents than previously available. We aimed to examine a variety of hierarchical-dimensional structures of psychopathology using a symptom-level approach and evaluate the models using more rigorous methods of model evaluation and selection. Specifically, we assessed four alternative models of adolescent psychopathology: bifactor, higher-order, four correlated-factors and a one-factor unidimensional model. As we planned to evaluate the structural validity through additional metrics beyond traditional fit indices which not been commonly examined in previous research, we did not have any specific expectations about which model would perform the best.

Extending previous research, we also aimed to examine the direct and indirect effects of high-risk personality traits on psychopathology across three hierarchical levels: general psychopathology, specific factors, and symptoms. To our knowledge, this is the first study to examine symptom-level associations with high-risk personality traits among adolescents. As such, we did not have any specific expectations about associations between the high-risk personality traits and individual symptoms. We did, however, expect that all high-risk personality traits would be positively associated with general psychopathology; impulsivity and sensation seeking would be positively associated with externalising related specific dimensions; and anxiety sensitivity and negative thinking would be associated with internalising related specific dimensions.

3.3 Methods

3.3.1 Participants

The sample was derived from two large cluster randomised controlled trials investigating the effectiveness of eHealth prevention programs in Australia – the Climate and Preventure (CAP) and Climate Schools Combined (CSC) studies (Newton et al., 2012; Maree Teesson et al., 2014). The

present study examined baseline data from these cohorts. The CAP cohort comprises 2,268 students with a mean age of 12.96 years ($SD = 0.46$) recruited through 27 schools in 2012. Within the CAP cohort, 972 were female (42.89%) and 1,941 were born in Australia (86.84%). The CSC cohort comprises 6,386 students with a mean age of 13.03 years ($SD = 0.61$) from 71 schools in 2014. Within the CSC cohort, 3,502 were female (54.83%) and 5,147 were born in Australia (84.17%). The combined sample contained 8,654 students, 53 of which were missing on all variables and were excluded from analyses, resulting in a final sample size of 8,601 (mean age 13.01 years, SD = 0.57) from 98 schools, of which 4,474 were female (51.71%) and 7,088 were born in Australia (84.88%).

3.3.2 Measures

3.3.3 Psychopathology

Item-level responses from measures of psychopathology used in both CAP and CSC baseline assessments were used in the present study. Due to the low prevalence of substance use and psychopathology in this general population sample, all items were recoded into binary indicators to reduce the number of sparse cells and improve the stability of the models and overall precision of the estimates. Cut points were determined based on inspection of the distribution of responses (further details provided below). The measures used to assess psychopathology are described below and a summary of the items, proportions and counts is provided in Appendix F Table S1.

Strengths and Difficulties Questionnaire (SDQ). The SDQ is a brief, 25-item questionnaire that measures emotional and behavioural difficulties over the past six months and is comprised of five sub-scales: conduct problems, emotional symptoms, hyperactivity, peer problems and prosocial behaviour (Goodman, 2001). Items were selected to load onto the fear, distress and conduct dimensions as informed by previous analyses (Carragher et al., 2016; Goodman et al., 2010). Reverse-scored items were removed due to poor performance and previously documented problems (Van De Looij-Jansen et al., 2011). Items from the SDQ were recoded into binary indicators with levels representing 'not true' or 'true' (i.e., 'somewhat true' or 'certainly true').

Kessler Psychological Distress Scale (K6). The K6 is a six-item screening tool for psychological distress due to symptoms of depression and anxiety over the past four weeks (Kessler et al., 2002; Kessler et al., 2003), and has been found to be a valid and reliable measure among adolescents (Ferro, 2019; Mewton et al., 2016). Two items were loaded onto the fear dimension, and the remaining four items loaded onto the distress dimension. Items were recoded as 'none of the time'

or 'any time' (i.e., 'a little of the time', 'some of the time', 'most of the time', 'all of the time').

Rutgers Alcohol Problem Index (RAPI). The RAPI measures alcohol-related consequences experienced over the past six months and has been validated amongst high-school aged people as a measure of alcohol-related problems (Neal et al., 2006; White & Labouvie, 1989). A shortened eight-item version that had previously demonstrated adequate validity and reliability was administered to the CAP cohort (Topper et al., 2011). As such, only these items have been used in the present study. Items were recoded as 'did not experience in the last six months' and 'experienced at least one time in the last six months'.

Patterns of Alcohol Use. Patterns of alcohol use over the past six months were assessed using three items adapted from the School Health and Alcohol Harm Reduction Project's 'Patterns of Alcohol Use' index (McBride et al., 2004). Specifically, there were three items measuring frequency of alcohol use in the past 6 months, quantity of alcohol consumed in the past 6 months and frequency of drinking above low risk levels in the past six months. Items were recoded into 'none or less than monthly' and 'once a month or more'.

3.3.4 High-risk personality traits

Substance Use Risk Profile Scale (SURPS) is a 23-item measure of personality risk for substance misuse, comprised of four distinct subscales: negative thinking, anxiety sensitivity, sensation seeking and impulsivity (Woicik et al., 2009). The SURPS asks participants to indicate the extent to which they agree with each item on a four-point scale (1 = strongly disagree, 2 = disagree, 3 = agree, 4 = strongly agree). Total scores were calculated for each subscale and used in subsequent analyses. The SURPS has demonstrated good validity and reliability as a measure of personality-related risk for substance use and co-occurring psychopathology among young people across multiple cohorts (Castellanos-Ryan et al., 2013; Newton, Barrett, et al., 2016; Woicik et al., 2009).

3.3.5 Analytic plan

Analyses in the present study were conducted in the following broad steps: 1) model estimation, 2) model evaluation via traditional goodness-of-fit and contemporary model reliability and replicability indices, 3) measurement invariance testing, and 4) finally the associations between personality traits and psychopathology dimensions were assessed via regression and indirect-effects models. Further details of each step are provided below.

First, we estimated four alternative structural models of psychopathology using confirmatory factor analysis (CFA): 1) a *one-factor* model with all items loading on a single latent variable representing general psychopathology; 2) a *four correlated-factors* model with four latent variables representing fear, distress, alcohol use/harms and conduct/inattention; 3) a *bifactor* model with all indicators loading onto a single latent variable representing general psychopathology as well as four orthogonal (i.e., uncorrelated) latent variables representing fear, distress, alcohol use/harms and conduct/inattention, and 4) a *higher-order model* comprising four lower-order factors representing fear, distress, alcohol use/harms and conduct/inattention and a higher-order general psychopathology latent variable that accounts for the correlations among the lower-order factors.

The structural models were based on prior symptom-level studies among adolescents, which have consistently found evidence for a general psychopathology factor, and at least two specific or correlated factors representing externalising and internalising symptoms (Afzali et al., 2017; Carragher et al., 2016; Haltigan et al., 2018; Levin-Aspenson et al., 2019). Notably, one study found that internalising bifurcated into fear and distress sub-dimensions (Levin-Aspenson et al., 2019), and another study found evidence for separate attention and externalising (i.e., antagonistic behaviours) factors (Haltigan et al., 2018). Although a variety of theoretical and empirical models of how externalizing psychopathology should be organized exist, research among adolescents supports separate conduct and substance misuse factors (Castellanos-Ryan & Conrod, 2011), which is consistent with the current HiTOP model (Krueger et al., 2021).

All models accounted for school-level clustering and were estimated in Mplus version 8.4 using robust weighted least squares (WLSMV) and robust maximum likelihood (MLR) estimation methods to generate a range of fit statistics.

Second, the structural validity of each model was evaluated with goodness-of-fit and latent variable reliability indices (Forbes, Greene, et al., 2021; Rodriguez et al., 2016a). Incremental fit indices, including root mean square error of approximation (RMSEA) comparative fit index (CFI, values >0.95) and Tucker-Lewis index (TLI) were used to assess model fit, where RMSEA values < 0.6, and CFI and TLI values > .95 indicate close fit (Brown, 2014). Models were also compared using the information criteria, including the Akaike information criterion (AIC), Bayesian information criterion (BIC), and the sample-size adjusted BIC (SSABIC), where lower values indicate superior fit (Raftery, 1995).

Given the tendency for goodness-of-fit statistics to be biased towards selecting bifactor models, additional reliability and replicability indices were calculated (Forbes, Greene, et al., 2021; Rodriguez et al., 2016a). Specifically, the *H* coefficient, which gives an indication of the construct replicability (*H*, ideally > .8), omega (ideally >.75), which represents the proportion of variance accounted for by a single latent variable, omega hierarchical (OmegaH, ideally >.8), indicates the proportion of variance accounted for by the general factor, and omega hierarchal subscale (OmegaHS, ideally >.75) which represents the variance accounted for by a specific factor after removing variance accounted for by the general factor. Additionally, we calculated the explained common variance which provides an indication of the importance of the general factor relative to the specific factors (ECV, ideally >.7), and the explained common variance of specific factors which gives an indication of the uniqueness of a specific factor (ECV_S, ideally >.7). Unidimensionality was examined by calculating the percent of uncontaminated correlations (PUC, values >.7 indicate unidimensionality) and absolute relative parameter bias (ARPB; 10-15% is acceptable). PUC indicates the proportion of unique correlations among indicators (i.e., parameter estimates) that can be explained by a general factor alone, thus high PUC indicates that the parameter estimates are relatively unbiased by multidimensionality and supports a unidimensional structure (Reise et al., 2013). ARPB compares the absolute difference between parameter estimates between a unidimensional model and a bifactor (or other multidimensional) model. For the higher-order model, these indices were calculated following a Schmid-Leiman transformation (SLT), which orthogonalises the latent variables. Following a SLT, the lower-order factors in a higher-order model are like the specific factors in a bifactor model. Whereas the latent variables from a correlated factors model are like the lower-order factors *prior* to SLT and are useful for understanding their reliability as standalone constructs. Models found to have acceptable structural validity according to the goodness-of-fit, reliability and replicability indices progressed to the next step.

Third, to examine the robustness of the models selected in the previous step and ensure that it was appropriate to combine data from both samples, measurement invariance was tested across the CAP and CSC groups within a multigroup CFA framework. Specifically, we tested invariance in the following sequence as recommended by Brown (2014): 0) test the model separately in each group 1) test invariance of the overall factor structure simultaneously (i.e., configural invariance); 2) test the invariance of the factor loadings (i.e., metric or weak factorial invariance); 3) test the invariance of item intercepts/thresholds (i.e., scalar or strong factorial invariance); and 4) test the invariance of item residual variances (i.e., residual or strict invariance). For higher-order models, we assessed

invariance using the procedure described by Rudnev and colleagues (2018), which assess invariance of the first-order factor alone, and the invariance of the first and higher-order factors simultaneously at each level of invariance.

As the chi-square difference test is too sensitive to be informative in the context of large sample sizes, invariance was evaluated by comparing changes in CFI and RMSEA (Brown, 2014; Chen, 2007; Kline, 2015). Factor structures with changes in CFI less than .01 and RMSEA less than .015 (from the previous model in the sequence) were considered to demonstrate invariance across groups. Structures demonstrating adequate invariance progressed to the next step. If there was evidence for non-invariance, which would suggest that factor structures or that the interpretation of the latent variables differed across the groups, then alternative tests of measurement invariance would be considered, such as partial measurement invariance, and we conducted additional post-hoc analyses to determine whether there are cohort-specific associations between the personality traits and psychopathology dimensions.

Finally, associations with the personality traits were added to the model(s) found to have adequate structural validity. Regression analyses were conducted to obtain total effect estimates for the association between each trait and general psychopathology. Indirect-effects models were estimated to obtain total, direct, and indirect effect sizes at the specific factor and symptom levels. This approach enabled us to test associations between personality traits and psychopathology across three levels of the structural model, and to disentangle unique associations from those that are accounted for by broader dimensions of psychopathology (Conway et al., 2021).

3.3.6 *Availability of data and analysis code*

The Mplus output files for these analyses are publicly available and can be accessed online. Data may be shared with other researchers upon reasonable request.

3.4 Results

3.4.1 *Structure of adolescent psychopathology*

Goodness-of-fit indices are presented in Table 3.1 and standardised factor loadings for each of the latent variable models using WLSMV are shown in Table 3.2. All models, except the one-factor model, were found to have acceptable fit according to traditional fit indices (i.e., CFI and TLI >.95).

Based on the information criteria (AIC, BIC, SSABIC), the bifactor model was the best fitting model, followed by the correlated factors and higher-order models. However, standardised factor loadings in the bifactor model were generally weak for the specific factors and some loadings were negative. In particular, standardised factor loadings on the fear, distress and conduct/inattention specific factors were weak, and the alcohol use/harms related indicators mostly loaded poorly onto the general factor. Further, a Heywood case (i.e., negative residual variance) was detected in the bifactor model on the fear factor (item "restless or fidgety"). Thus, the bifactor model was not considered for further analysis. Standardised factor loadings in the one-factor, four-correlated factors and higher-order models were all positive and reasonably strong (> 0.4). In the higher-order model, standardised factor loadings indicate that the general psychopathology factor was more reflective of fear ($b = 0.948$) and distress ($b = 0.876$) dimensions followed by conduct/inattention ($b = 0.744$) and alcohol use/harms ($b = 0.388$) dimensions.

Table 3.1 Fit Indices for Different Structural Models of Adolescent Psychopathology (N=8,589)

Model	No. of parameters	WLSMV					MLR		
		χ^2	df	CFI	TLI	RMSEA (90% CI)	AIC	BIC	SSABIC
One-factor	58	10859.603	377	0.807	0.793	0.057 (0.056-0.058)	171456.65	171863.03	171678.72
Four correlated factors	64	2564.967	371	0.960	0.956	0.026 (0.025-0.027)	161016.20	161467.90	161264.50
Higher-order	62	2944.731	373	0.953	0.949	0.028 (0.027-0.029)	161203.80	161641.41	161444.38
Bifactor	87	2586.392	348	0.959	0.952	0.027 (0.026-0.028)	159600.40	160214.50	159938.00

Note. χ^2 = Chi-square statistic; df = degree of freedom; CFI = comparative fit index; TLI = Tucker–Lewis index; RMSEA = root mean square error of approximation; CI = confidence interval; AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; SSABIC = sample size adjusted BIC; WLSMV = weighted least square mean and variance adjusted. The bifactor could not be estimated using the default integration methods for MLR in Mplus. In order to compare the models, the MLR models were then estimated using the INTEGRATIONS = montecarlo(5000) command in Mplus.

Table 3.2 Standardised Factor Loadings on General and Specific (Fear, Distress, Alcohol Use/Harms, Conduct/Inattention) Factors Using WLSMV Estimator and Inter-Factor Correlations

Symptom	Item ID	One factor	Four factors	Higher-order		Bifactor	
		General	Specific	General	Specific	General	Specific
Fear							
Nervous in new situations	SD16	**0.559**	**0.668**	-	**0.677**	**0.665**	**-0.168**
Many fears	SD24	**0.498**	**0.640**	-	**0.637**	**0.624**	**-0.216**
Nervous	K61R	**0.422**	**0.556**	-	**0.546**	**0.498**	**0.315**
Restless or fidgety	K63R	**0.513**	**0.639**	-	**0.638**	**0.617**	**0.802**
Distress							
Somatic symptoms	SD3	**0.573**	**0.643**	-	**0.645**	**0.665**	**-0.010**
Worries	SD8	**0.642**	**0.721**	-	**0.721**	**0.728**	**0.066**
Unhappy	SD13	**0.755**	**0.842**	-	**0.844**	**0.812**	**0.204**
Hopeless	K62R	**0.754**	**0.828**	-	**0.826**	**0.638**	**0.590**
Depressed	K64R	**0.754**	**0.835**	-	**0.836**	**0.673**	**0.530**
Effort	K65R	**0.559**	**0.641**	-	**0.641**	**0.557**	**0.323**
Worthless	K66R	**0.810**	**0.881**	-	**0.881**	**0.656**	**0.682**
Alcohol use/harms							
Frequency	AUC1	**0.712**	**0.820**	-	**0.816**	**0.242**	**0.791**
Binge	AUC2	**0.836**	**0.915**	-	**0.912**	**0.235**	**0.901**
Quantity	AUC3	**0.709**	**0.820**	-	**0.819**	**0.236**	**0.796**
Acted bad	AH1	**0.831**	**0.942**	-	**0.942**	**0.305**	**0.902**
Shame/embarrassment	AH2	**0.892**	**0.952**	-	**0.952**	**0.337**	**0.894**
Neglected responsibilities	AH3	**0.807**	**0.933**	-	**0.935**	**0.310**	**0.892**
Tolerance	AH4	**0.845**	**0.943**	-	**0.945**	**0.405**	**0.850**
Personality change	AH5	**0.858**	**0.927**	-	**0.926**	**0.390**	**0.838**
Tried to cut down	AH6	**0.808**	**0.877**	-	**0.874**	**0.410**	**0.767**
Memory loss	AH7	**0.760**	**0.845**	-	**0.844**	**0.397**	**0.738**
Crazy	AH8	**0.857**	**0.917**	-	**0.917**	**0.486**	**0.772**
Conduct/inattention							
Restless	SD2	**0.586**	**0.734**	-	**0.736**	**0.496**	**0.648**
Temper	SD5	**0.563**	**0.729**	-	**0.734**	**0.609**	**0.278**
Fidgety	SD10	**0.633**	**0.794**	-	**0.799**	**0.547**	**0.673**
Fight a lot	SD12	**0.535**	**0.671**	-	**0.665**	**0.516**	**0.393**
Easily distracted	SD15	**0.602**	**0.732**	-	**0.732**	**0.573**	**0.410**
Lies or cheats	SD18	**0.543**	**0.667**	-	**0.661**	**0.535**	**0.329**
Steals	SD22	**0.522**	**0.652**	-	**0.644**	**0.511**	**0.358**
First order factors							
	Fear	-	-	**0.948**	-	-	-
	Distress	-	-	**0.876**	-	-	-
	Alcohol use/harms	-	-	**0.388**	-	-	-
	Conduct/ inattention	-	-	**0.744**	-	-	-
Inter-factor correlations							
Fear with Distress		-	**0.892**	-	-	0.00	0.00
Fear with Alcohol		-	**0.164**	-	-	0.00	0.00

Symptom	Item ID	One factor	Four factors	Higher-order		Bifactor	
		General	Specific	General	Specific	General	Specific
Use/harms							
Fear with Conduct/inattention		-	**0.668**	-	-	0.00	0.00
Distress with Alcohol Use/harms		-	**0.309**	-	-	0.00	0.00
Distress with Conduct/inattention		-	**0.624**	-	-	0.00	0.00
Alcohol use with Conduct/inattention		-	**0.431**	-	-	0.00	0.00

Note. SD = items from Strengths and Difficulties Questionnaire; AH = Alcohol Harms, items from Rutgers

Alcohol Problem Index (RAPI); K6 = Kessler 6 Plus scale (K6+); AUC = Alcohol use, AUDIT-C items;

WLSMV = weighted least square mean and variance adjusted. Factor loadings and correlations with a p value ≤

0.05 are shown in bold.

Model reliability indices are shown in Table 3.3. Overall, the general psychopathology factor showed good internal reliability (omega range 0.96-0.97) and construct reliability (H range 0.93-0.97) across the one-factor and higher-order models. The specific factors (fear, distress, alcohol use/harms and conduct/inattention), also showed good internal reliability (omegaS range 0.72-0.98) across the four-correlated factors and higher-order models. Construct reliability (H range 0.73-0.98) in the four-correlated factors model was good. However, in the higher-order model, only the alcohol use/harms specific factor had adequate reliability (i.e., $H > 0.7$).

Omega hierarchical subscale (OmegaHS) indices were low for fear, distress, and conduct/inattention factors, indicating that the majority of variance in these factors may be attributable to the general factor. However, OmegaHS was high for the alcohol use/harms factor in the higher-order model, suggesting that the variance in this specific factor may not be attributable to the general factor.

Overall, the general factor appears to have good reliability across the one-factor and higher-order models and the specific factors appear to have poor reliability, except for the alcohol use/harms factor, across the bifactor and higher-order models. Although the correlated factors model demonstrated better fit and reliability, the lower-order factors of a higher-order model are comparable to the correlated factors model (i.e., the correlated factors model is similar to the lower-order level of the higher-order model). Thus, support for the reliability of the factors in the correlated-factors model also suggests there is evidence for the lower-order factors of a higher-order model. Furthermore, the reliability indices for the lower-order factors are based on residualised factors (i.e., the Schmid-Leiman transformation is applied before the indices are calculated). As such, the lower-order factors following the SLT are very similar to the specific factors in a bifactor model whereas the correlated factors model gives a closer approximation to the lower-order factors (prior to the SLT) as standalone constructs. An advantage of the higher-order model is that it allows inclusion of both the narrower constructs and a general psychopathology factor. We therefore selected the higher-order model on the basis that there was evidence for the general factor having good reliability, along with the evidence for the reliability of the correlated/lower-order factors. However, model fit indices suggest that perhaps the higher-order general factor may not be required to account for the associations between factors over and above use of correlations. Therefore, additional external validity was assessed for the correlated factors model (See Appendix F Table S7). The higher-order model and standardised factor loadings are shown in Figure 3.2.

Table 3.3 Reliability Indices Alternative Models of Adolescent Psychopathology

Index	Factor	One factor	Four factor	Bifactor	Higher-Order (SLT)
H	General Psychopathology	**0.97**	-	**0.93**	**0.93**
	Fear	-	**0.73**	0.67	0.14
	Distress	-	**0.93**	0.66	0.54
	Alcohol use/harms	-	**0.98**	**0.97**	**0.96**
	Conduct/inattention	-	**0.88**	0.70	0.67
Omega	General Psychopathology	**0.96**	-	**0.97**	**0.97**
OmegaS	Fear	-	0.72	**0.79**	0.72
	Distress	-	**0.91**	**0.92**	**0.91**
	Alcohol use/harms	-	**0.98**	**0.98**	**0.98**
	Conduct/inattention	-	**0.88**	**0.87**	**0.88**
OmegaH	General Psychopathology	-	-	0.66	0.66
OmegaHS	Fear	-	-	0.07	0.07
	Distress	-	-	0.19	0.21
	Alcohol use/harms	-	-	**0.84**	**0.83**
	Conduct/inattention	-	-	0.35	0.39
ECV	General Psychopathology	-	-	0.42	0.44
ECV_S	Fear	-	-	0.04	0.01
	Distress	-	-	0.06	0.05
	Alcohol use/harms	-	-	0.40	0.41
	Conduct/inattention	-	-	0.08	0.09
ECV_S_NEW	Fear	-	-	0.36	0.10
	Distress	-	-	0.28	0.23
	Alcohol use/harms	-	-	**0.85**	**0.85**
	Conduct/inattention	-	-	0.42	0.45
PUC		-	-	**0.75**	**0.75**
ARPB		-	-	0.64	0.55

Note. Results in bold indicate acceptable reliability. Indices for Higher-Order model cannot be calculated, indices presented are based on Schmid-Leiman transformed (SLT) model. ECV = Explained Common Variance, ARPB = Absolute Relative Parameter Bias, ECV_S = Explained Common Variance of specific factors, H = measure of construct replicability, Omega = internal reliability of general factor/s, OmegaS = internal reliability of specific factor/s, OmegaH = Omega Hierarchical, OmegaHS = Omega Hierarchical subscale, PUC = Percent of Uncontaminated Correlations, SLT = Schmid-Leiman transformation.

Following inspection of factor loadings, model fit and reliability indices, additional models were examined including bifactor and higher-order models comprised of general internalising and general externalising factors (rather than a single general psychopathology factor). However, these models were found to have inadequate structural validity (see supplementary materials in Appendix F for further details).

Figure 3.2 Higher-Order Structural Model of Adolescent Psychopathology with Standardised Parameter Estimates
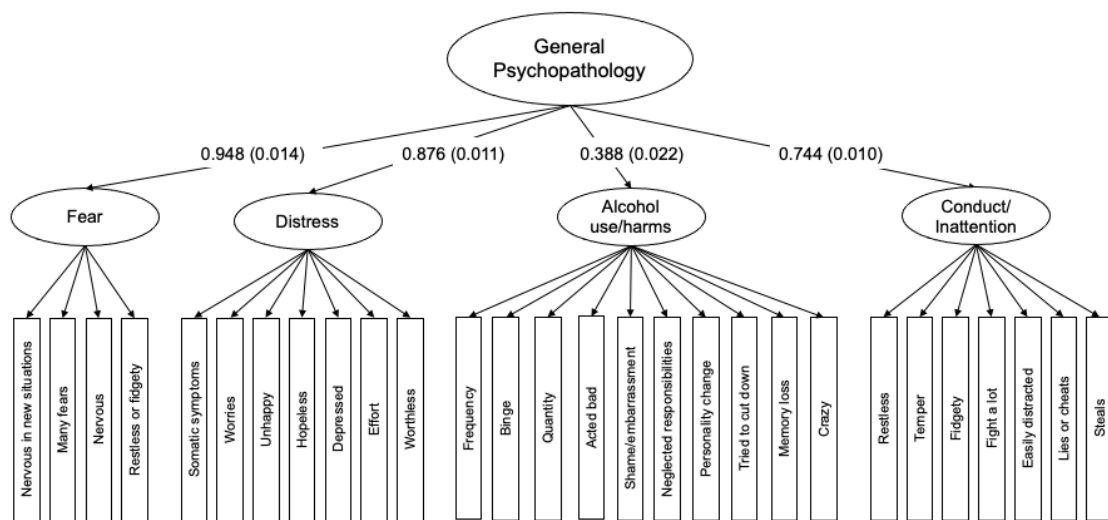
Note. All estimates statistically significant (p≤ 0.05). The standardised factor loadings for indicators of psychopathology are presented in Table 3.2.

The reliability of the higher-order model was further corroborated by measurement invariance tests, as shown in Table 3.4. The baseline model fit the data well in both the CAP and CSC cohorts. However, a high correlation (0.987) between two items (AH1, "Acted bad" and AH3, "Neglected responsibilities") was found in the CAP cohort. One of the items was removed (AH1, "Acted bad") from the model in subsequent analyses and this higher-order model demonstrated invariance across the CAP and CSC cohorts.

Table 3.4 Results of measurement invariances tests of a higher-order model of psychopathology

Model	χ^2	df	Comparison	$\chi^2 \Delta$	df	CFI	CFI Δ	RMSEA	RMSEA Δ
0. CAP participants (*n*=2260)	894.422*	346	NA	-	-	0.986	-	0.026 (0.024-0.029)	-
0. CSC participants (*n*=6329)	1926.085*	346	NA	-	-	0.952	-	0.027 (0.026-0.028)	-
1. Configural model	2664.86*	693	NA	-	-	0.973	-	0.026 (0.025-0.027)	-
2. First-order metric	2728.503*	717	1 vs. 2	252.347	24	0.972	-0.001	0.026 (0.025-0.027)	0
3. First- & second-order metric	2634.176*	719	2 vs. 3	6.562	2	0.974	0.002	0.025 (0.024-0.026)	-0.001
4. First-order scalar	2680.26*	743	3 vs. 4	151.608	24	0.974	0	0.025 (0.024-0.026)	0
5. First- & second-order scalar	2654.42*	747	4 vs. 5	24.551	4	0.974	0	0.024 (0.023-0.025)	-0.001
6a. Residual variances free	2687.871*	719	NA	-	-	0.973		0.025 (0.024-0.026)	-
6b. Residual variances fixed	2654.42*	747	6a vs. 6b	183.005	28	0.974	0.001	0.024 (0.023-0.025)	-0.001

Note. * *p* <.001. $\chi^2\Delta$ computed using Mplus DIFFTEST function; CFI Δ = difference in CFI from previous model; RMSEA Δ = difference in RMSEA from previous model. Initial baseline model in the CAP cohort revealed a correlation between AH1 & AH3 of 0.987. The AH1 item was removed from subsequent analyses, and the above table shows the results of measurement invariance tests with AH1 removed.

3.4.2 High-risk personality risk traits and associations with psychopathology dimensions and symptoms

The standardised total and direct effects are available in the supplementary material (Appendix F Tables S3 to S6). Figure 3.3 shows the standardised direct effect estimates and 99% confidence intervals for each of the personality traits and general and specific factors of psychopathology. Anxiety sensitivity, negative thinking, impulsivity, and sensation seeking all had significant, positive total effects with general psychopathology. Differential patterns of association emerged with specific factors of psychopathology (Figure 3.3) and in symptom-level analyses (Figure 3.4).

Figure 3.3 Effect sizes and standard errors for standardised direct effect of each personality trait on first order psychopathology factors (fear, distress, conduct/inattention, and alcohol use/harms) and total effect on general
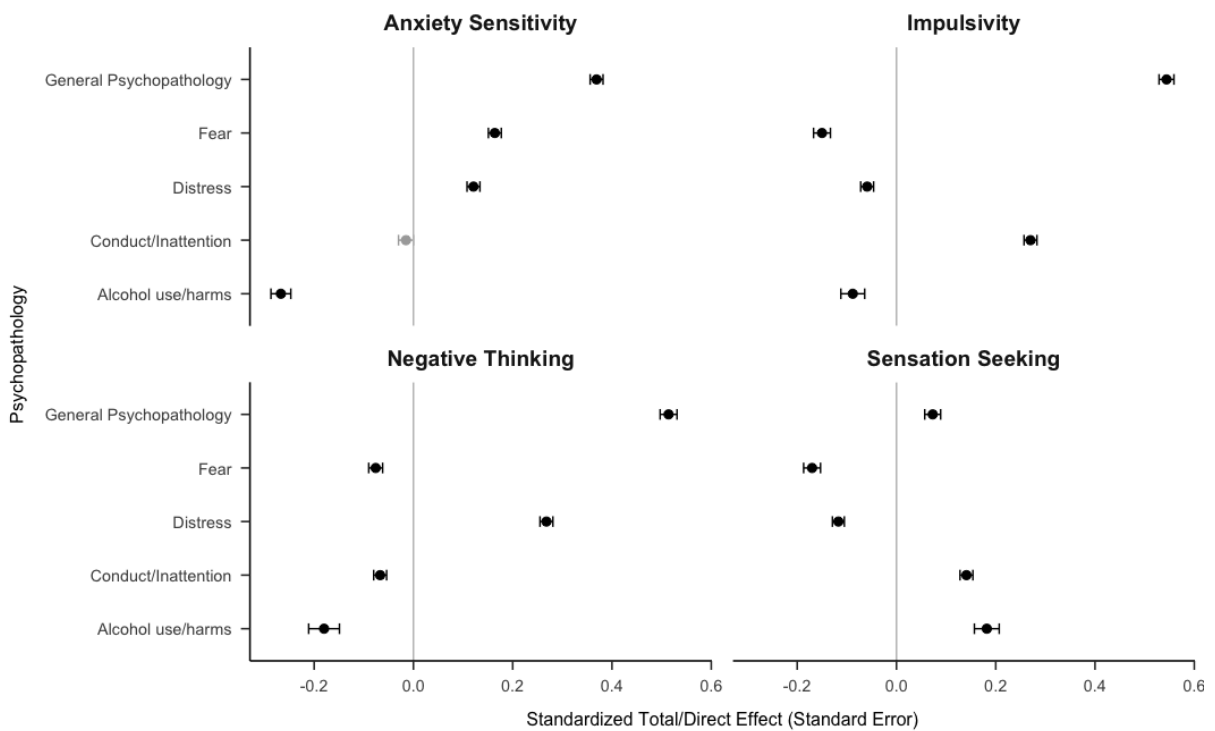
Note. Significant effects (p <.001) shown in black, non-significant (p >.001) effect shown in grey. Vertical grey solid lines show 0.0 effect size.

Figure 3.4 Effect sizes and standard errors for standardised direct effects of each personality profile on symptoms of psychopathology
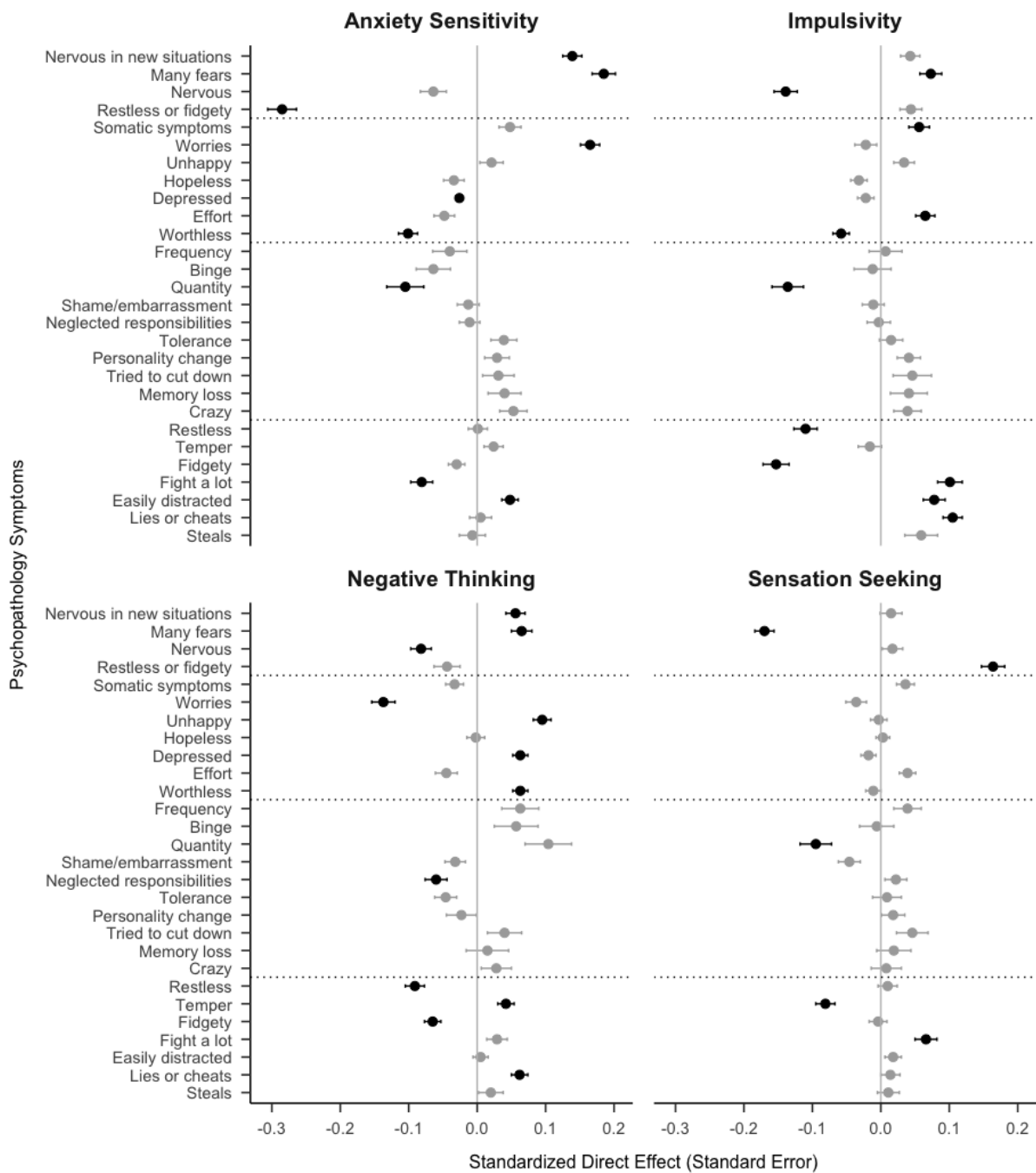
Note. Significant effects (p <.001) shown in black, non-significant (p >.001) effect shown in grey. Black dotted lines mark boundaries between first-order factors, vertical grey solid lines show 0.0 effect size.

Anxiety Sensitivity: Anxiety sensitivity had a significant positive direct effect with fear and distress, with only 58% and 65% of the variance accounted for by for general psychopathology (Appendix F Table S3). There was also a significant negative direct effect of anxiety sensitivity with alcohol use/harms, which represents a change in direction from the total effect (i.e., the direct effect reversed in sign compared to the total effect). This may be due to a suppressor effect, and it is likely that the association between alcohol use/harms and anxiety sensitivity was accounted for by general psychopathology (Watson et al., 2013). The direct effect with conduct/inattention was not statistically significant, indicating general psychopathology also accounted for the association between anxiety sensitivity and conduct/inattention symptoms. Overall, these results indicate that the adolescents with greater levels of anxiety sensitivity had significantly higher fear and distress levels (but not alcohol use/harms or conduct/inattention) than adolescents with lower levels of anxiety sensitivity.

Symptom-level indirect-effects models revealed that 24 of 28 associations between symptoms and personality risk traits were accounted by higher-order factors (i.e., general psychopathology, and the specific dimension that the symptom is loaded on). For the remaining direct effects, between 53% and 79% of the variance a large proportion of variance accounted for by the higher-order factors. There were significant direct effects for anxiety sensitivity and "nervous in new situations" and "many fears" with small direct effects ($b = 0.139$ and 0.185, $p < 0.001$, respectively), over and above levels of fear and general psychopathology. Similarly, there was a significant and small direct effect for anxiety sensitivity with "worries", over and above levels of distress and general psychopathology ($b = 0.165$, $p<0.001$). Finally, the direct effect between "easily distracted" and anxiety sensitivity had a small effect size ($b = 0.048$, $p<0.001$), over and above conduct/inattention and general psychopathology. All other symptom-level associations were either non-significant or the association was fully accounted for by the higher-order factors.

Negative thinking: Negative thinking, had a *positive* direct effect with distress, with only 50% of variance accounted for by general psychopathology ($b = 0.268$, $p<.001$; Appendix F Table S4). There were *negative* direct effects of negative thinking with fear, conduct/inattention, and alcohol use/harms specific factors ($b = -0.076$, -0.067, -0.180, respectively, ps $<.001$), representing a reversal of their total effects, indicating that the association was accounted for by general psychopathology. Overall, this indicates that adolescents with greater levels of negative thinking had significantly higher distress levels (but not fear, alcohol use/harms or conduct/inattention) than adolescents with lower levels of negative thinking.

At the symptom level, the associations with 21 of 28 symptoms were accounted for by higher-order factors. Of the remaining symptoms, the effects were small and between 75% and 88% of the variance was accounted for by the higher-order factors. Notably, there were significant direct effects for negative thinking and "unhappy", "depressed", and "worthless" ($b = 0.095$, 0.063 and 0.063, ps < 0.001, respectively), over and above distress and general psychopathology. The remaining symptom-level associations were either non-significant or the association was fully accounted for by the higher-order factors.

Impulsivity: Impulsivity had a small, positive direct effect with conduct/inattention, with only 53% of variance accounted for by general psychopathology ($b = 0.270$, $p < .001$). There were negative direct effects with alcohol use/harms, distress, and fear, which represented a reversal of their total effects, indicating that the association was accounted for by general psychopathology ($b = -0.088$, -0.059, -0.150, $p < .001$). Overall, this indicates that adolescents with greater levels of impulsivity had significantly higher conduct/inattention levels (but not fear, distress, or alcohol use/harms) than adolescents with lower levels of impulsivity.

At the symptom level, the associations between impulsivity and 22 of 28 symptoms were accounted by the higher-order factors. The remaining direct effects were small, with a large proportion of variance accounted for by the higher-order factors (72% to 83%). Notably, there were significant, positive direct effects with the symptoms "fight a lot", "easily distracted" and "lies or cheats", over and above the conduct/inattention and general psychopathology factors ($b = 0.101$, 0.078, 0.105, $p < .001$, respectively). Direct effects with alcohol use/harms were either fully accounted for by general psychopathology or were not significant, suggesting that the effects of impulsivity with alcohol use/harms were accounted for by the higher-order factors.

Sensation seeking: Sensation seeking had small, positive direct effects with alcohol use/harms and conduct/inattention factors with only 10% and 13% of variance accounted for by general psychopathology, respectively ($b = 0.182$, 0.141, ps < .001, respectively, see Appendix F Table S6). There were also small negative direct effects with distress and fear ($b = -0.117$, -0.170, ps < .001, respectively), and the association was mostly accounted for by general psychopathology (100% and 93%, respectively). Overall, this indicates that adolescents with greater levels of sensation seeking had significantly higher alcohol use/harms and conduct/inattention levels, and significantly lower levels of fear than adolescents with lower levels of impulsivity.

At the symptom level, the associations between sensation seeking and 26 of 28 indicators of psychopathology were accounted for by the higher-order factors. There was a small negative direct effect with "many fears" (b = -0.170, p <0.001), and a small positive direct effect with "fight a lot" (b = 0.066, p < 0.001).

3.5 Discussion

The current study extends prior work on the underlying structure of psychopathology by using a symptom-level approach and more rigorous methods of assessing the structural validity, reliability, and replicability of different statistical models. Our results align with previous research on the structure of psychopathology in adolescents and extend this work by illuminating important patterns of association with four high-risk personality traits that have implications for the development of targeted prevention and early intervention programs and our understanding of the underlying structure of psychopathology.

3.5.1 High-risk personality traits and psychopathology

Overall, the results indicate that personality measures could be used to identify adolescents at risk of developing general psychopathology, as well as certain specific forms of psychopathology. Findings showed that all four personality traits were associated with general and specific dimensions of psychopathology in theoretically expected ways and consistent with previous research. Consistent with the four-factor model of vulnerability, our results broadly indicated that inhibited traits (i.e., negative thinking and anxiety sensitivity) were more closely related to internalising forms of psychopathology (i.e., fear and distress), and disinhibited traits (i.e., impulsivity and sensation seeking) were associated with externalising forms of psychopathology (i.e., alcohol use/harms and conduct/inattention (Castellanos-Ryan & Conrod, 2012). These findings also align with prior research with young people indicating that neuroticism is positively associated with fear, distress and broad externalising dimensions (Watts, Poore, Lilienfeld, et al., 2019), and that different facets of neuroticism are differentially related to internalising and externalising dimensions (Brandes et al., 2019).

Given that associations between each of the four personality traits and substance use are well established, we anticipated that there would be positive associations with the alcohol use/harm factor. However, we found that only sensation seeking was positively associated with alcohol use/harms above and beyond general psychopathology in our sample. Because most research has

typically focused on a broad externalising factor and sensation seeking (Carragher et al., 2016; Castellanos-Ryan et al., 2016), our results are consistent with only one other study which reported on a bifactor model comprised of a general externalising factor and a substance use and conduct specific factor. Castellanos-Ryan and Conrod (2011) found that sensation seeking was uniquely linked with substance use and that impulsivity was related to the specific conduct factor (along with general externalising). This suggests that impulsivity may be related to broader externalising (i.e., the overlap between substance use and conduct/antisocial problems) and may also have unique links to conduct/behavioural problems, whereas sensation seeking may be more specifically related to substance misuse.

Consistent with previous research, we found that anxiety sensitivity was related to the internalising dimensions of fear and distress (Carragher et al., 2016; Castellanos-Ryan et al., 2016). However, we also found that anxiety sensitivity was related to lower alcohol use/harms after accounting for general psychopathology. Although this finding was unexpected, literature on the association between anxiety and alcohol use provides important context for interpreting our results. A recent systematic review revealed inconsistent findings for the association between alcohol use and anxiety (Dyer et al., 2019), and general population research has shown that anxiety may not increase alcohol use until after age 14 (Birrell et al., 2015). This is consistent with longitudinal research that has found dynamic associations among anxiety symptoms and alcohol use in early adolescence (Pardee et al., 2014). Specifically, young adolescents with higher initial levels of anxiety demonstrated more rapid increases in alcohol use, compared to peers with low or declining anxiety symptoms. In contrast, there was evidence to suggest that social anxiety specifically had protective effects in early adolescence before later increasing risk for substance misuse.

Within the present study, our finding that greater anxiety sensitivity was related to lower alcohol use/harms may mean that anxiety sensitivity does not have a meaningful unique association with alcohol use/harms, and that the association is better explained by general psychopathology. This is in line with findings from a recent systematic review and meta-analysis that found that anxiety sensitivity did not predict increases in alcohol use over time (Bartel et al., 2018). Alternatively, anxiety sensitivity may protect against alcohol related harms in early adolescence or delay the onset/escalation of alcohol use until later in adolescence. For example, as the alcohol use/harms factor in the present study is more heavily defined by alcohol-related harms, it is possible that anxiety sensitivity is protective against experiencing alcohol-related harms within this age group. Indeed, at the symptom level we found that anxiety sensitivity, impulsivity and (to a lesser extent) sensation seeking generally had negative direct effects with alcohol use items (i.e., frequency,

binge, and quantity), but positive direct effects with most of the alcohol harm items. Furthermore, given that in the present sample the prevalence of alcohol use and related harms was relatively low (which is expected given the mean age was 13 years), it is possible that anxiety sensitivity may delay the onset of alcohol use or slow the escalation of alcohol consumption until later in adolescence. For example, it's possible that once individuals with high anxiety sensitivity have experienced the stress dampening effects of alcohol, their association with alcohol may change such that anxiety sensitivity leads to greater alcohol use (Stapinski et al., 2015). Ultimately, longitudinal research is needed to further unpack the association between anxiety sensitivity, alcohol use, and psychopathology more broadly within the hierarchical-dimensional model of psychopathology.

As expected, negative thinking was associated with greater general psychopathology. Negative thinking was also directly related to distress, whereas associations with fear, alcohol use/harms and conduct/inattention were accounted for by general psychopathology. This suggests that negative thinking may be a broader risk factor for psychopathology and that interventions targeting negative thinking may result in reductions in a wide range of psychiatric symptoms. This is consistent with other research linking related traits, such as neuroticism, emotion regulation and dysregulation, to general psychopathology (Brandes et al., 2019; Haltigan et al., 2018; Santens et al., 2020). Indeed, it has even been suggested that general psychopathology reflects emotional/behavioural dysregulation broadly, and maps closely with trait neuroticism. Examination of the intersection between neurotic/inhibited traits and psychopathology over the adolescent period would be a valuable avenue for future research.

In the present study, the general psychopathology factor was more heavily defined by fear and distress dimensions, which complicates the conclusions that could be drawn from the associations between symptom dimensions and the personality traits. However, this is consistent with other studies of general psychopathology among adolescents which have shown that general psychopathology is typically defined by either thought disorder or internalising dimensions, depending on the symptom domains included in the model (Gomez et al., 2019; Watts et al., 2020). Current knowledge of the onset and temporal sequencing of internalising and externalising problems during adolescence suggest that it would be reasonable for a general psychopathology factor to be more reflective of internalising problems in early adolescence, as seen in the present study, compared to later adolescence (Birrell et al., 2015; Slade et al., 2015; Solmi et al., 2021).

3.5.2 Clinical and classification implications

Our findings have important implications for research on the early detection and prevention of mental and substance use disorders. Adolescents characterised by a fear of anxiety related sensations (anxiety sensitivity); a sense of hopelessness or low positive affect (negative thinking); difficulties regulating behavioural responses (impulsivity); and/or a desire for novel experiences (sensation seeking) may be at greater risk for developing a wide range of psychiatric problems. Individuals with higher levels of fear or distress may benefit most from receiving interventions targeting anxiety sensitivity and negative thinking; and adolescents with greater levels of alcohol misuse/harms or conduct/inattention problems may benefit from interventions targeting impulsivity and sensation seeking. Indeed, this assumption is corroborated by prior research demonstrating the effectiveness of a personality-targeted prevention program reducing substance use and co-occurring emotional problems by addressing these specific personality traits (Lammers et al., 2017; Newton et al., 2020; O'Leary-Barrett et al., 2013). However, further research is needed to determine whether these effects hold when examining substance use and mental health outcomes with a hierarchical-dimensional framework.

From a classification perspective, our findings support the utility of conceptualising psychopathology in a hierarchical-dimensional framework and align with prior research on the structure of psychopathology among adolescents. We found evidence for a higher-order model of psychopathology comprised of a general psychopathology dimension, and four specific dimensions: fear, distress, alcohol use/harms and conduct/inattention. While most previous research has selected a bifactor model of psychopathology, when considering model reliability and replicability along with traditional fit indices we found that a higher-order model fit the data best. Although this differs from past research, it is consistent with other more recent studies on hierarchical-dimensional models of psychopathology that have considered additional metrics of model reliability and replicability, underscoring the importance of assessing these indices in future research (Lees et al., 2020; Sunderland et al., 2020). Further, the four specific factors are consistent with prior research indicating that internalising may be comprised of fear and distress specific sub-dimensions and externalising may be comprised of substance misuse and conduct/behavioural sub-dimensions factors (Blanco et al., 2015; Levin-Aspenson et al., 2019; Platt et al., 2017; Slade & Watson, 2006). Further studies are needed, particularly longitudinal research, to confirm the validity and reliability of this underlying structure.

3.5.3 Limitations and future directions

There are some limitations that should be considered when interpreting our findings. Importantly, the present study is cross-sectional and cannot determine causality between personality and psychopathology and the generalisability of our findings are limited by the use of a non-representative community sample of Australian adolescents. Self-reported alcohol use/harms and conduct/inattention problems can be affected by self-report biases among, for example, children and young adults with ADHD and young adults following treatment (Hoza et al., 2012; Nirenberg et al., 2013; Sodano et al., 2021). Although the self-reported psychopathology outcomes did not have corroborating information, such as parent or teacher reports, data were collected using structured and validated instruments. Within this context, self-report methods have been shown to be a valid and reliable approach to measuring substance use and mental health outcomes in adolescents (Smith et al., 1995; Smith, 2007; van der Ende et al., 2020). In addition, although our study incorporated a wide variety of mental health symptoms, there are some notable forms of psychopathology that were not included. We were unable include psychosis-related symptoms, for example, as these were only assessed in one of the cohorts, and other common youth-onset disorders such as obsessive-compulsive disorder and eating pathology were not assessed. It is also worth noting that six of the seven items in the negative thinking subscale were worded positively (e.g., 'I am happy', 'I am very enthusiastic about my future') and then reverse scored. As such, this subscale may be more reflective of low positive thinking, rather than a direct measure of negative thinking. This is akin to evidence that negative and positive affect are independent dimensions, rather than opposite poles of a single dimension (Curran, Howard, et al., 2014; Jovanović & Gavrilov-Jerković, 2016; Watson & Tellegen, 1985). Ultimately, as this study was a secondary analysis of data from two RCT cohorts our data were limited to what was available. Additional evidence using more extensive and robust measures would be of value. Furthermore, longitudinal studies with greater coverage of psychiatric disorders may provide more comprehensive insight into the underlying structure of psychopathology and personality-based causal pathways.

Another potential limitation of this study concerns some of the observed differential patterns of association at the symptom level (i.e., symptom level negative direct effects, but positive total/higher-order effects), which could reflect potential measurement error or model misspecification. For example, the 'restless or fidgety' item from the K6 and the observed negative association with anxiety sensitivity and positive association with sensation seeking (positive direct effect) suggests this item could reasonably serve as an indicator of externalising/conduct/inattention. As such, an individual's interpretation of the question may

influence whether 'restless or fidgety' is an indicator of fear (e.g., restless/fidgety behaviour could be an expression of fear or anxiety-related symptoms) or conduct/inattention (e.g., restless/fidgety behaviour could be an expression of hyperactivity or attention problems). Similarly, the unique positive association between anxiety sensitivity and 'worries' (and negative association with negative thinking), may suggest that 'worries' would be a more appropriate indicator for fear rather than distress. It is also possible that the symptom level effects may reflect nuances in our sample. Thus, further longitudinal research is needed to confirm the reliability of these effects and clarify the placement of these potentially cross-loading symptoms.

3.5.4   Conclusions

Although there is extensive evidence linking personality with psychopathology, much of the research has failed to take into account the empirical structure of psychopathology. Findings from the present study describe the complex links between four high-risk personality traits and their associations with a hierarchical-dimensional framework of psychopathology in a large sample of early adolescents. The results support the four-factor model of vulnerability as a useful tool for identifying adolescents at risk of experiencing psychopathology and provide useful information for the development and optimisation of prevention and early intervention programs. Consistent with prior research, the present study indicates that a tendency toward low positive affectivity (negative thinking), a fear of anxiety related sensations (anxiety sensitivity); difficulties regulating behavioural responses (impulsivity) and/or a desire for novel experiences (sensation seeking) may be associated with a greater risk for developing mental health problems. Although further longitudinal research is needed to better understand the complex interactions between personality and psychopathology, the present study highlights the importance of symptom-level analyses in delineating personality related risk for psychopathology and the role personality may play in the development of individual symptoms through to broad dimensions of psychopathology. More broadly, the findings contribute to the ongoing the debate surrounding the structure and classification of adolescent psychopathology.

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Chapter 4

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Co-development of general psychopathology and high-risk personality traits during adolescence

Preface

Chapters 2 and 3 sought to improve our understanding of the structure of psychopathology among young people and adjudicate between competing models using modern statistical approaches and more rigorous tests of external validity. However, as identified in Chapter 2, there are only a small number of longitudinal studies examining general psychopathology in young people, highlighting the need for more causally driven research. Furthermore, the findings from the systematic review (Chapter 2) highlighted the close relationship between psychopathology and certain aspects of personality, particularly neuroticism and behavioural disinhibition. Capitalising on the same cohort and the best fitting higher-order model of psychopathology from Chapter 3, this chapter examines the co-development of general psychopathology and high-risk personality traits over three years (13 to 16 years of age). This is critical to explore given how little is known about what general psychopathology represents, or the factors that contribute to the development and maintenance of psychopathology during adolescence.

This chapter addresses the fourth research question of this thesis: *"How do high-risk personality traits and general psychopathology influence each other during adolescence?"* This study is currently under review with the Journal of Psychopathology and Clinical Science.

Supplementary materials are available in Appendix G and online (https://osf.io/xdftb), along with analysis code and output.

4.1 Abstract

There is strong evidence for a general psychopathology dimension which captures covariance among all forms of psychopathology, however questions remain about what this dimension represents and whether certain aspects of personality underlie general psychopathology. This study examined the co-development of general psychopathology and four high-risk personality traits: anxiety sensitivity, negative thinking, sensation seeking, and impulsivity. Data from the control groups of two large randomised controlled trials of Australian adolescents (N = 2,083, mean age at baseline = 13.49 years) were analysed. Adolescents completed self-report measures of psychopathology symptoms and personality at baseline, one-, two-, and three-years post-baseline. A general psychopathology dimension was extracted from a higher-order model. Latent curve models with structured residuals, controlling for age, sex, and cohort, showed that spikes in anxiety sensitivity and impulsivity were associated with spikes in general psychopathology at subsequent time points, and spikes in general psychopathology were associated with spikes in negative thinking at subsequent time points. These findings contribute to our understanding of the substantive meaning and validity of general psychopathology and have implications for personality-based prevention and intervention targets.

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4.2 Introduction

Most mental disorders emerge during adolescence with the peak age of onset for all disorders being 14.5 years (Solmi et al., 2021). Personality is an important risk factor for psychopathology, with childhood temperament and personality associated with increased odds of experiencing subsequent mental health problems (De Fruyt et al., 2017; Tackett & Mullins-Sweatt, 2021). Despite well-established links between personality and psychopathology, relatively few longitudinal studies have examined co-development of personality and psychopathology over adolescence (Wilson & Olino, 2021). Extant research has tended to focus on non-pathological (e.g., five-factor model or Big 5) traits, such as neuroticism and extroversion (Etkin et al., 2021; Mann et al., 2020) and prospective associations with specific disorders or symptom domains (De Bolle et al., 2012, 2016). Furthermore, the advent of hierarchical-dimensional models of psychopathology and consistent evidence for a general factor capturing comorbidity among all mental disorders, provides new avenues for examining personality-psychopathology associations (Kotov et al., 2021). However, the substantive meaning of what a general factor of psychopathology actually represents remains unresolved. Whilst most evidence to date suggests general psychopathology likely represents a complex interaction between impulsive responses and negative emotionality or affectivity (Smith et al., 2020; Southward et al., 2022), very little is known about the mechanisms by which different aspects of personality are related to general psychopathology.

Personality and psychopathology can be related in multiple ways (Tackett & Mullins-Sweatt, 2021). Personality can predispose people to experiencing certain mental health problems (vulnerability/risk model); the experience of psychopathology can lead to changes in personality (scar/complication model); or personality can impact the presentation or severity of psychopathology but not necessarily play a causal role (pathoplasty/exacerbation model). It is also possible that personality and psychopathology sit on the same continuum, ranging from general traits and subclinical characteristics through to mental disorders (continuum/spectrum model). These aren't necessarily contradictory explanations, but rather highlight the range of plausible mechanisms underlying the association between personality and psychopathology (Tackett & Mullins-Sweatt, 2021; Wilson & Olino, 2021).

There are few longitudinal studies examining associations between personality and psychopathology within the context of hierarchical-dimensional conceptualisations of

psychopathology. Using cross-lagged panel models, Etkin and colleagues (2022) examined associations between the Big 5 personality traits and a bifactor model of psychopathology in adolescents. Results indicated bidirectional associations between general psychopathology and neuroticism from ages 14 to 15, suggesting evidence for both scar/complication and pathoplasty/exacerbation models (Etkin et al., 2022). There were also small prospective pathoplasty effects for extroversion and conscientiousness, such that high extroversion and low conscientiousness predicted high general psychopathology from ages 15 to 16. These findings echo earlier work by De Bolle and colleagues (2012, 2016) who found evidence for the continuum/spectrum, pathoplasty and scar/complication models in relation to general personality traits (emotional stability, extroversion, imagination, benevolence, and conscientiousness), maladaptive traits (disagreeableness, emotional instability, introversion, and compulsivity), and internalising and externalising psychopathology during the transition from childhood to early adolescence. Using the same sample, De Bolle and colleagues (2016) compared the strength of association and found that maladaptive traits were more closely related to internalising and externalising than general traits.

It is possible that previous studies reporting associations between Big 5 traits and general and specific dimensions of psychopathology captured general or 'superficial' effects, beneath which are nuanced and dissociable patterns of association between facets of personality and psychopathology (e.g., Brandes et al., 2019).For example, bidirectional associations have been consistently found between neuroticism and multiple forms of mental health problems, including general psychopathology (Brandes et al., 2019; Brandes & Tackett, 2019). However, neuroticism itself is comprised of several specific characteristics, or facets, and it is not yet known if or how bidirectional associations are driven by these distinct facets. Some facets of personality may contribute to the development of general psychopathology, while other facets may be influenced by prior general psychopathology. Understanding these dynamics may be especially useful, not only for the identification of at-risk adolescents, but may also indicate specific symptom domains of concern or potentially point to cognitive or behavioural mechanisms driving the development of general psychopathology. This has significant potential for the identification of more salient intervention targets.

An alternative to studying the Big 5 traits is to focus on more granular or maladaptive traits with strong links to mental health problems. For example, the four-factor model of vulnerability describes four personality-based risk factors substance use problems and co-occurring

psychopathology (Castellanos-Ryan & Conrod, 2012). These four traits are negative thinking, anxiety sensitivity, impulsivity and sensation seeking. Negative thinking, which reflects a tendency to experience hopelessness and low positive affect, and anxiety sensitivity, which refers to a fear of anxiety-related sensations (arising from beliefs that such sensations could lead to harmful consequences) are both associated with mood and anxiety related problems, as well as substance use problems. Impulsivity, which broadly reflects a failure to inhibit behaviours likely to result in negative consequences, is associated with conduct and substance use problems. In contrast, sensation seeking, which reflects a willingness to take risks for the sake of novel experiences, is associated more specifically with substance use problems. Although initially conceptualised as a model of risk for substance use problems among adolescents, the four traits have cross-sectional and prospective associations with multiple forms of psychopathology, including internalising, externalising and general psychopathology (Afzali et al., 2017; Carragher et al., 2016; Castellanos-Ryan et al., 2016; Lynch et al., 2023; Chapter 3; Newton, Barrett, et al., 2016). One study reported that negative thinking and impulsivity assessed at age 14 were stronger predictors of general psychopathology at age 16 than neuroticism (Castellanos-Ryan et al., 2016).

A critical limitation of previous studies is the reliance on statistical methods that do not separate between-person and within-person effects (Curran, Howard, et al., 2014; Hamaker et al., 2015; Hopwood et al., 2022). Specifically, researchers have found that results from cross-lagged panel models (CLPM) can lead to inaccurate conclusions about within-person associations between two constructs, especially when the constructs are 'trait' like. Thus, associations between personality and psychopathology, which both have trait like elements, identified in CLPM analyses may have been incorrectly interpreted as within-person associations. Similarly, although latent growth models and other longitudinal models help describe associations overtime, they do not provide insight into changes in associations from one time to the next, and thus can't be used to test different explanatory models of personality-psychopathology associations.

New statistical methods, such as the latent curve model with structured residuals (LCM-SR; or the closely related random intercept cross-lagged panel model), disaggregate between-person and within-person sources of variance, offering a more accurate test of different explanatory models than previously possible (Curran, Howard, et al., 2014). LCM-SR allows determination of whether fluctuations in a construct *within* individuals at one time point are associated with fluctuations in another construct at future time point (or at the same time point), after accounting for differences *between* individuals (e.g., sex or gender). For example, if someone is experiencing higher levels

of impulsivity than they usually do, does this predict increases or decreases in general psychopathology at the next time point? Or do changes in general psychopathology at one time predict fluctuations in personality at the next time? The theory underlying aetiological models of psychopathology and personality posits that effects occur within a given individual, rather than across individuals (Hopwood et al., 2022). Therefore, methods that allow for direct assessment of within-person variances are essential to advancing our understanding of the aetiological mechanisms underlying personality and psychopathology.

4.2.1 Present study

There are very few longitudinal studies examining the co-development of personality and general psychopathology over adolescence (Wilson & Olino, 2021). Furthermore, previous research has relied on methods which tend to conflate between-person and within-person sources of variance, potentially masking important associations or leading to erroneous conclusions. To address these gaps, we examined associations between general psychopathology and four high-risk personality traits during the transition from early adolescence to mid-adolescence using novel and sophisticated statistical techniques to disaggregate between-person and within-person sources of variance.

4.3 Methods

4.3.1 Participants

This study examined longitudinal data from two large cluster randomised controlled trials investigating the effectiveness of eHealth prevention programs in Australia – the Climate and Preventure (CAP) and Climate Schools Combined (CSC) studies. The interventions evaluated in these trials aimed to prevent the uptake and reduce harmful substance use and/or mental health problems. Given that effects of the intervention may alter the natural progression of personality and psychopathology developmental processes, only students allocated to the control conditions of these trials are included. Research protocols have been published elsewhere (Newton et al., 2012; Maree Teesson et al., 2014), as well as the main intervention outcomes (Newton, Conrod, et al., 2016; Maree Teesson et al., 2020). All students, including those allocated to the control condition, received health education as usual during their Year 8 Health and Physical Education curriculum lessons. In Australia, health education, including lessons on mental health, alcohol and drugs is a mandatory part of the secondary-school health curriculum. Students completed surveys

in class, through either an online or paper survey. This study examined data collected at baseline, 12-, 24- and either 30- or 36-months post-baseline[3].

4.3.2   Measures

4.3.2.1 High-risk personality traits

Four personality traits associated with increased risk for substance use and co-occurring mental health problems were assessed using the Substance Use Risk Profile Scale (SURPS). The SURPS is a 23-item measure of personality risk for substance use problems and co-occurring psychopathology, comprised of four distinct subscales: negative thinking, anxiety sensitivity, sensation seeking and impulsivity (Woicik et al., 2009). The SURPS has demonstrated good validity and reliability as a measure of personality-related risk for substance use and co-occurring psychopathology among young people (Castellanos-Ryan et al., 2013; Newton, Barrett, et al., 2016; Woicik et al., 2009). Group and longitudinally (i.e., age, sex, and cohort) invariant factor scores for each subscale were estimated using moderated non-linear factor analysis (see below for further details).

4.3.2.2 General psychopathology

General psychopathology was estimated as a latent factor drawn from a higher-order model of adolescent psychopathology delineated in a separate study (Lynch et al., 2023; Chapter 3). In that study, baseline data from the CAP and CSC studies were used to examine multiple competing structures of psychopathology, including correlated factors, bifactor and higher-order models. Results indicated that a higher-order model comprised of a general psychopathology dimension, and four specific dimensions (fear, distress, alcohol use/harms and conduct/inattention) outperformed alternative structures when compared using contemporary model reliability and replicability indices along with traditional fit indices. Measurement invariance tests also indicated the higher-order structure was invariant across the CAP and CSC cohorts. For the present study, group and longitudinally invariant factor scores were extracted for general psychopathology via moderated non-linear factor analysis (MNLFA).

Indicators of the lower order factors included items from the Strengths and Difficulties

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[3] The fourth data collection occurred approximately 30-months post-baseline in the CSC cohort, and 36-months post-baseline in the CAP cohort.

Questionnaire (SDQ; Goodman, 2001), the Kessler Psychological Distress Scale (K6; Kessler et al., 2002), Rutgers Alcohol Problem Index (RAPI; Neal et al., 2006), and two items about quantity of alcohol consumed in the past 6 months and frequency of drinking at or above low risk levels in the past 6 months (McBride et al., 2004). Wording of the specific items and their corresponding factors can be found in the supplementary material (Appendix G Table M1).

4.3.3 Analysis plan

Analyses were conducted in two broad phases: 1) measurement invariance assessment using moderated nonlinear factor analysis, and 2) assessment of time-specific and developmental trajectories using latent curve models with structured residuals (LCM-SR). Both phases involved sequential, iterative model building processes. Step-by-step details for each phase of analysis are provided in the supplementary material (Appendix G). The overarching analytic strategy is briefly summarised below.

All analyses were conducted in Mplus version 8.4 for Mac (Muthén & Muthén, 2017). Mplus input files were created with the assistance of R packages aMNLFA (Automated Moderated Nonlinear Factor Analysis Using 'M-plus'; Gottfredson et al., 2019) and Mplus Automation (Hallquist & Wiley, 2018). Analysis code and Mplus output files are available online.

4.3.3.1 Measurement invariance

MNLFA was used to assess the measurement invariance of personality and psychopathology outcomes and generate factor scores adjusted for any measurement bias (Curran, McGinley, et al., 2014). The adjusted factors were then used in subsequent analyses. Building on the multiple-indicators-multiple causes approach to measurement invariance, MNLFA simultaneously assesses differential item functioning (DIF) and measurement invariance across multiple grouping variables and ultimately aims to generate factors scores that have been corrected for measurement bias. Drawing on the general procedures outlined by Bauer (2017) and Gottfredson and colleagues (2019), we examined DIF and mean and variance impact effects in an iterative process. As recommended by Curran and colleagues (2014), the MNLFA procedure was applied to a cross-sectional calibration sample (i.e., one measurement per participant randomly drawn from the set of available repeated measures for each participant) to preserve the assumption of independence. Once a final model was reached, the model parameters were then applied to the full longitudinal dataset to generate adjusted factors scores for all available measurements for each participant.

The factor scores used in the main analyses were adjusted for potential measurement bias relating to age, sex, and cohort (i.e., CAP or CSC). For personality, each trait was assessed in a series of univariate analyses (i.e., each SURPS subscale was examined separately). For general psychopathology, the lower-order factors from the previously described higher-order model were assessed separately for invariance in a series of univariate analyses. The final parameter values from the MNLFA procedure were then used to specify a higher-order model and generate adjusted factor scores for general psychopathology. Further details on this procedure are provided in the supplementary materials (Appendix G).

4.3.3.2 Latent curve models with structured residuals

Next, we estimated a series of LCM-SR models to examine associations between general psychopathology and the four high-risk personality traits (Curran, Howard, et al., 2014; Wellman et al., 2020). We 1) estimated univariate models to identify the optimal shape of growth for each construct and specified structured residuals for each time point, 2) tested the inclusion of autoregressive paths using the best-fitting model, and 3) combined the best-fitting univariate models into a series of bivariate models. Once an unconditional LCM-SR model was established we then regressed the latent curve and intercept factors onto baseline age, sex, and study cohort to account for any attributable variance.

Goodness-of-fit for all models was assessed using root mean square error of approximation (RMSEA), comparative fit index (CFI) and Tucker-Lewis index, where RMSEA values < 0.06, and CFI and TLI values > .95 indicate close fit (TLI; Brown, 2014). Models were also compared using the information criteria, including the Akaike information criterion (AIC), Bayesian information criterion (BIC), and the sample-size adjusted BIC (aBIC), where lower values indicate superior fit (Raftery, 1995). Changes in model fit between nested models were formally evaluated with the likelihood ratio test using a scaled difference chi-square. If there was no statistically significant improvement in model fit, the best fitting model was determined based on overall fit, parsimony, and theoretical basis for components.

4.3.3.3 School-level clustered data

As the data were collected through schools (n=26, average cluster size 79.923), we assessed the school-level intraclass correlation coefficients (ICCs) for all constructs at each time point (see

Appendix G Table S1). The ICC ranged from 0.016 to 0.080, indicating there was only a small amount of variance at the school level. Attempts to account for school-level clustering resulted in model convergence issues, primarily due to the small number of schools. Recent simulation studies have shown that ignoring the clustered data structure has minimal impact, with substantive interpretations consistent across models that do and do not account for school-level clustering (Bailey et al., 2020; Choi, 2022). As such, we proceeded without accounting for school-level clustering.

4.4 Results

Table 4.1 presents demographics and attrition rates for the total sample and separately for each cohort (combined N = 2,083, mean age 13.49 years, SD = 0.44). The overall retention rate at the final time point (30- or 36-months post baseline) was 71% (1,485/2,083).

Table 4.1 Participant demographic information and follow up rates

		Cohort	
	Overall, N = 2,083[1]	**CSC**, N = 1,556[1]	**CAP**, N = 527[1]
Age (years)	13.49 (0.44)	13.50 (0.47)	13.45 (0.36)
(Missing)	2	0	2
Sex			
Male	691 / 2,081 (33%)	517 / 1,556 (33%)	174 / 525 (33%)
Female	1,390 / 2,081 (67%)	1,039 / 1,556 (67%)	351 / 525 (67%)
(Missing)	2	0	2
School type			
Public	493 / 2,083 (24%)	398 / 1,556 (26%)	95 / 527 (18%)
Private	713 / 2,083 (34%)	520 / 1,556 (33%)	193 / 527 (37%)
Catholic	877 / 2,083 (42%)	638 / 1,556 (41%)	239 / 527 (45%)
Country of birth			
Australia	1,745 / 2,073 (84%)	1,278 / 1,549 (83%)	467 / 524 (89%)
Other English-speaking country	120 / 2,073 (5.8%)	86 / 1,549 (5.6%)	34 / 524 (6.5%)
Non-English-speaking country	208 / 2,073 (10%)	185 / 1,549 (12%)	23 / 524 (4.4%)
(Missing)	10	7	3
Follow up			
Baseline	2,083 / 2,083 (100%)	1,556 / 1,556 (100%)	527 / 527 (100%)
12-month	1,799 / 2,083 (86%)	1,327 / 1,556 (85%)	472 / 527 (90%)
24-month	1,674 / 2,083 (80%)	1,227 / 1,556 (79%)	447 / 527 (85%)
30-month	1,078 / 1,556 (69%)	1,078 / 1,556 (69%)	0 / 0 (0%)
36-month	407 / 527 (77%)	0 / 0 (0%)	407 / 527 (77%)
30- / 36-month	1,485 / 2,083 (71%)	1,078 / 1,556 (69%)	407 / 527 (77%)

Note. [1] Mean (SD); n / N (%)

Participants who were present at baseline only, compared to participants who completed any follow ups, were more likely to have higher negative thinking at baseline (OR 1.37 95% CI 1.01 to 1.85, *p* = .044). No other differences emerged across sex, study cohort or mean baseline scores for general psychopathology, anxiety sensitivity, impulsivity or sensation seeking (see Appendix G Tables S2 to S4).

4.4.1.1 Measurement invariance

Results from MNLFA analyses indicated that factor scores generated from MNLFA models were highly correlated with a base model without non-invariance terms (*r* = 0.94 to 1.00, *p*<.001, Appendix G Table S5) suggesting factor scores generated by our model were robust against non-invariance across sex, age, and cohort. To reduce model complexity in subsequent analyses, parameter estimates from the final MNLFA models were used to generate sex, cohort, and age invariant factor scores for each construct.

4.4.2 Preliminary unconditional univariate and bivariate latent curve models with structured residuals

A summary of the model fit and nested model comparisons is provided in the supplementary material (Appendix G Table S6). Below we briefly summarise key decisions and outcomes.

4.4.2.1 Unconditional univariate between-person models

For all constructs, a model with a random intercept and linear slope fit the data well. Quadratic slope models were also examined for each construct; however, there were negative variances present in all of these. Inspection of the mean observed scores at each time point also indicated that a linear model may be more suitable for the data. Therefore, quadratic slope models were excluded from subsequent analyses.

4.4.2.2 Unconditional univariate within-person models

Next, the intercept and linear growth curve models were expanded to include autoregressive effects between time-adjacent structured residuals to determine the stability of each construct over time. For general psychopathology, allowing the autoregressive parameters to be freely estimated appeared to fit the data better (Model 17) as determined via examining model fit indices. A negative residual variance was detected at T4; however, this issue did not appear in subsequent

bivariate models. Thus, Model 17 was retained.

For negative thinking, there was no statistically significant difference between the freely estimated versus constrained models, however inspection of the model fit indices suggests that the constrained model was a slightly better fit. Further, the constrained model improved fit over the base intercept and linear slope model. For each of the remaining personality constructs, the inclusion of autoregressive parameters did not improve fit according to the chi-square differences test compared to the base intercept + linear slope models. Given that this also indicates that the inclusion of the autoregressive parameters does not degrade model fit, these were retained in subsequent analyses (Curran, Howard, et al., 2014). The chi-square differences test comparing freely estimated versus constrained autoregressive parameters were also non-significant, however the fit indices overall indicated the constrained models fit slightly better. Thus, for all personality constructs the models with autoregressive parameters constrained to equality were selected for subsequent analyses.

4.4.2.3 Unconditional bivariate models

Univariate models for each personality construct and general psychopathology were combined into unconditional bivariate models without cross-lagged parameters between constructs for each of the personality and general psychopathology models (Models 27, 34, 43 and 50). These models all had acceptable fit and were then expanded to test the inclusion of bidirectional cross-lags.

Specifically, we added the regression of the residual for general psychopathology on the residual for each personality construct, first constraining these to equality (Models 28, 35, 42 and 51), and then allowing them to be freely estimated (Models 29, 36, 43 and 52). For all constructs, results of the chi-square differences test indicated that these regressions did not improve or degrade model fit, nor was there a difference between the constrained vs. unconstrained models. Inspection of model fit indices indicated that the constrained models (Models 28, 35, 42 and 51) fit the data marginally better and were thus retained for all constructs. We then removed these regressions and repeated the process for the regression of residual personality on residual general psychopathology. There was again no indication that the inclusion of these regressions improved, or degraded model fit, nor was there a difference between the constrained (Models 30, 37, 46, 53) and unconstrained models (Models 31, 38, 47, 54). Thus, the constrained models were retained (Models 30, 37, 46, 53). Both sets of regressions were then combined into unconditional bivariate models with general psychopathology (Models 32, 39, 48, 55), and these fit the data well.

The final models were estimated with study cohort, sex, and age at baseline as time-invariant covariates. Summaries of the standardised and unstandardised model results are provided in the supplementary material (Appendix G Tables S7-S10). The within-person results from these final models are described below. Table 4.2 displays the standardised and unstandardised within-person coefficients, and Table 4.3 displays the autoregressive coefficients (i.e., the within-construct, within-person effects).

Table 4.2 Standardised and unstandardised parameter estimates for the within-person concurrent and cross-lagged paths

	Vulnerability / pathoplasty			Complication / scar			Concurrent / continuum			
	Pers. T1 -> P T2	Pers. T2 -> P T3	Pers. T3 -> P T4	P T1 -> Pers. T2	P T2 -> Pers. T3	P T3 -> Pers. T4	Pers. T1 -> P T1	Pers. T2 -> P T2	Pers. T3 -> P T3	Pers. T4 -> P T4
Negative Thinking x General Psychopathology										
b (SE)	0.097 (0.051)	0.097 (0.051)	0.097 (0.051)	**0.105 (0.04)****	**0.105 (0.04)****	**0.105 (0.04)****	**0.133 (0.046)****	**0.128 (0.02)*****	**0.128 (0.02)*****	**0.128 (0.02)*****
β (SE)	0.077 (0.043)	0.087 (0.046)	0.112 (0.059)	**0.107 (0.044) ***	**0.109 (0.043) ***	**0.134 (0.054) ***	**0.399 (0.089) *****	**0.324 (0.042) *****	**0.305 (0.038) *****	**0.442 (0.056) *****
Anxiety Sensitivity x General Psychopathology										
b (SE)	**0.080 (0.037)***	**0.080 (0.037)***	**0.080 (0.037)***	0.035 (0.027)	0.035 (0.027)	0.035 (0.027)	**0.095 (0.013)*****	**0.078 (0.011)*****	**0.078 (0.011)*****	**0.078 (0.011)*****
β (SE)	**0.055 (0.026) ***	**0.067 (0.031) ***	**0.105 (0.054)**	0.042 (0.031)	0.044 (0.033)	0.041 (0.031)	**0.319 (0.040) *****	**0.219 (0.029) *****	**0.230 (0.030) *****	**0.347 (0.090) *****
Impulsivity x General Psychopathology										
b (SE)	**0.072 (0.033)***	**0.072 (0.033)***	**0.072 (0.033)***	0.094 (0.048)	0.094 (0.048)	0.094 (0.048)	**0.155 (0.052)****	**0.121 (0.021)*****	**0.121 (0.021)*****	**0.121 (0.021)*****
β (SE)	**0.071 (0.035) ***	**0.085 (0.040) ***	**0.127 (0.065) ***	0.081 (0.044)	0.089 (0.046)	0.083 (0.045)	**0.354 (0.079) *****	**0.243 (0.036) *****	**0.272 (0.038) *****	**0.413 (0.104) *****
Sensation Seeking x General Psychopathology										
b (SE)	-0.013 (0.043)	-0.013 (0.043)	-0.013 (0.043)	-0.028 (0.031)	-0.028 (0.031)	-0.028 (0.031)	-0.005 (0.02)	0.003 (0.01)	0.003 (0.01)	0.003 (0.01)
β (SE)	-0.007 (0.023)	-0.011 (0.037)	-0.030 (0.096)	-0.031 (0.034)	-0.035 (0.039)	-0.038 (0.042)	-0.023 (0.096)	0.009 (0.029)	0.010 (0.032)	0.051 (0.280)

Notes. P = general psychopathology, Pers. = personality; *b* = unstandardised estimate; β = standardised estimate, SE = standard error. *p<.05, **P<.01, ***p<.001

Table 4.3 Standardised and unstandardised parameter estimates for the within-person autoregressive paths

	General Psychopathology			Personality		
	T1 -> T2	T2 -> T3	T3 ->T4	T1 -> T2	T2 -> T3	T3 ->T4
Negative Thinking						
b (SE)	0.185 (0.098)	**0.220 (0.055)*****	0.070 (0.121)	0.131 (0.069)	0.131 (0.069)	0.131 (0.069)
β (SE)	0.169 (0.010)	**0.218 (0.052) *****	0.084 (0.139)	0.116 (0.064)	0.122 (0.065)	**0.159 (0.078) ***
Anxiety Sensitivity						
b (SE)	**0.231 (0.083)****	**0.204 (0.044)*****	-0.131 (0.153)	**0.123 (0.046)****	**0.123 (0.046)****	**0.123 (0.046)****
β (SE)	**0.203 (0.083) ***	**0.228 (0.046) *****	-0.192 (0.257)	**0.113 (0.041) ****	**0.114 (0.044) ****	**0.128 (0.048) ****
Impulsivity						
b (SE)	**0.233 (0.092)***	**0.202 (0.049)*****	-0.136 (0.169)	0.109 (0.074)	0.109 (0.074)	0.109 (0.074)
β (SE)	0.208 (0.096)	**0.228 (0.050)**	-0.2 (0.287)	0.103 (0.073)	0.108 (0.143)	0.113 (0.121)
Sensation Seeking						
b (SE)	0.200 (0.127)	**0.183 (0.039)*****	-0.306 (0.231)	0.020 (0.072)	0.020 (0.072)	0.020 (0.072)
β (SE)	0.166 (0.120)	**0.209 (0.041) *****	-0.8 (1.315)	0.015 (0.052)	0.02 (0.069)	0.025 (0.025)

Notes. *b* = unstandardised estimate; β = standardised estimate, SE = standard error. *p<.05, **P<.01, ***p<.001

Figure 4.1 Final model results for conditional bivariate LCM-SR for general psychopathology and negative thinking
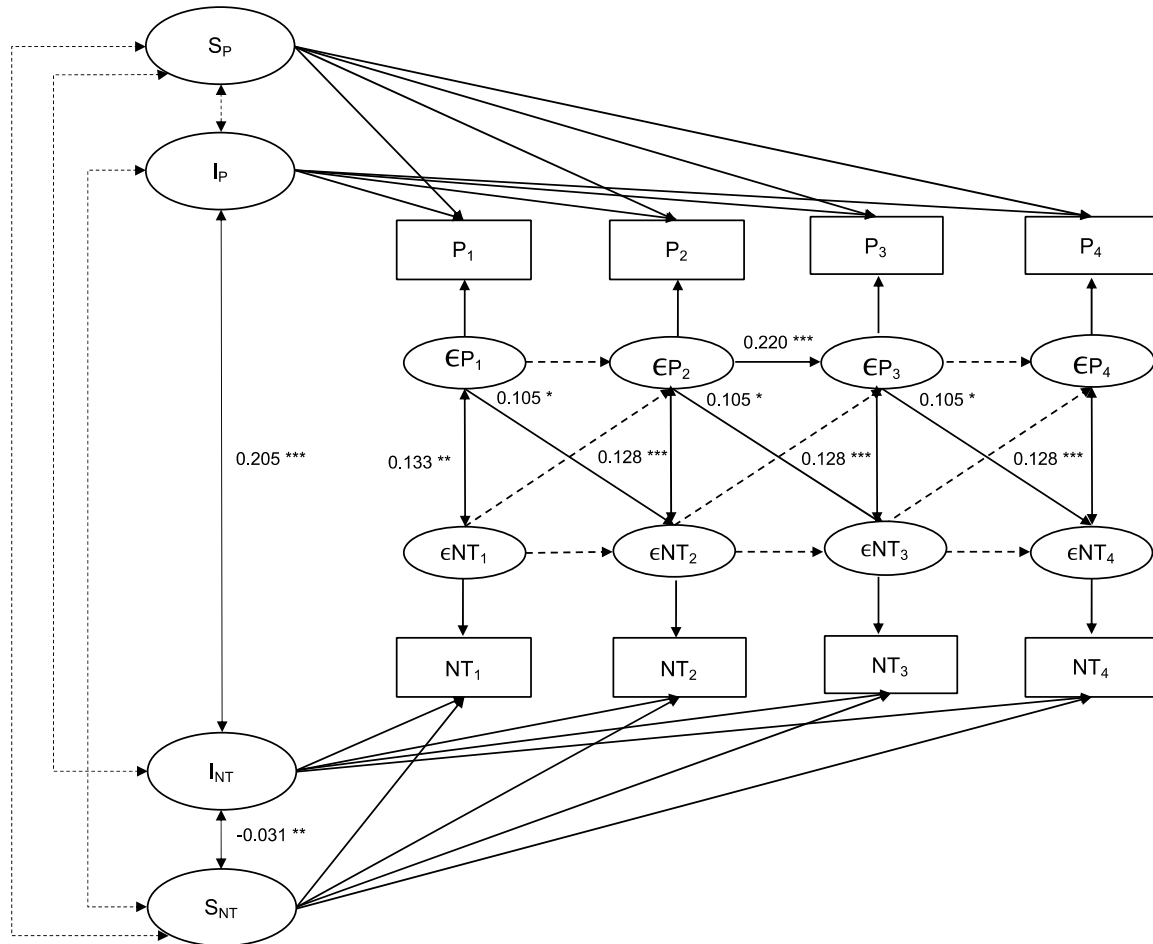
Note. P = general psychopathology; NT = negative thinking; I = intercept; S = slope; all values are unstandardised estimates; dashed lines are estimated but not significant. Sex and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

Figure 4.2 Final model results for conditional bivariate LCM-SR for general psychopathology and anxiety sensitivity
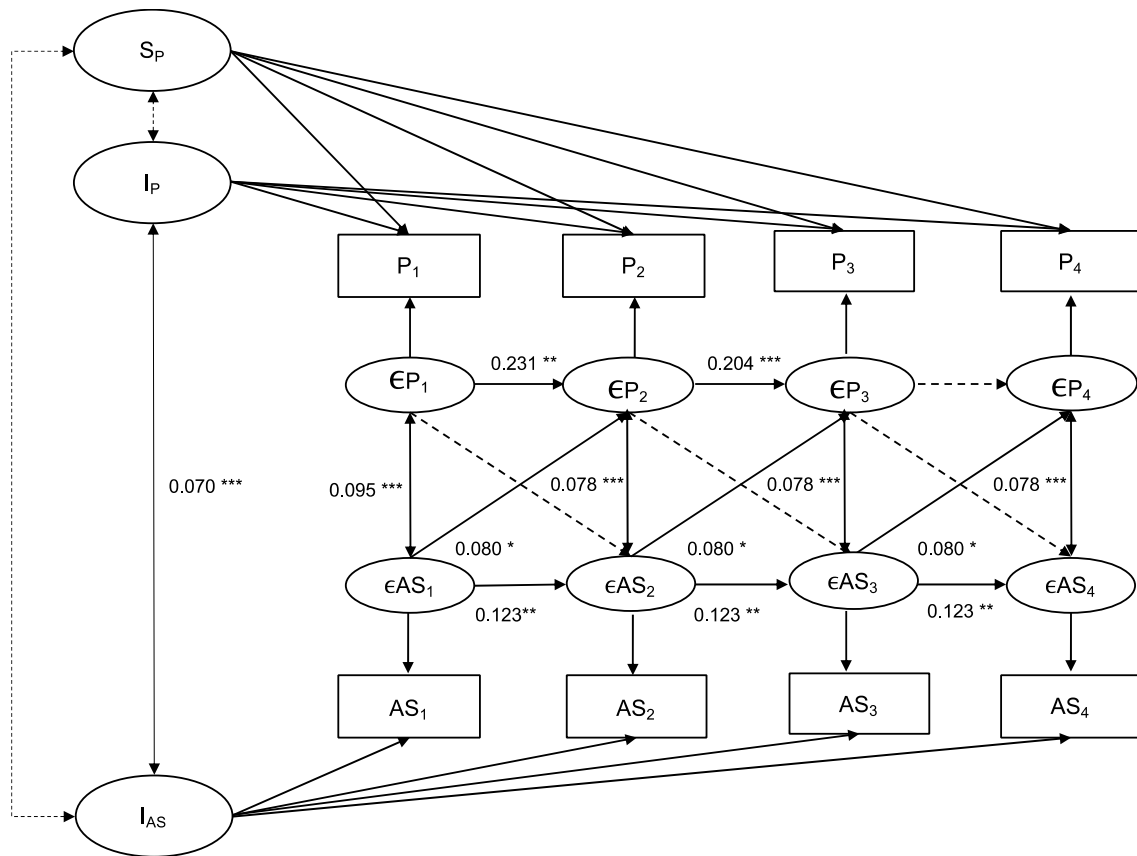
Note. P = general psychopathology; AS = anxiety sensitivity; all values are unstandardised estimates; dashed lines are estimated but not significant. Sex and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

Figure 4.3 Final model results for conditional bivariate LCM-SR for general psychopathology and impulsivity
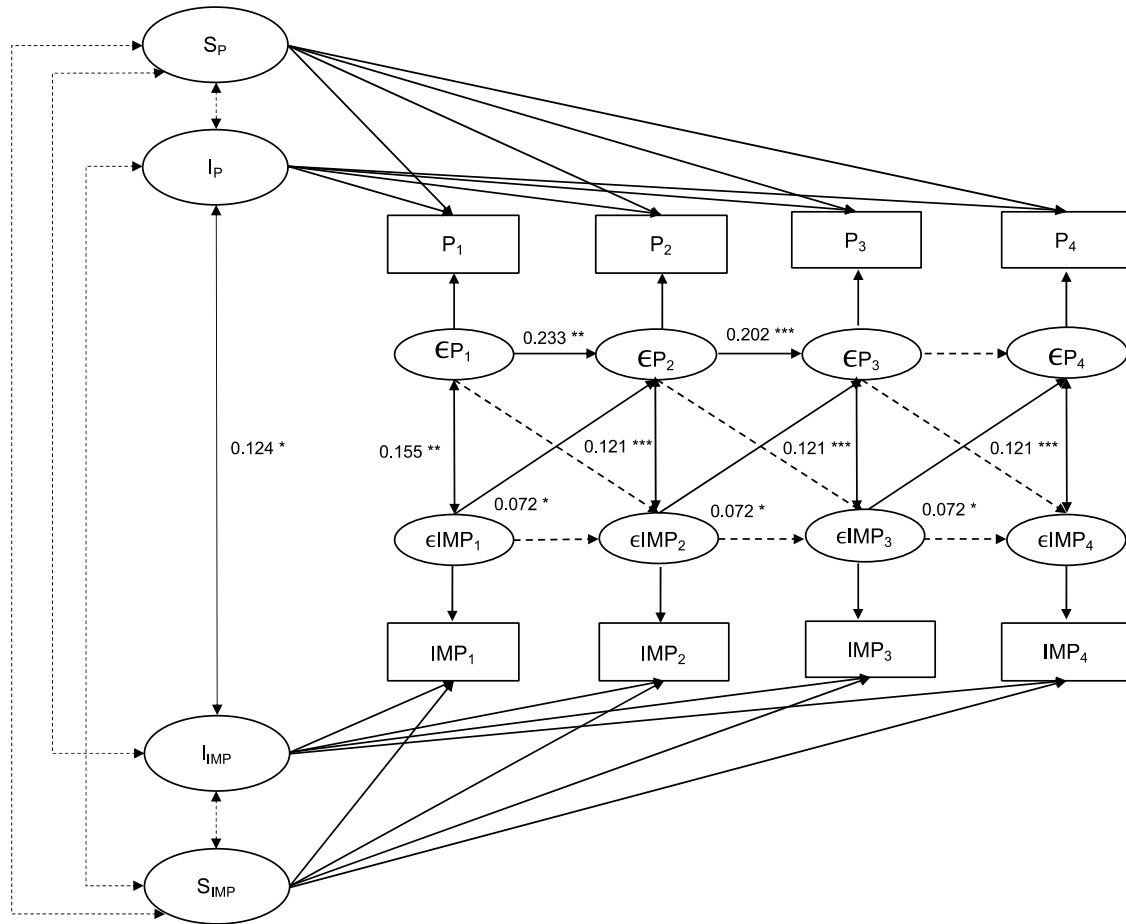
Note. P = general psychopathology; IMP = impulsivity; all values are unstandardised estimates; dashed lines are estimated but not significant. Study cohort, sex, and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

Figure 4.4 Final model results for conditional bivariate LCM-SR for general psychopathology and sensation seeking
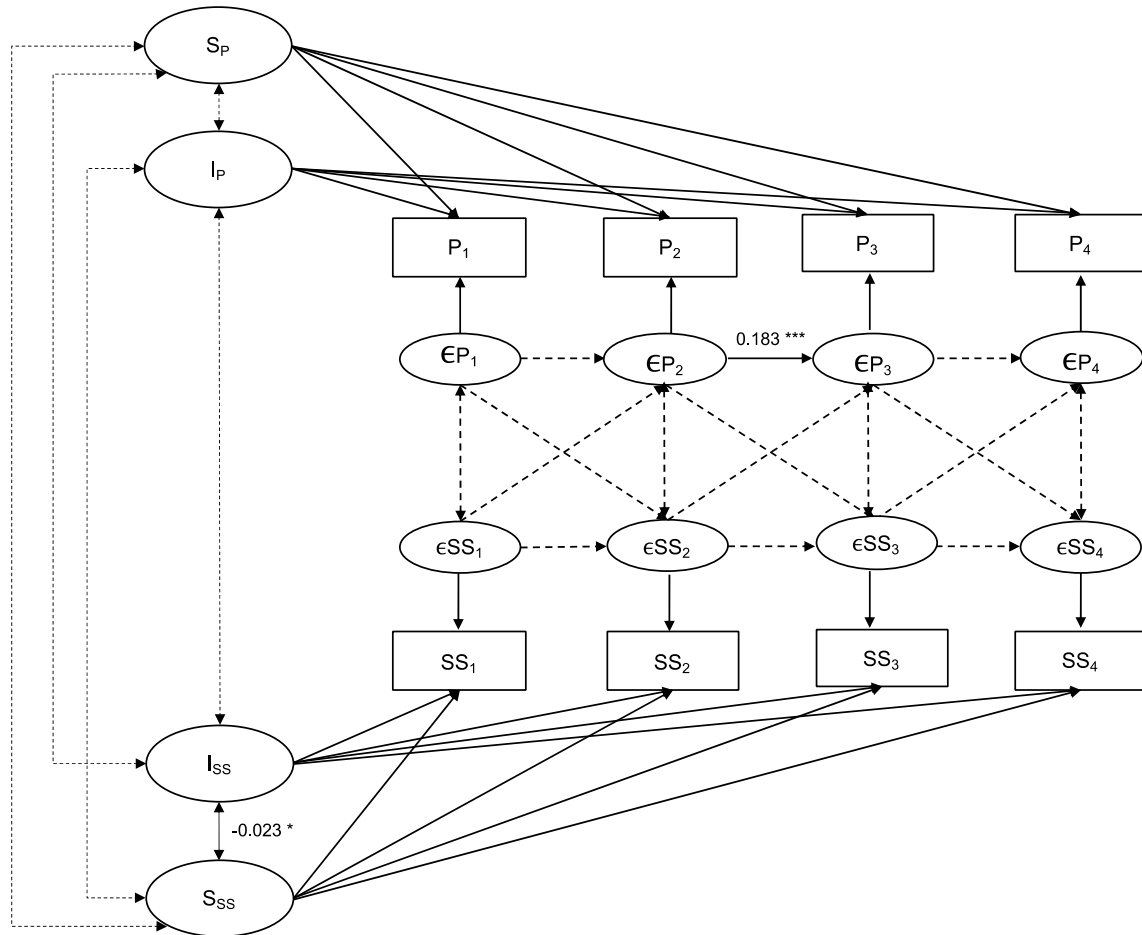
Note. P = general psychopathology; SS = sensation seeking; all values are unstandardised estimates; dashed lines are estimated but not significant. Study cohort, sex, and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

4.4.3   Negative thinking and general psychopathology

Figure 4.1 shows the final, unstandardised model results for the LCM-SR involving general psychopathology and negative thinking. The cross-lagged parameters from negative thinking to general psychopathology were not significant, however, as shown in Figure 4.1 and Table 4.2, the cross-lagged parameters from general psychopathology to negative thinking were large and significant (Orth et al., 2022). This indicates that adolescents who experienced higher levels of general psychopathology than they usually do at one time point, tended to also experience higher levels of negative thinking than they were expected to at the next time point.

As shown in Table 4.3, the autoregressive parameters for the structured residuals for negative thinking were not significant, and for general psychopathology only the T2 to T3 parameter was statistically significant. This indicates that adolescents experiencing higher levels of general psychopathology at T2 (than expected based on their underlying trajectory), tended to also experience higher levels of general psychopathology at T3.

4.4.4   Anxiety sensitivity and general psychopathology

Figure 4.2 shows the final, unstandardised model results for the LCM-SR involving general psychopathology and anxiety sensitivity. As shown in Table 4.2, there was a medium cross-lagged effect from anxiety sensitivity to subsequent general psychopathology. Whereas the cross-lagged parameters from general psychopathology to anxiety sensitivity were not statistically significant. This indicates that adolescents experiencing higher levels of anxiety sensitivity than they usually do at one time point, tended to experience higher levels of general psychopathology than they usually would at the next time point.

As shown in Table 4.3, the autoregressive parameters for the structured residuals for anxiety sensitivity were large and significant, indicating that there were enduring adolescent specific deviations, or increases, in anxiety sensitivity over the follow up period. That is, adolescents experiencing higher than their usual level of anxiety sensitivity, consistently tended to experience higher levels of anxiety sensitivity than they usually would at the next time point. For general psychopathology, there were large autoregressive effects from T1 to T2 and T2 to T3, indicating that adolescents experiencing higher general psychopathology than they usually do, tended to also experience higher than usual general psychopathology at the next time point, but only up until age 15 (T3).

4.4.5   Impulsivity and general psychopathology

Figure 4.3 shows the final, unstandardised model results for the LCM-SR involving general psychopathology and impulsivity. As shown in Table 4.2, there was a medium cross-lagged effect from impulsivity to general psychopathology, indicating that adolescents with higher than usual levels of impulsivity tended to also have higher than usual levels of general psychopathology at the next time point. The cross-lagged effect from general psychopathology to impulsivity was non-significant.

As shown in Table 4.3, the autoregressive parameters for the structured residuals for impulsivity were not statistically significant. For general psychopathology there were medium, significant effects from T1 to T2 and T2 to T3. This suggests that adolescents experiencing higher general psychopathology than they usually would, tend to experience higher than usual general psychopathology at the next time point but only up until age 15 (T3), whereas any adolescents experiencing deviations in their usual level of impulsivity tended to fall back to their usual level quite quickly.

4.4.6   Sensation seeking and general psychopathology

Figure 4.4 shows the final, unstandardised model results for the LCM-SR involving general psychopathology and sensation seeking. The cross-lagged parameters from sensation seeking to general psychopathology, and general psychopathology to sensation seeking, were not statistically significant. The autoregressive parameters for the structured residuals for sensation seeking were also not statistically significant. For general psychopathology, as shown in Figure 4.4, only the autoregressive effect from T2 to T3 was statistically significant. Altogether, the findings from this model suggest that fluctuations in sensation seeking and general psychopathology were not related. Standardised and unstandardised within-person coefficients are reported in Tables 4.2 and 4.3.

4.5 Discussion

The present study aimed to empirically investigate longitudinal associations between a higher-order general psychopathology factor and four high-risk personality traits from early to mid-adolescence. By using a statistical approach that separates between-person and within-person variance, we were able address questions about who is most likely to develop general psychopathology in adolescence, and when and how high-risk personality traits are associated with general psychopathology. Very few studies to date have examined longitudinal associations between general psychopathology and personality (e.g., Mann et al, 2020; Etkin et al., 2022) and none have examined high-risk personality traits.

The analytic approach used in the present study allowed us to examine how person-specific and time-specific changes in general psychopathology and personality influence one another. This allowed us to explicitly test the scar/complication, pathoplasty and continuum/spectrum models of personality-psychopathology associations. Adolescents who experienced increases in general psychopathology, compared to their typical developmental trajectory, tended to experience spikes in negative thinking at subsequent time points. This finding is consistent with the scar/complication model of personality-psychopathology development. In contrast, adolescents who experienced increases in anxiety sensitivity, tended to experience increases in general psychopathology at subsequent time points, relative to their usual developmental trajectories. A similar effect was also found for impulsivity, such that adolescents who experienced heightened impulsivity beyond that of their typical trajectory, tended to experience spikes in general psychopathology at the next time point. These findings are consistent with a pathoplasty model of personality-psychopathology, which proposes that personality traits influence the manifestation, course, and severity of psychopathology.

Although this is the first study to examine cross-lagged associations between general psychopathology and these specific personality traits, our findings are relatively consistent with previous research. For example, a recent investigation of longitudinal associations between general psychopathology and Big 5 traits found that neuroticism predicted subsequent general psychopathology, and vice versa (i.e., scar/complication and pathoplasty effects both occurred), suggesting a pattern of exacerbation between neuroticism and general psychopathology (Etkin et al., 2021). Arguably, negative thinking, anxiety sensitivity and impulsivity represent nuanced features of neuroticism (Castellanos-Ryan et al., 2013). By extension, the results of the present

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study suggest that focusing on broader personality traits may mask underlying and differing patterns of association with general psychopathology. Moreover, these underlying associations between aspects of broader neuroticism may explain the bidirectional associations between neuroticism and general psychopathology previously observed by Ektin and colleagues (2022).

Sensation seeking was unrelated to general psychopathology at the within-person level in the present study. This, in part, may be explained by the underlying symptoms captured by the general psychopathology factor. Specifically, the general psychopathology factor in the present study was heavily defined by fear and distress lower-order factors, followed by a conduct-inattention factor, and then modestly defined by the alcohol use/harms factor (standardized factor loadings = 0.948, 0.876, 0.744 and 0.388, respectively; see Chapter 3). However, previous research also suggests sensation seeking is more specifically related to substance use problems and, to a lesser extent, conduct/hyperactivity problems, rather than other forms of psychopathology (Castellanos-Ryan & Conrod, 2011). As such, it seems likely that sensation seeking may contribute to the development of more specific dimensions comprised of substance use related symptoms, particularly alcohol use (Castellanos-Ryan & Conrod, 2011; O'Connor et al., 2021). Thus, sensation seeking may be more suitable for the identification of adolescents at risk of developing substance use related problems, rather than general psychopathology.

There were strong concurrent associations between general psychopathology and negative thinking, anxiety sensitivity and impulsivity. This indicates that deviations in these traits coincide with deviations in general psychopathology. This is consistent with previous research (Etkin et al., 2022), including cross-sectional research (Afzali et al., 2017; Carragher et al., 2016; Castellanos-Ryan et al., 2016). A notable departure from previous research, is that sensation seeking was not concurrently (or prospectively) associated with general psychopathology. Again, this may be due to sensation seeking being more directly associated with substance use, and the composition of our general psychopathology factor being more defined by fear and distress symptom domains, rather than alcohol use/harms. These individual level within-time associations are often interpreted as indicating support for the continuum/spectrum model.

Previous research has reported that negative thinking, anxiety sensitivity and impulsivity are correlated with neuroticism (r = 0.50, 0.23 and 0.41, respectively), and arguably represent distinct aspects of neuroticism (Castellanos-Ryan et al., 2013). Sensation seeking appears to be more directly related to substance use problems than other externalising related problems, and is more

closely associated with extroversion (Castellanos-Ryan et al., 2013; Castellanos-Ryan & Conrod, 2012, 2011). Given the close associations between neuroticism and general psychopathology, it is not surprising that, in the context of hierarchical-dimensional models of psychopathology, negative thinking and anxiety sensitivity appear to be prospectively *and* concurrently associated with greater internalising and general psychopathology (Carragher et al., 2016; Castellanos-Ryan et al., 2016; Lynch et al., 2023; Chapter 3), and either unrelated or inversely related to externalising. Similarly, impulsivity and sensation seeking appear to be more closely related to externalising related dimensions, with impulsivity more closely related to conduct/general externalising and sensation seeking more closely aligned with substance use problems and related harms (Castellanos-Ryan et al., 2016; Castellanos-Ryan & Conrod, 2011). In the present study, the concurrent and prospective findings also lend support to the notion that dispositional negative affect and impulsivity are core features of general psychopathology (Smith et al., 2020; Southward et al., 2022).

Within-construct carry-over effects were also observed. Deviations from a person's usual trajectory for negative thinking, impulsivity and sensation seeking at one time point tended not to carry over to the next time point. In contrast, spikes in anxiety sensitivity on one occasion were associated with future spikes in anxiety sensitivity. This suggests that heightened anxiety sensitivity at one point tends to carry over to subsequent timepoints throughout early to mid-adolescence. However, this finding should be interpreted with caution. It is possible that the need to remove the slope factor for anxiety sensitivity from this model meant that there was more available variance in the within-person component of the model (Mund & Nestler, 2019).

For general psychopathology, evidence for time-specific carry-over effects varied across models and measurement windows. Specifically: between ages 13 and 14, there was a significant, positive autoregressive effect for general psychopathology in two of the four models (impulsivity and anxiety sensitivity models); between ages 14 and 15 all four models had a significant, positive autoregressive effect; and finally, there were no significant autoregressive effects between 15 and 16 years or age. Together, these results suggest that spikes in general psychopathology tend to consistently carry-over between the ages of 14 and 15, and for individuals with higher than usual levels of anxiety sensitivity or impulsivity at age 13, an adolescent's heightened general psychopathology may commence from age 13 and continue through to 15. This aligns with evidence for the peak age of onset for any mental disorder being 14.5 years and reinforces the importance of continuous, reliable measures of psychopathology and of delivering prevention and

early intervention during early to mid-adolescence (Fusar-Poli et al., 2021; Solmi et al., 2021).

4.5.1 Limitations

Whilst the general psychopathology factor in this study was comprised of a broad range of mental health symptoms, some common symptom domains were not assessed in the trials including psychosis and eating pathology. Moreover, the general psychopathology factor was more heavily defined by fear, distress, and conduct-inattention than alcohol use/harms. Second, 67% of the sample were female. To account for this, we used factor scores adjusted for sex-related measurement bias in the primary analyses and included sex as a covariate in final models. Third, this study was a secondary analysis of data from two RCT cohorts which had slightly different follow up intervals between T3 and T4 (6 months post T3 in CSC vs. 12 months in CAP), which may have limited our ability to detect autoregressive effects between T3 and T4. Unfortunately, low covariance coverage within the CAP sample impaired our ability to conduct sensitivity analyses to examine potential influences of the uneven assessment periods. Thus, time-specific effects between T3 and T4 should be interpreted with caution. Finally, there was substantial missing data due to attrition. Although attrition analyses indicated there were some differences in baseline levels of negative thinking, there were no differences in other personality or general psychopathology variables.

4.5.2 Implications and future directions

The findings from the present study shed light on the association between personality and psychopathology during adolescence and have implications for the timing and targeting of prevention efforts as well as substantive interpretations of general psychopathology. Results support the idea that general psychopathology likely reflects interactions between dispositional negative emotionality, impulsive emotional responsiveness, and nonspecific impairment (Carver et al., 2017; Smith et al., 2020; Southward et al., 2022). The different pattern of effects for negative thinking compared to anxiety sensitivity and impulsivity suggests that a core functional mechanism of general psychopathology may be a sensitivity or responsivity to aversive and rewarding stimuli, which results in negative emotionality (or potentially manifests as other maladaptive traits or symptoms). Understanding the substantive meaning of general psychopathology is essential for elucidating the causes of psychopathology and facilitating significant advancements in prevention and should be a top priority for future research.

The present study corroborates existing evidence for early adolescence as an ideal time for preventive interventions. In the present study, general psychopathology at age 15 was consistently predicted by general psychopathology at age 14; and for adolescents experiencing spikes in anxiety sensitivity or impulsivity, general psychopathology at age 14 was also predicted by general psychopathology at age 13. This suggests that early adolescence may be an optimal time to implement programs to prevent development of general psychopathology. Although there were no carry-over effects in general psychopathology from age 15 to 16 in the present study, given the likely onset of new symptom domains during this period, it seems plausible that a booster, or early intervention, at age 15 could also reduce growth in general psychopathology beyond mid-adolescence, and thus could warrant further empirical investigation. Further research spanning a longer developmental period could shed further light on the optimal time to deliver interventions, and whether timing varies among different personality risk profiles.

Results also reinforce personality as a means of identifying adolescents at risk of developing multiple forms of psychopathology (as represented by general psychopathology) and highlight the potential for tailoring interventions to different personality risk profiles. Certain personality traits, such as sensation seeking, may be more useful for the early detection and prevention of more specific symptom domains, whereas other traits, such as impulsivity and anxiety sensitivity, may be able to identify those at risk of developing psychopathology more broadly, while also hinting at potential mechanisms of change. Negative thinking, on the other hand, may only be useful for identifying individuals with existing or emerging general psychopathology.

This three-year study examined longitudinal associations between a higher-order general psychopathology factor and four high-risk personality traits among adolescents. Spectrum, scar/complication, vulnerability/risk and pathoplasty models were supported. Developmental spikes in impulsivity and anxiety sensitivity preceded spikes in general psychopathology, which were followed by spikes in negative thinking. Spikes in general psychopathology persisted from age 14 to 15, suggesting this may be a critical developmental window for the progression of general psychopathology. The modifiable processes underlying personality-general psychopathology associations, and the functional utility of general psychopathology, need further research. Such evidence could help develop interventions that disrupt the mechanisms linking personality and psychopathology, and ultimately prevent the onset of multiple forms of psychopathology simultaneously. This study advances understanding of the role of certain aspects of personality in the development of general psychopathology and highlights the potential of

general psychopathology preventative interventions that are tailored to different personality traits and delivered during early adolescence to effectively and efficiently target those at greatest risk.

<div align="right">Chapter 5</div>

The 3-year effects of a personality-targeted prevention program on general and specific dimensions of psychopathology: A cluster randomised controlled trial

Preface

The findings from [Chapters 3](#) and [4](#) included cross-sectional and longitudinal associations between high-risk personality traits and general and specific dimensions of psychopathology in adolescents. These chapters provided clear evidence for the interaction between personality and psychopathology among adolescents. The findings indicate that an intervention focussed on helping adolescents better manage their personality traits (particularly anxiety sensitivity and impulsivity), could help reduce growth in general (and/or specific) dimensions of psychopathology. This chapter investigates the impact of a school-based, personality-targeted prevention program on the trajectories of general and specific dimensions of psychopathology over three years (13 to 16 years of age). Notably, this is the first study to examine the impact of a school-based preventative intervention on growth in general and specific dimensions of psychopathology.

This chapter addresses the fifth research question of this thesis: What impact does a personality-targeted prevention program have on the trajectories of general and specific dimensions of psychopathology?

This study is currently under review with the Journal of Consulting and Clinical Psychology.

Supplementary materials are available in [Appendix H](#) and [online](#) (https://osf.io/9haem) along with the analysis code and output files.

5.1 Abstract

Objective: To examine the effect of a personality-targeted prevention program (*Preventure*) on trajectories of general and specific dimensions of psychopathology during adolescence.

Methods: In 2012, adolescents (N=2,190) from 26 schools participated in a cluster randomised controlled substance use prevention trial. This study compared schools allocated to deliver *Preventure* (n = 13 schools; n=466 students; Mage = 13.42 years) with a control group (n=7 schools; n=235 students, Mage = 13.47 years; 64% Female). All participants were assessed for psychopathology symptoms at baseline, 6-, 12-, 24- and 36-months post-baseline. Outcomes were a general psychopathology factor and four specific factors: fear, distress, alcohol use/harms and conduct/inattention), extracted from a higher-order model. Participants who screened as 'high-risk' on at least one of four personality traits (negative thinking, anxiety sensitivity, impulsivity and sensation seeking) were included in intention-to-treat analyses. Intervention effects were examined using multi-level mixed models accounting for school-level clustering.

Results: Among high-risk adolescents, growth in general psychopathology was slower in the *Preventure* group compared to the control group (b = -0.07, p = .038) across the 3 years. After controlling for effects on general psychopathology, there were no significant, additional effects on the lower order factors. There were personality-specific effects on general psychopathology within the impulsivity subgroup (b = -0.16, p = .024). Intervention effects across high- and low-risk adolescents were also detected on general psychopathology (b = -0.04, p = .034) and alcohol use/harms beyond the effect on general psychopathology (b = -0.07, p = .021), suggesting a possible 'herd-immunity' effect.

Conclusions: This study provides evidence for the effectiveness of personality-targeted intervention in altering trajectories of general psychopathology during adolescence. The finding that general psychopathology may respond to changes in thinking and responding to stressors has implications for the substantive interpretation of general psychopathology factors and prevention and early intervention efforts.

5.2 Introduction

An estimated 23% of US adolescents experience a mental disorder within a 12-month period (Polanczyk et al., 2015). Furthermore, these disorders account for one quarter of Years Lived with Disability (Erskine et al., 2015) and 10-20 years reduction in life expectancy (Chesney et al., 2014). With the onset of half of all mental disorders peaking by age 14, preventative interventions aimed at early adolescents have the potential to significantly reduce the burden of disease attributed to mental and substance use disorders (Solmi et al., 2021).

Prevention programs have historically focused on preventing or delaying the onset of a specific disorder or symptom domain (Forbes et al., 2019). Yet there is considerable evidence that many disorders are highly comorbid, with up to two-thirds of adolescents with a mental or substance use disorder estimated to have at least one other disorder (Kessler et al., 2012). The extensive overlap between mental disorders has led to speculation that there are several underlying transdiagnostic dimensions that better account for commonly co-occurring disorders (e.g., internalising and externalising dimensions). More recently, a general psychopathology dimension, which captures shared variance across all forms of psychopathology, has gained increasing attention in the literature (Kotov et al., 2017; Smith et al., 2020). General psychopathology and other transdiagnostic dimensions of psychopathology represent compelling prevention targets, which may lead to more efficient prevention and intervention efforts, and in turn reduce the sizeable burden of psychopathology (Forbes et al., 2019).

5.2.1 Hierarchical-dimensional models of psychopathology

As described in previous chapters, there is extensive evidence for models of psychopathology comprised of hierarchically organised dimensions, with a general psychopathology dimension at the apex, and several spectra and subfactors which sit underneath. A hierarchical conceptualisation of psychopathology implies that by targeting general psychopathology, it may be possible to prevent the full spectrum of lifetime mental disorders (Forbes et al., 2019). To achieve this, there are two unresolved issues in the literature that need to be addressed. The first is whether longitudinal trajectories of general psychopathology can be modified through preventative interventions. The second is coming to a consensus on what general psychopathology actually is (Forbes et al., 2019). Current leading theories are that general psychopathology represents either dispositional negative emotionality, impulsive responsivity, thought dysfunction or low cognitive functioning, or a non-specific index of impairment rather than a common underlying vulnerability

(Smith et al., 2020; Southward et al., 2022).

5.2.2 Preventure

Preventure is a personality-targeted, group-based intervention delivered in schools designed to reduce and prevent substance misuse and mental health symptoms among adolescents. Using the Substance Use Risk Profile Scale (SURPS), students who exceed a specific threshold are allocated to one of four high-risk personality risk factor groups (impulsivity, sensation seeking, negative thinking and anxiety sensitivity). Students who do not exceed the threshold (i.e., 'low-risk' students) receive health education as usual. *Preventure* provides psychoeducation and uses a general cognitive-behavioural skills training framework, that is tailored to each target personality trait. The effectiveness of *Preventure* in reducing and preventing alcohol and illicit drug use and symptoms of other common disorders, including depression, anxiety, panic, hyperactivity and conduct related problems has been demonstrated in multiple randomised controlled trials in North America, Europe, and Australia (Conrod et al., 2006, 2008; Lammers et al., 2017; Newton et al., 2020, 2021; Newton, Conrod, et al., 2016; O'Leary-Barrett et al., 2013). This impact across multiple symptom domains suggests that *Preventure* may be effective in reducing general psychopathology, as well as specific dimensions. Preventure has also been found to have indirect benefits for the 'low-risk' students within schools that delivered Preventure compared to controls (Conrod et al., 2013). This is known as a herd-effect, as it reflects reduced risk in the general school population resulting from a significant portion of individuals within a school community receiving the intervention.

5.2.3 The present study

The present study examined for the first time the effect of *Preventure* on trajectories of general and specific dimensions of psychopathology among adolescents. We hypothesised that *Preventure*, compared to control (health education as usual), would slow the growth in general and specific dimensions (fear, distress, alcohol use, conduct/inattention) of psychopathology among adolescents with high-risk personality profiles. In addition, we conducted exploratory analyses to determine whether there were specific intervention effects within the personality risk groups. Specifically, we hypothesised that, compared to the control group, those in the *Preventure* group would demonstrate reduced growth in 1) distress for individuals in the negative thinking subgroup; 2) fear and distress for individuals in the anxiety sensitivity subgroup; 3) alcohol use/harms for individuals in the sensation seeking subgroup, and 4) conduct problems for

individuals in the impulsivity subgroup. We also examined whether there was evidence of 'herd-immunity' effects (i.e., the effects of the intervention held across high- and low-risk students).

5.3 Methods

5.3.1 Design and participants

We analysed data from the Climate and Preventure (CAP) study – a four arm, cluster randomised controlled trial conducted between 2012 and 2015 (Newton et al., 2012). The trial was designed to compare the efficacy of different approaches to the prevention of substance misuse. Participating secondary schools (N=26) were block randomied by an external researcher using Research Randomizer (https://www.randomizer.org/) to one of four conditions: 1) *Preventure* (a selective, personality-targeted substance use prevention program delivered to high-risk students); 2) *Climate Schools* (a universal digital alcohol and cannabis use and related harms prevention program delivered to all students); 3) *Climate Schools and Preventure* (CAP; both universal and selective programs delivered), or 4) *control* (health education as usual). Only students who received parental consent, and consented themselves, were eligible to participate.

The trial was powered to detect effect sizes of 0.3 in binary substance use outcomes, based on previous substance use prevention trials (Newton et al., 2012). The present study collapsed the two arms that delivered *Preventure* (i.e., *Preventure* arm and the CAP arm) into the intervention group (high-risk n = 466) and compared with the control (health education as usual) group (high-risk n = 235). This was done to improve power to detect changes in continuous latent variables representing broader forms of psychopathology. Furthermore, previous analysis of the CAP study has demonstrated that *Climate Schools* alone does not affect mental health outcomes, and that the effect of *Preventure* on mental health is generally unaffected when combined with *Climate Schools* (Newton et al., 2020). The CONSORT diagram in Figure 5.1 summarises participant flow and retention rates for each condition included in the present study. The intention to treat sample for the present study was 701 high-risk students (Mage= 13.44 years, SD=0.44; 35.2% Female). Baseline group-level characteristic are presented in Table 5.1.

This study was approved by the University of New South Wales Human Research Ethics Committee (HC11274), the Sydney Catholic Education Office (772), and the New South Wales Department of Education and Training (2011201). The trial follows the Consolidated Standards of Reporting Trials (CONSORT) guidelines and was prospectively registered with the Australian

and New Zealand Clinical Trials Registry (ACTRN12612000026820). Full details of the study design, including sample size calculations, have been published elsewhere (Newton et al., 2012).

Figure 5.1 CONSORT figure for participant flow throughout the trial in the Preventure and control groups
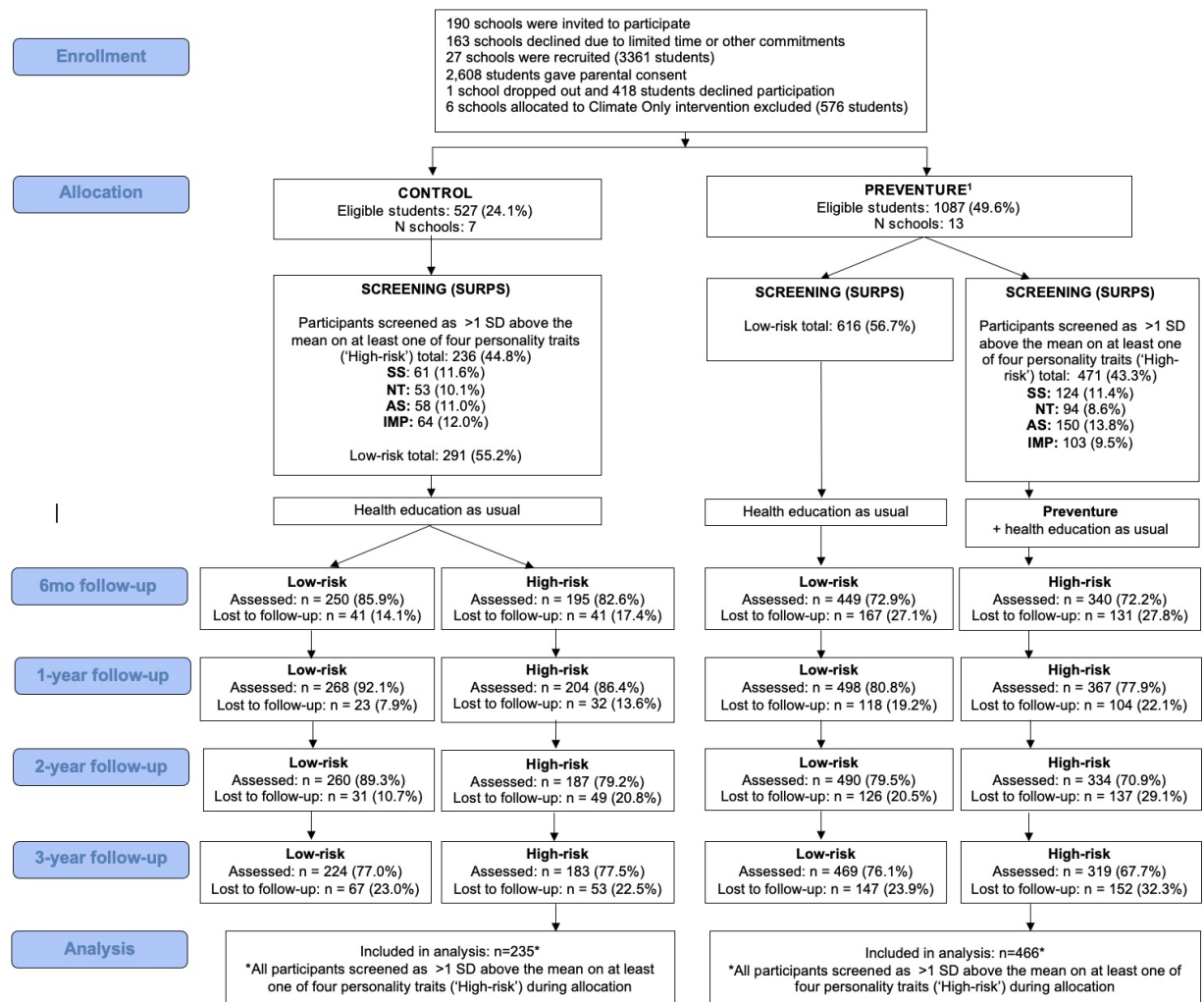
Notes. [1] The *Preventure* group is comprised of the *Climate Schools and Preventure* arm and *Preventure*-only arm of the CAP study. See methods for further details.

CAP: Climate Schools and Preventure; SURPS: Substance Use Risk Profile Scale; SS: sensation seeking; NT: negative thinking; AS: anxiety sensitivity; IMP: impulsivity.

Table 5.1 Participant characteristics

	Control, N = 235	**Preventure**, N = 466
Age (years) M (SD)	13.47 (0.37)	13.42 (0.44)
(Missing)	1	0
Sex N (%)		
Male	84 / 234 (36%)	369 / 466 (79%)
Female	150 / 234 (64%)	97 / 466 (21%)
(Missing)	1	0
Country of birth N (%)		
Australia	205 / 234 (88%)	388 / 465 (83%)
Other English-speaking country	19 / 234 (8.1%)	43 / 465 (9.2%)
Other Non-English-speaking country	10 / 234 (4.3%)	34 / 465 (7.3%)
(Missing)	1	1

5.3.2   Procedure

5.3.2.1   Screening

Students completed self-report questionnaires, either online or paper surveys, in class at baseline, 6-, 12-, 24- and 36-months post-baseline (for full protocol see Newton et al., 2012). At baseline, all students completed the Substance Use Risk Profile Scale (SURPS), a 23-item questionnaire that assesses four personality risk factors for substance use: anxiety sensitivity, negative thinking, impulsivity, and sensation seeking. The SURPS has demonstrated good reliability and validity, including among Australian adolescents (Newton, Barrett, et al., 2016). Students scoring more than one standard deviation (SD) above their school mean on any of the personality risk profiles were categorised as high-risk and allocated to the personality group on which they were furthest from the school mean.

5.3.2.2   Intervention

In schools allocated to either the *Preventure* or CAP conditions, high-risk students according to the SURPS were invited to participate in the *Preventure* intervention corresponding to their high-risk personality type. *Preventure* involves two 90-minute group sessions delivered one week apart by a clinical psychologist and a trained co-facilitator (at least four years of undergraduate training in Psychology). The content of the intervention is tailored to each personality group, and the

sessions are conducted separately for each group. As reported previously, 81 groups (162 sessions) with an average of five students per group were completed (Teesson et al., 2017). The majority of students attended both sessions (first session = 90% [n = 422]; second session = 84% [n = 394]). Implementation fidelity was examined in five groups. The facilitator was found to adhere 'almost totally' to the Preventure manual in 65% of the sessions, and 'totally' in the remaining sessions, indicating a high level of intervention fidelity (for further details see Newton, Conrod, et al., 2016). The intervention incorporates psychoeducation, components of cognitive behavioural therapy and motivational interviewing. The first session involves psychoeducation focused on characteristics and unhelpful coping behaviours specific to the target personality trait. In the second session, students are supported to identify and challenge personality-specific thoughts that lead to problematic emotional and behavioural reactions. More detailed information about *Preventure* is available elsewhere (Conrod, 2016). Students in the CAP arm also received the *Climate Schools* program – an online drug and alcohol universal prevention program comprised of 12 x 40-minute lessons presented in a cartoon format (Newton et al., 2012). Students in all arms received health education as usual in accordance with the Australian national curriculum.

5.3.3   Measures

5.3.3.1 Psychopathology

Fear was assessed by four items, including two items from the emotional problems subscale of the Strengths and Difficulties Questionnaire (SDQ; Goodman, 2001) and two items from the Kessler Psychological Distress Scale (K6; Kessler et al., 2002). *Distress* was assessed by seven items, with three items from the SDQ and four items from the K6. *Alcohol use/harms* were assessed by eight items, including six items from the Rutgers Alcohol Problem Index (RAPI; Neal et al., 2006) and two items about quantity of alcohol consumed in the past six months and frequency of drinking at above low risk levels in the past six months (McBride et al., 2004). Finally, *conduct/inattention* was assessed with seven items from the conduct problems and hyperactivity subscales of the SDQ. Further details on the measures of psychopathology have been published elsewhere (Lynch et al., 2023; Chapter 3; Newton et al., 2012).

Due to the low prevalence of psychopathology symptoms in this general population sample, all items were dichotomised (i.e., symptom present or absent) to improve the stability of the models and overall precision of the estimates. Item wording, response coding and factor specification is provided in the supplementary materials (Appendix H Table M1).

5.3.4   Statistical analyses

5.3.4.1   Structural model of psychopathology

The higher-order model used in the present study was identified in a previous study examining the underlying structure of psychopathology (Lynch et al., 2023; Chapter 3). In that study, baseline data from the CAP study and a second eHealth prevention trial (Climate Schools Combined (CSC); Teesson et al., 2020) were used to examine multiple structures, including correlated factors, bifactor and higher-order models. The higher-order model featuring four lower-order factors (fear, distress, alcohol use/harms, and conduct/inattention) and a higher-order general factor, demonstrated good model fit and reliability and was found to be invariant across the CAP and CSC cohorts, indicating the structure was robust and represented the CAP data well. As such, we used the same higher-order model in the present study. Two amendments were made to the items underlying the alcohol use/harms factor to reduce item redundancy and improve interpretability. First, we removed the frequency of alcohol use item, as this item was used to determine whether the other two alcohol use items should be skipped, which creates a linear dependency between the items that can cause issues (e.g., with model identification). Second, the two remaining alcohol use items in the original study were coded as 'never OR less than monthly' or 'once a month or more', whereas in the present study this was recoded as 'never' or 'any'. This was done to align the interpretation with the other symptoms of psychopathology. In addition, two alcohol harms items were removed due to a high correlation with other items (AH1), empty cell warnings and convergence issues (AH4). In the present study, a two-level higher-order model (clustered by school and participant id) was estimated using maximum likelihood estimation with robust standard errors (MLR), as it is robust to non-normality, non-independence of observations and categorical indicators.

5.3.4.2   Measurement invariance

Moderated nonlinear factor analysis (MNLFA) was used to examine the measurement invariance of the psychopathology dimensions across age, sex, personality group (i.e., anxiety sensitivity, negative thinking, impulsivity, and sensation seeking) and intervention (i.e., *Preventure* or no *Preventure*; Bauer, 2017). Analyses were conducted in Mplus version 8.4 for Mac (Muthén & Muthén, 2017), in combination with R packages *aMNLFA* (Gottfredson et al., 2019) and *Mplus Automation* (Hallquist & Wiley, 2018). Further details about the procedure are provided in the supplementary materials.

5.3.4.3 Intervention effects

Bayesian Plausible Values (BPV) are a set of factor score values generated from the best fitting structure model using multiple imputations. BPVs tend to be more reliable than standard factor scores and can overcome measurement related biases (Asparouhov & Muthen, 2010). Within-level BPVs were estimated for each participant at each time point with 100 imputations in Mplus version 8.4 for Mac (Muthén & Muthén, 2017). Parameter estimates from the higher-order model estimated with MLR were used as starting values to generate plausible values using the Bayes estimator.

Multilevel mixed effects models were then used to examine intervention effects in R using the *mitml* and *lme4* packages (Bates et al., 2015; Grund et al., 2021). Within-level BPVs for each factor were regressed onto linear and quadratic time variables. The best-fitting random effects structure included random intercepts at the individual and school levels. When assessing impact on lower-order factors, we examined models both with and without general psychopathology included as a fixed effect to determine whether there were direct effects on any of the lower-order factors over and above any effects accounted for by general psychopathology. Further details about the assessment of the shape of change, and random and fixed effect structures are available online. Sex was included as a fixed effect in all models to account for any sex-related differences. The 100 BPV datasets are analysed using regular complete-data methods and then pooled according to Rubin's rules to form the final parameter estimates (Grund et al., 2021). Analysis code and output files are available online.

5.3.4.4 Exploratory analyses

To assess the personality specific hypotheses, data subsets comprised of students in the personality group of interest were created (e.g., students in the impulsivity group who received *Preventure* were compared with control students who would have been allocated to the impulsivity group). Additional exploratory analyses were conducted to assess intervention effects on the whole sample (including low-risk students).

5.4 Results

5.4.1 Structure of psychopathology, measurement invariance and attrition

Within-level standardised factor loadings for the higher-order model are shown in Table 2 (observations = 8,752; AIC = 154255.7; BIC = 154652; ssBIC = 154474.1). All loadings were statistically significant ($p \leq 0.05$).

Results from MNLFA analyses indicated that factor scores generated from MNLFA models were highly correlated with a base model without non-invariance terms (r = 0.93 to 0.99, p < .001, Appendix H tables S5.1 and S5.2). As such, the base model without any non-invariance terms was used for intervention effect analyses.

Attrition analyses indicated that although attrition was more likely to occur within the Preventure group (completed all follow-ups vs missed at least one follow-up: OR 1.89 [CI 1.38 to 2.60, p<0.001]; completed any follow-ups vs. zero follow-ups: OR 2.32 [95% CI 1.07 to 5.81, p=0.048, Table S5.3]), there were no interaction effects between group allocation and baseline measures of the psychopathology outcomes, suggesting no evidence for differential attrition based on psychopathology (see Appendix H, Table S5.5). Additional attrition analysis indicated there were no differences between participants who were present at baseline only compared to participants who completed any follow ups (see Appendix H, tables S5.3-S5.5). Attrition was most commonly attributed to students being absent on the day of the survey or failing to use their unique identifying code and therefore could reasonably be assumed as missing at random.

Table 5.2 Within-level standardised factor loadings for the higher-order model of psychopathology using MLR

Factor / Symptom	Item ID	*β*	SE
Fear			
Nervous in new situations	SD16	0.577	0.020
Many fears	SD24	0.546	0.021
Nervous	K61R	0.734	0.020
Restless or fidgety	K63R	0.767	0.013
Distress			
Somatic symptoms	SD3	0.538	0.015
Worries	SD8	0.664	0.020
Unhappy	SD13	0.777	0.010
Hopeless	K62R	0.910	0.006
Depressed	K64R	0.898	0.007
Effort	K65R	0.774	0.011
Worthless	K66R	0.925	0.006
Alcohol use/harms			
Binge	AUC2	0.897	0.009
Quantity	AUC3	0.913	0.006
Shame/embarrassment	AH2	0.942	0.009
Neglected responsibilities	AH3	0.960	0.006
Personality change	AH5	0.955	0.006
Tried to cut down	AH6	0.948	0.009
Memory loss	AH7	0.917	0.015
Crazy	AH8	0.921	0.012
Conduct/inattention			
Restless	SD2	0.788	0.013
Temper	SD5	0.633	0.019
Fidgety	SD10	0.811	0.012
Fight a lot	SD12	0.755	0.021
Easily distracted	SD15	0.761	0.02
Lies or cheats	SD18	0.674	0.019
Steals	SD22	0.695	0.031
General psychopathology			
Fear		0.954	0.005
Distress		0.956	0.004
Alcohol Use/harms		0.288	0.039
Conduct/inattention		0.654	0.018

Note. SE = standard error; SD = items from Strengths and Difficulties Questionnaire; AH = Alcohol Harms, items from Rutgers Alcohol Problem Index (RAPI); K6 = Kessler 6 Plus scale (K6+); AUC = Alcohol use, AUDIT-C items. All loadings were statistically significant (*p* value ≤ 0.05). MLR = model likelihood estimated with robust standard errors.

5.4.2 Intervention effects

Figure 5.2. shows the mean BPV pooled across high-risk students for the general and specific fear, distress, alcohol use/harms and conduct/inattention psychopathology factors over the three-year follow-up period. Information used to determine the shape of change for all outcomes, and the best-fitting random and fixed effect structures are provided in the supplementary material. For all outcomes, the best-fitting random-effects structure included random intercepts at the individual and school levels. For the lower-order factors, the best fitting structure to control for general psychopathology included fixed effects of general psychopathology. Comparisons between linear and quadratic change models for all outcomes indicated that linear models fit best. Fixed effect coefficients from the linear mixed effect models for general and specific fear, distress, alcohol use/harms and conduct/inattention psychopathology factors are shown in Table 5.2.

Participants in the *Preventure* group, compared to the control group, demonstrated reduced growth in general psychopathology across three years (Table 5.3). There was also evidence for reduced growth in *distress* among participants who received *Preventure* compared to the control group, but this was no longer significant after accounting for general psychopathology. There were no statistically significant intervention effects on fear, alcohol use/harms or conduct/inattention either before or after accounting for general psychopathology. However, there were notable decreases in the standardised effect sizes in the models controlling for general psychopathology, particularly for fear.

Figure 5.2 Changes in general and specific psychopathology from baseline to 36-months post-baseline among high-risk students
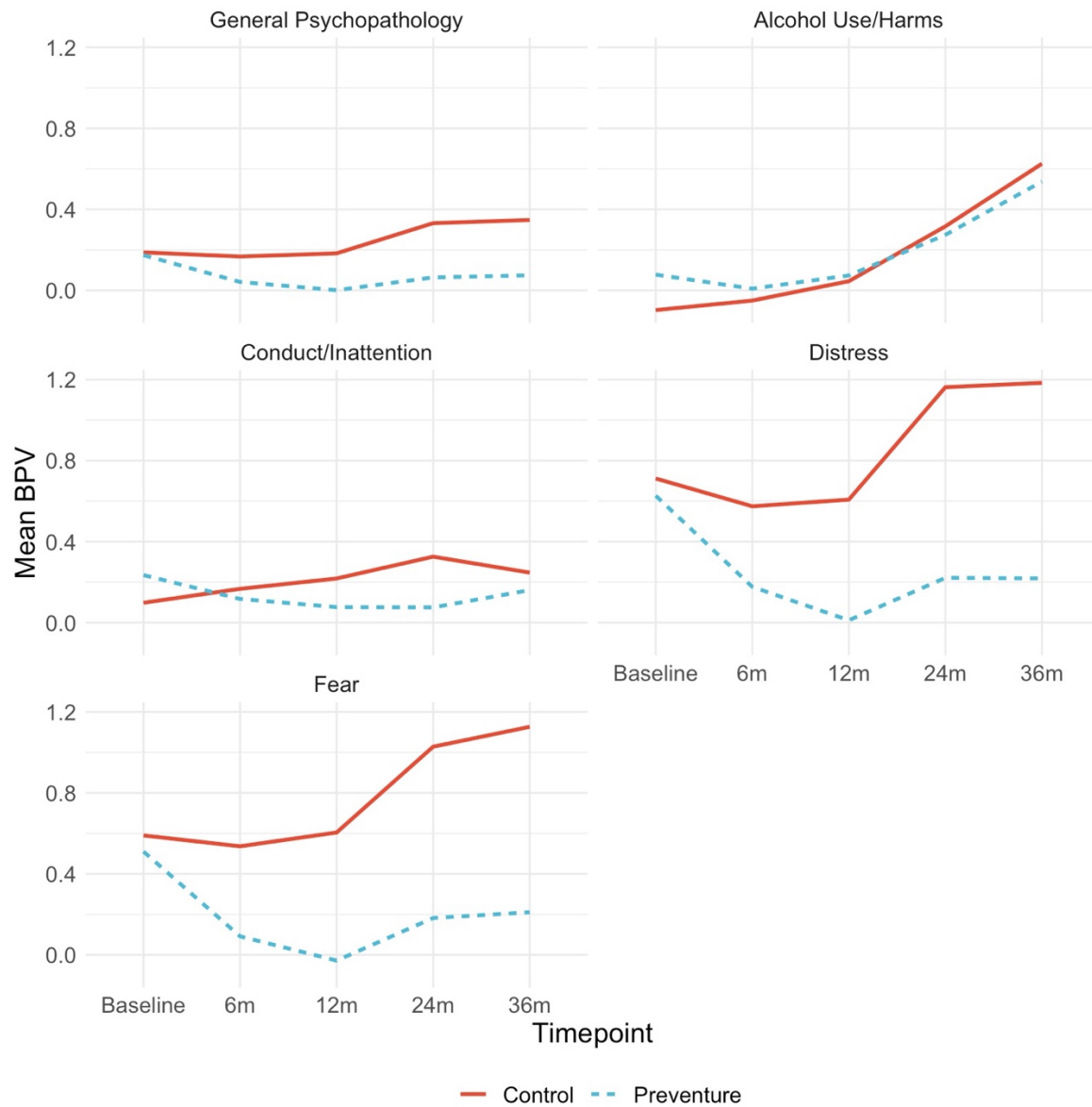
Note. BPV = Bayesian Plausible Value

Table 5.3 Pooled fixed-effects coefficients from the mixed-effects model for general psychopathology, fear, distress, alcohol use/harms and conduct/inattention in the high-risk sample (n=701, observations = 2746)

	Model 1			Model 2 (controlling for general psychopathology)		
General Psychopathology	*Estimate (SE)*	*p*	*95% CI*	*Estimate (SE)*	*p*	*95% CI*
Intercept	-0.06 (0.10)	.525	-0.25 to 0.13			
Main effects						
Preventure	0.10 (0.10)	.335	-0.10 to 0.30			
Time (years)	**0.06 (0.03)**	**.015**	**0.01 to 0.12**			
Female	**0.37 (0.09)**	**<.001**	**0.20 to 0.54**			
Intervention effects						
Preventure x Time	**-0.07 (0.03)**	**.038**	**-0.13 to 0.00**			
Fear	*Estimate (SE)*	*p*	*95% CI*	*Estimate (SE)*	*p*	*95% CI*
Intercept	-0.21 (0.32)	.510	-0.84 to 0.42	-0.01 (0.08)	.899	-0.17 to 0.15
Main effects						
Preventure	0.28 (0.34)	.404	-0.38 to 0.94	-0.03 (0.09)	.711	-0.20 to 0.14
Time (years)	**0.21 (0.09)**	**.020**	**0.03 to 0.38**	0.004 (0.04)	.920	-0.08 to 0.08
Female	**1.21 (0.29)**	**<.001**	**0.65 to 1.78**	0.02 (0.06)	.737	-0.10 to 0.15
General psychopathology	-	-	-	**3.16 (0.03)**	**<.001**	**3.10 to 3.21**
Intervention effects						
Preventure x Time	-0.22 (0.11)	.056	-0.44 to 0.01	0.002 (0.05)	.960	-0.10 to 0.10
Distress	*Estimate (SE)*	*p*	*95% CI*	*Estimate (SE)*	*p*	*95% CI*
Intercept	-0.20 (0.32)	.544	-0.83 to 0.44	0.00 (0.08)	.958	-0.16 to 0.15
Main effects						
Preventure	0.35 (0.34)	.309	-0.32 to 1.02	0.04 (0.09)	.649	-0.13 to 0.21
Time (years)	**0.21 (0.09)**	**.017**	**0.04 to 0.37**	-0.0009 (0.04)	.981	-0.08 to 0.08
Female	**1.32 (0.29)**	**<.001**	**0.75 to 1.90**	0.12 (0.07)	.064	-0.01 to 0.25
General psychopathology	-	-	-	**3.20 (0.03)**	**<.001**	**3.14 to 3.26**
Intervention effects						
Preventure x Time	**-0.24 (0.11)**	**.028**	**-0.46 to -0.03**	-0.03 (0.05)	.631	-0.13 to 0.08
Alcohol use/harms	*Estimate (SE)*	*p*	*95% CI*	*Estimate (SE)*	*p*	*95% CI*
Intercept	**-0.25 (0.10)**	**.012**	**-0.45 to -0.06**	**-0.23 (0.10)**	**.017**	**-0.43 to -0.04**
Main effects						
Preventure	0.21 (0.11)	.049	0.00 to 0.42	0.19 (0.11)	.079	-0.02 to 0.39
Time (years)	**0.25 (0.03)**	**<.001**	**0.18 to 0.31**	0.23 (0.03)	**<.001**	0.16 to 0.29
Female	**0.16 (0.08)**	**.048**	**0.00 to 0.33**	0.06 (0.08)	.452	-0.10 to 0.22
General psychopathology	-	-	-	0.29 (0.03)	**<.001**	0.24 to 0.34
Intervention effects						
Preventure x Time	-0.08 (0.04)	.069	-0.16 to 0.01	-0.06 (0.04)	.166	-0.14 to 0.02
Conduct/inattention	*Estimate (SE)*	*p*	*95% CI*	*Estimate (SE)*	*p*	*95% CI*
Intercept	-0.01 (0.12)	.936	-0.25 to 0.23	0.06 (0.07)	.431	-0.09 to 0.20

Main effects

Preventure	0.14 (0.13)	.283	-0.11 to 0.39	0.04 (0.08)	.601	-0.12 to 0.20
Time (years)	0.05 (0.04)	.148	-0.02 to 0.13	0.002 (0.03)	.950	-0.06 to 0.07
Female	**0.24 (0.11)**	**.032**	**0.02 to 0.46**	-0.09 (0.07)	.189	-0.22 to 0.04
General psychopathology	-	-	-	**0.83 (0.03)**	**<.001**	**0.78 to 0.89**
Intervention effects						
Preventure x Time	-0.06 (0.05)	.219	-0.15 to 0.03	-0.003 (0.04)	.930	-0.09 to 0.08

Note. Estimates obtained from 100 BPV datasets. Time coded as baseline = 0, 6m= 0.5, 12m = 1, 24m = 2, 36m = 3. Results under 'Model 2' show mixed effects models for fear, distress, alcohol use/harms and conduct/inattention controlling for general psychopathology.

5.4.3   Exploratory analyses

Personality-specific effects. There were no statistically significant intervention effects detected within the *negative thinking, anxiety sensitivity* or *sensation seeking* target personality subgroups (see Appendix H Tables S5.6, S5.7 and S5.9). Within the *impulsivity* subgroup there was reduced growth in general psychopathology in the *Preventure* group, compared to the control group. ($b = -0.16$, $p = .024$; Appendix H Table S5.8).

Herd-immunity effects. Additional exploratory analyses with the whole sample (i.e., both high- and low-risk students), indicated there was reduced growth in *general psychopathology* ($b = -0.04$, $p = .034$) in the *Preventure* group compared to the control group (see Appendix H Table S5.10). There was also reduced growth in *alcohol use/harms* ($b = -0.08$, $p = .007$), and this remained after controlling for *general psychopathology* ($b = -0.07$, $p = .021$). There were no significant intervention effects on *fear*, *distress, or conduct/inattention* either before or after accounting for *general psychopathology.* However, there were notable decreases in the standardised effect sizes in the models controlling for *general psychopathology* suggesting that intervention effects on the specific dimensions were likely accounted for by effects on *general psychopathology*.

5.5 Discussion

This study found for the first time that a personality-targeted intervention delivered in schools, can be effective in reducing growth in general psychopathology among high-risk students from early- to mid-adolescence. The intervention was shown to produce effects on certain specific dimensions of psychopathology (distress, and to a lesser extent fear and conduct/inattention), however, overall, results indicated that the impact on specific dimensions of psychopathology were reflected in the effects on general psychopathology. These findings provide the first empirical evidence that development of general psychopathology can be modified through a brief, selective preventative intervention delivered during early adolescence.

In previous analyses of *Preventure* trials, significant decreases in anxiety, depression, conduct, hyperactivity, and alcohol consumption have been observed (Newton, Conrod, et al., 2016; O'Leary-Barrett et al., 2013). Results from the current study suggest that decreases in these different symptom areas are synonymous with decreases in general psychopathology. *Preventure* was designed to provide brief, personality-specific coping skills and equip students to identify and challenge personality-specific thoughts that lead to problematic emotional and behavioural reactions. Therefore, while the mechanisms to explain these broad decreases in psychopathology are unclear, they may be attributed to transdiagnostic processes believed to underlie general psychopathology, such as emotion dysregulation or negative emotionality (Smith et al., 2020).

While no other studies have examined the impact of a school-based intervention, one previous randomised controlled trial examined trajectories of general, internalising, and externalising psychopathology among children with histories of institutional rearing (Wade et al., 2018). In this study, children who were randomised into foster care demonstrated declines in externalising and general psychopathology from age 8 to 16 years, compared to children who remained institutionalised. When considered with the results of the present study, this suggests that general psychopathology may represent broad deficits in coping and responding to stressors. Critically, these findings together indicate that general psychopathology is a useful intervention target and may be influenced by changes to a child's socioenvironmental context as well as changes to how individuals think and respond to stressors.

The personality specific outcomes of this study are particularly novel, providing evidence of possible greater effectiveness among students with an impulsive personality profile. Specifically,

subgroup analyses indicated that growth in general psychopathology among students in the impulsive subgroup was slower in comparison to students in the control group. However, there were no other significant intervention effects found in the other personality subgroups. It is possible that there was insufficient power within these subgroups due to small sample sizes. Nevertheless, the potential personality specific effects of *Preventure* warrant further examination as this may help clarify who benefits most from the intervention, or, conversely, identify personality subgroups for whom the intervention could be improved.

Findings from the present study also indicated that *Preventure* may have herd-immunity-like effects, as the impact on general psychopathology held when low-risk students, who did not receive the intervention, were included in analyses. In addition, there were significant effects on *alcohol use/harms* even after accounting for the effect on general psychopathology. This suggests that the program has benefits for the whole cohort. Although other *Preventure* studies have identified universal effects on alcohol related outcomes (Conrod et al., 2013; Slade et al., 2021), to our knowledge this is the first study to examine effects on other symptom domains. The mechanisms through which the effects of *Preventure* transfer to low-risk students who did not directly receive the intervention are unclear. It seems reasonable to suggest that the impact of *Preventure* on high-risk students leads to changes in the social interactions between high- and low-risk students, in turn reducing socioenvironmental risks for all students. Future research should attempt to better understand the factors and processes that may underlie these effects.

Results should be considered in light of some potential limitations. First, as the present study combined the *Preventure* only and the combined *Preventure and Climate Schools* intervention groups (to improve power), it is possible that Climate Schools could be influencing the results. However, Climate Schools focuses on preventing alcohol and cannabis use and related harms, and previous research has shown Climate Schools to be effective with alcohol related outcomes, but not other broader mental health outcomes (Newton et al., 2020; Slade et al., 2021). Furthermore, *Preventure* has previously been shown to be effective with and without the combined Climate Schools Program (Newton et al., 2020). In the present study, general psychopathology was more heavily defined by fear, distress, and conduct/inattention than alcohol use/harms. Therefore, it seems reasonable to suggest that the impacts on psychopathology in the present study can be attributed to *Preventure*. Second, there was a low prevalence of alcohol use and mental health symptoms in the present sample, and as such there may have been limited variability within the data. Third, although a broad range of mental health symptoms were included, there were some common symptom domains missing from our model, such as psychosis, eating pathology and

other substance misuse. Finally, there was also an imbalance in the ratio of males and females across the intervention groups following randomisation. To account for this, we adjusted for sex in intervention effect analyses however future research may wish to strive for a more balanced sample.

The most important conclusion from this study is that a personality-targeted selective prevention program can reduce the development of general psychopathology across three years during adolescence. The findings are consistent with arguments that a general psychopathology dimension can be a useful and efficient target for the prevention of a broad range of symptom domains. Importantly, the findings also contribute to our understanding of the nature of general psychopathology and suggest this factor may represent a general tendency toward poor behavioural and emotional control. Overall, the findings should encourage further research on the prevention of broad, transdiagnostic dimensions of psychopathology, and the upscaling of interventions which demonstrate effects in preventing general psychopathology.

Chapter 6

General discussion

6.1 Background

Psychopathology is the leading burden of disease among young people worldwide (Erskine et al., 2015; Whiteford et al., 2013). Over the last decade the prevalence of mental disorders in young people has reached a crisis point. At the same time, growing disillusionment with existing categorical diagnostic systems has led to a renaissance of research investigating empirically based structural models of psychopathology culminating in the development of the Hierarchical Taxonomy of Psychopathology. Understanding the underlying structure of psychopathology is necessary for explicating the precursors, course, and consequences of mental ill health. Hierarchical-dimensional models, such as HiTOP, indicate there is a general psychopathology dimension that underlies all mental illness. Broad dimensions of psychopathology open new avenues for prevention and intervention research. Implicit within the existence of a general psychopathology dimension is the opportunity to prevent the development of multiple mental disorders simultaneously. Despite strong evidence for the existence of this general psychopathology dimension, we still know very little about what the dimension actually represents.

The overall aim of this thesis was to further examine general psychopathology and underlying specific symptom domains among adolescents, thereby providing insights into the nature of general psychopathology, its developmental origins, and its utility as a preventive intervention target. Three major gaps were identified in Chapter 1 of this thesis. First, the literature to date had poorly evaluated alternative structural models of psychopathology in young people. Second,

despite well-established links with personality, limited research had examined the co-development of personality and psychopathology in adolescence within the context of hierarchical-dimensional conceptualisations of psychopathology. Third, no empirical research had examined the impact of preventative interventions on general psychopathology, despite the advantages of providing a broader target. Furthermore, methodological limitations were identified in the existing literature, including insufficient adjudication between alternative structural models, inadequate disaggregation of between-person and within-person sources of variance, and limited longitudinal research. This thesis was designed to address these limitations and provide insight into the complex inter-relations between personality and psychopathology in young people. Five research questions were formulated to address the gaps identified and provide an innovative and critical contribution to our understanding of psychopathology in young people:

1. What are the risk and protective factors for general and specific dimensions of psychopathology in young people?
2. What is the underlying structure of psychopathology in young people?
3. How are high-risk personality traits associated with different levels of a hierarchical-dimensional model of psychopathology?
4. How do high-risk personality traits and general psychopathology influence each other during adolescence?
5. What are the impacts of a personality-targeted prevention program on trajectories of general and specific dimensions of psychopathology?

Overall, this thesis offers a methodologically rigorous approach to advancing our understanding of the structure of psychopathology and its association with high-risk personality traits in young people. The remainder of this chapter will give an overview of each of the studies in this thesis, summarise key findings, strengths, and limitations of the research, and discuss implications and future directions.

6.2 Summary of chapters and overview of findings

The key findings from each chapter in relation to each of the five major questions of this thesis is provided in Table 6.1. Each chapter and the key findings are summarised below.

Chapter 1 outlined the prevalence and burden of psychopathology in young people and highlighted the need for better prevention and early intervention. An overview of evidence for alternative

conceptualisations of psychopathology was provided, with extensive evidence supporting a shift towards empirically based, hierarchical-dimensional structures. Chapter 1 also briefly outlined the advantages and opportunities for general psychopathology as an intervention target, particularly for young people, and demonstrated a clear need for a better understanding of the development of general psychopathology during adolescence. Finally, Chapter 1 summarised the high-risk personality traits in the four-factor model of vulnerability and outlined their suitability for advancing our understanding of the structure, development, and prevention of broad dimensions of psychopathology.

Chapter 2 presented a systematic review of the literature on transdiagnostic risk and protective factors for general and specific dimensions of psychopathology. An array of risk factors spanning biological, socioenvironmental, and psychological research domains emerged. Most notably, factors relating to negative affectivity/neuroticism and behavioural disinhibition were identified as promising, modifiable risk factors for general psychopathology. Chapter 2 also identified critical methodological considerations, including the need for more longitudinal research and further exploration and evaluation of alternative structural models of psychopathology.

Chapter 3 explored the structure of psychopathology in a large sample of Australian adolescents and assessed external validity in relation to high-risk personality traits. Following rigorous model evaluation, a higher-order model comprised of a general psychopathology dimension and four specific dimensions (fear, distress, alcohol use/harms, and conduct/inattention) outperformed alternative structures. Associations with four high-risk personality traits were then explored across each level of the higher-order model. General psychopathology was associated with anxiety sensitivity, negative thinking, impulsivity, and sensation seeking. After accounting for these associations with general psychopathology, there were some remaining direct associations with specific dimensions of psychopathology. Negative thinking and anxiety sensitivity were more closely related to fear and distress, whereas impulsivity and sensation seeking were more closely related to alcohol use/harms and conduct/inattention. Sensation seeking was also directly associated with alcohol use/harms (after accounting for its association with general psychopathology). Taken together, these findings suggested that each of the personality traits have unique patterns of association with specific symptom domains. Furthermore, several significant associations between personality traits and individual symptoms remained after accounting for general and specific psychopathology.

Chapter 4 explored the co-development of general psychopathology and high-risk personality traits over the course of three years, from early to mid-adolescence. Given the potential opportunities for prevention, this study focused on general psychopathology. The major findings from this study were that general psychopathology at age 13 was concurrently associated with negative thinking, anxiety sensitivity and impulsivity, but not sensation seeking. Longitudinally, anxiety sensitivity and impulsivity predicted general psychopathology at subsequent time points. In contrast, general psychopathology predicted subsequent negative thinking. These findings suggest that anxiety sensitivity and impulsivity are especially useful predictors of increases in general psychopathology between the ages of 13 to 16, and that negative thinking may increase as a consequence of earlier increases in general psychopathology. Importantly, this research provides further evidence that sensation seeking may be more useful as a predictor of substance use problems specifically, rather than of broader psychopathology dimensions. Increases in general psychopathology persisted from age 14 to 15, suggesting that this is a particularly critical age for increases in co-occurring mental health problems.

Chapter 5 evaluated the impact of *Preventure*, a school-based personality-targeted substance use prevention program, on general and specific dimensions of psychopathology. *Preventure* was found to reduce growth in general psychopathology among students with a high-risk personality profile over three years. There were no effects on specific dimensions beyond the effect on general psychopathology. Exploratory analyses were also conducted to examine the impact within personality risk subgroups and across high- and low-risk students. There were personality-specific effects on general psychopathology among adolescents in the impulsivity subgroup. There was also evidence for reduced growth in general psychopathology across high- and low-risk adolescents. The findings that a brief intervention successfully reduced growth in general psychopathology for high-risk adolescents (and their low-risk peers) are novel and impressive.

Table 6.1 Summary of research questions and key findings from this thesis

Research question	Chapter aim and overview	Key findings
What are the risk and protective factors associated with general psychopathology and specific dimensions of psychopathology?	**Chapter 2**: Review the biological, socio-environmental, and psychological risk and protective factors for general and specific dimensions of psychopathology in young people aged 10-24 years; 41 studies were included in the review.	Outcome: general psychopathology ↑ Earlier pubertal timing/onset of menarche ↑ Executive functioning deficits ↑ Genetic risk for ADHD ↑ Genetic risk for schizophrenia ↑ Maternal depression ↑ Stressful life events ↑ Low extroversion ↑ Low effortful control ↑ High negative affectivity ↑ High neuroticism ↑ High rumination
What is the underlying structure of psychopathology in young people?	**Chapter 2**: Review theoretical and methodological approaches to modelling psychopathology in young people	- 50 structural models from 41 studies; 25 bifactor models - Most common structure comprised of general psychopathology, internalising and externalising
	Chapter 3: Evaluate alternative structural models of psychopathology in adolescents (N=8,654)	- Higher-order model comprised of general psychopathology, fear, distress, alcohol use/harms and conduct/inattention spectra performed better than alternative structures
How are high-risk personality traits associated with different levels of a hierarchical-dimensional model of psychopathology?	**Chapter 3**: Examine associations with four high-risk personality traits: Negative thinking, anxiety sensitivity, impulsivity and sensation seeking across general, specific and symptom levels.	General psychopathology ↑ Negative thinking ↑ Anxiety sensitivity ↑ Impulsivity ↑ Sensation seeking Distress ↑ Anxiety sensitivity ↑ Negative thinking Fear ↑ Anxiety sensitivity ↓ Sensation seeking Alcohol use/harms ↓ Anxiety sensitivity ↓ Negative thinking ↓ Impulsivity ↑ Sensation seeking Conduct/inattention ↑ Impulsivity ↑ Sensation seeking Symptom level ↑↓ Several significant associations between personality traits and

Research question	Chapter aim and overview	Key findings
		individual symptoms remained after accounting for general and specific psychopathology
How do high-risk personality traits and general psychopathology influence each other during adolescence?	**Chapter 4:** Examine the co-development of **general psychopathology** and high-risk personality traits	- Initial levels of general psychopathology associated with NT, AS and IMP - AS and IMP → General psychopathology - General psychopathology → NT - Increases in general psychopathology carried over from age 14 to 15
What are the impacts of a personality-targeted prevention program on general and specific dimensions of psychopathology?	**Chapter 5**: Examine the impact of *Preventure* on general psychopathology and fear, distress, alcohol use/harms and conduct/inattention specific dimensions.	- *Preventure* found to reduce growth in general psychopathology - Personality-specific effects on general psychopathology within impulsivity subgroup, no other significant intervention effects observed within other personality subgroups. - Reduced growth in general psychopathology evident across high- and low risk adolescents

6.3 Strengths and limitations

Overall, this thesis advances the knowledge base on the structure of psychopathology and substantive meaning of general psychopathology and its utility in the prevention of mental health problems among young people. The review of the literature identified several gaps and methodological considerations, including a predominance of studies using bifactor models despite concerns about the reliability and replicability of latent variables derived from such models; a narrow focus on structure rather than meaning and interpretation of transdiagnostic dimensions; reliance on diagnostic indicators rather than symptoms; and a lack of longitudinal, causally driven studies. A major strength of this thesis is that it addressed these gaps by: harmonising longitudinal data from two large randomised controlled trials of Australian adolescents; adopting a symptom level approach to modelling the structure of psychopathology; applying rigorous tests of model fit, reliability and replicability; and sophisticated statistical analytic techniques.

The study described in Chapter 3 addressed concerns about structural models by applying more rigorous tests of model fit, reliability and replicability to adjudicate between bifactor, higher-order and correlated factor models. This led to the selection of a higher-order model of psychopathology, which was then used in the studies described in Chapters 4 and 5, which provided further evidence for the robustness of this model by demonstrating longitudinal and group related invariance. Furthermore, results from Chapters 4 and 5 provide additional evidence for the external validity of the higher-order model and demonstrate meaningful and theoretically expected findings in relation to the higher-order general psychopathology factor. The sophisticated analytic approach applied in Chapter 4 separated between-person and within-person sources of variance to examine developmental associations between general psychopathology and high-risk personality traits. The findings of this thesis add to the literature on general psychopathology by drawing attention to the complex, developmental associations with high-risk personality traits, and demonstrating that it is an actionable intervention target that can be modified through helping young people to develop skills to manage personality-based risks. Finally, this thesis integrated data from two large randomised controlled trials of Australian adolescents, applied rigorous, sophisticated statistical methods to explore each of the central research questions and addresses important gaps and methodological limitations of the extant literature.

Despite the significant and original contributions of this thesis to our understanding of general psychopathology and the complex interactions with personality traits among adolescents, the findings from this program of work must be interpreted with consideration to several limitations. As discussed

in the empirical chapters, the generalisability of findings may be limited due to the non-representative community sample of Australian adolescents and the use of self-report measures, and the unequal gender distributions in Chapters 4 and 5 due to the randomisation procedure. Other previously noted limitations relate to complexities arising from secondary data analysis, such as inconsistencies in follow up intervals across the two samples (Chapter 4), the collapsing of intervention groups to ensure sufficient power to detect effects in continuous outcomes (Chapter 5), and the scope of personality and psychopathology constructs that were assessed (Chapters 3-5). Although a broad range of mental health symptoms were included in the analyses, there were some common forms of psychopathology that were not assessed in the original trials and consequently were not able to be incorporated into the higher-order model of psychopathology (e.g., psychosis, eating pathology and obsessive-compulsive disorder). Similarly, this thesis examined high-risk personality traits using a measure designed to identify adolescents at risk of substance use problems and co-occurring emotional and conduct problems. Although the traits examined in the present thesis are highly correlated with the Big 5 traits, particularly neuroticism and the excitement-seeking facet of extroversion, future research should consider using more comprehensive measures of general personality. For example, the NEO-PI (McCrae et al., 2016) which measures both broad personality dimensions and narrower facets and nuances of personality, would allow for a more detailed investigation of the interactions between personality and psychopathology and potentially identify other aspects of personality that may be useful predictors of, or more salient intervention targets for, general or specific psychopathology outcomes. Chapter 3 identified individual symptoms with cross-domain direct effects, over and above general and specific dimensions of psychopathology. Given that original positioning of these symptoms aligns with the broader literature, and that the factor loadings for these symptoms were high (indicating appropriate positioning), modifications to the symptom level were not examined in the subsequent chapters. As the structure of psychopathology continues to be debated, there is potential to clarify the position of these symptoms within the broader structure of psychopathology in future, structural research. Despite these limitations, the results of this thesis establish a foundation for future research to further unpack the complex associations between personality and psychopathology during adolescence.

6.4 Implications

The research questions and overall aims of this thesis were shaped by a translational perspective within the context of a movement toward data-driven, hierarchical-dimensional conceptualisations of psychopathology. This perspective acknowledges that comorbidity among mental and substance use disorders is not only common but can be leveraged to better understand aetiology and enhance

prevention efforts. Collectively, the empirical chapters provide robust evidence for a higher-order structure comprised of four lower-order dimensions (fear, distress, alcohol use/harms, and conduct/inattention problems). Importantly, these studies are among the first to explore aetiological and intervention research questions together. Extending beyond traditional structural studies, the findings from this thesis have important implications for the substantive interpretation of general psychopathology, the targeting and timing of prevention efforts, and set the stage for further aetiological and intervention research.

6.4.1   Prevention targets and timing

Findings from this thesis indicate that effective and efficient prevention and health policy should consider interventions that target, or have effects on, broad dimensions of psychopathology. This thesis also provides further evidence for personality measures, such as the SURPS, as useful tools for identifying individuals at risk of experiencing co-occurring mental health and substance use problems. Adolescents characterised by elevated anxiety sensitivity, negative thinking, impulsivity and/or sensation seeking are more likely to develop a wide range of psychiatric problems. Results from Chapter 3 indicate that these different aspects of personality are concurrently associated with general psychopathology *and* have unique associations with different specific forms of psychopathology. This suggests that these aspects of personality demonstrate the usefulness of personality as a tool for identifying adolescents at risk for experiencing general psychopathology and hints at the symptom domains most likely to be experienced. For example, adolescents with elevated sensation seeking may be more likely to experience alcohol or substance use related problems whereas adolescents with elevated impulsivity may be more vulnerable to conduct/inattention related problems. Adolescents with higher levels of anxiety sensitivity may be more vulnerable to internalising problems generally, such as fear and distress related symptom domains; and adolescents with greater negative thinking may be more vulnerable to experiencing distress more specifically. Further research is needed to better understand the predictive utility of different aspects of personality in relation to specific dimensions of psychopathology.

Findings from Chapter 4 revealed complex and important longitudinal associations in relation to the co-development of general psychopathology and these high-risk personality traits. Specifically, anxiety sensitivity and impulsivity predicted general psychopathology, whereas general psychopathology predicted negative thinking. This indicates that certain aspects of neuroticism *contribute to* the development of general psychopathology while others may instead be *amplified by* the experience of general psychopathology. Although prior research has indicated that bidirectional

associations exist between general psychopathology and neuroticism, these findings demonstrate that different aspects of neuroticism play different roles in the development of psychopathology. From an intervention perspective, these findings suggest that impulsivity and anxiety sensitivity may be more salient prevention targets, while negative thinking may be more useful in early or indicated interventions.

The results from Chapter 5 indicate that growth in general psychopathology during adolescence can be effectively reduced by the *Preventure* intervention. This was the first study to show that general psychopathology could be modified through a preventative intervention. Reducing growth in general psychopathology has the potential to prevent the development of multiple forms of mental or substance use disorders simultaneously with significant potential to reduce the enormous burden and disease and social costs attributed to them. In addition, in Chapter 4, predictive relationships were observed between anxiety sensitivity and impulsivity and increases in general psychopathology. Such increases in general psychopathology tended to persist from 14 to 15 years of age and predicted increases in negative thinking. These findings highlight the potential benefits of personality-based approaches to screening, prevention, and intervention.

In summary, certain aspects of personality contribute to trajectories of general psychopathology, and other aspects share high concurrent associations. This information can be used to improve early identification of individuals prior to symptom onset, and tailor interventions towards modifiable aspects of personality, such as emotion regulation and impulse control, to prevent or reduce symptoms or the impact and burden of mental health problems. These findings represent some of the first steps towards personalised prevention.

6.4.2   *Interpretation of general psychopathology*

Despite substantial evidence for the general factor of psychopathology, the construct remains somewhat of a black box. Beyond the statistical understanding that general psychopathology represents shared variance among indicators or lower-order factors, the field is unclear on the mechanisms that drive this shared variance. As outlined in Chapter 1, there is an ongoing dispute about whether general psychopathology represents a substantive mechanism or a methodological artefact. Although this thesis did not directly aim to adjudicate between interpretations, the findings imply that general psychopathology possesses some functional utility, at least within a general population sample during a critical developmental period for psychopathology.

Chapter 6. General discussion

The findings from Chapters 3 and 4 suggest that general psychopathology represents a general vulnerability to, or propensity for, developing multiple forms of psychopathology and point to potential underlying personality-based mechanisms. The concurrent associations between general psychopathology and anxiety sensitivity, impulsivity and negative thinking are consistent with a shared aetiology or integrated dimensional model of personality and psychopathology.

Among the proposed functional explanations of general psychopathology described in Chapter 1, findings from this thesis are consistent with the idea that general psychopathology likely reflects the synthesis of dispositional negative emotionality, impulsive responsivity to emotion and nonspecific impairment (Carver et al., 2017; Smith et al., 2020; Southward et al., 2022). Specifically, in Chapter 4, anxiety sensitivity and impulsivity were found to precede increases in general psychopathology, which in turn preceded increases in negative thinking.

The intervention effects observed in Chapter 5 also hold implications for the substantive meaning of what a general psychopathology dimension represents. For example, the finding that growth in general psychopathology can be reduced through an intervention that applies motivational interviewing and CBT techniques tailored to neurotic and disinhibited personality traits, suggests general psychopathology may directly or indirectly reflect a tendency toward poor behavioural or emotional control. Furthermore, the observation that this effect remained when both high- and low-risk students were included in analyses, suggests that general psychopathology is also influenced by changes to an adolescent's socioenvironmental context. These findings are consistent with the large body of evidence demonstrating that emotion regulation and dysregulation contribute to the development and/or maintenance of almost all common forms of psychopathology, including internalising and externalising symptoms (Brenning et al., 2022; Cavicchioli et al., 2022; Cludius et al., 2020; Lincoln et al., 2022; Sloan et al., 2017). Emotion dysregulation has been found to mediate the association between childhood maltreatment and several specific symptom domains (Weissman et al., 2019) and appears to amplify personality-based risk factors, including impulsivity and behavioural disinhibition, which in turn leads to more severe expressions of psychopathology (Beauchaine, 2015). The findings from this thesis add to this literature and suggest that emotion regulation (or dysregulation) may be a potential causal mechanism underlying general psychopathology.

It is also plausible that this interpretation is specific to adolescents (a subset of the general population with emerging symptoms and psychopathologies), or non-clinical samples. One recent study examined whether the inclusion of undiagnosed cases affected empirical evidence for general psychopathology (Watts et al., 2021). Using data from three large, USA representative samples, cases without a single

psychiatric diagnosis were systematically removed in 10% increments and structural models were re-estimated at each increment. As undiagnosed cases were removed, empirical support for general psychopathology weakened: the general factors of psychopathology explained less variance in psychopathology and the correlation between externalising and internalising factors became negligible or negative. The authors tentatively conclude that this lends weight to the 'statistical artefact' interpretation as the construct did not generalise to the entire population. An alternative interpretation raised by the authors, is that general psychopathology may be a more meaningful construct among people with sub-clinical or emerging psychopathology (e.g., adolescents). Indeed, this may in part explain why prevention studies involving non-clinical samples (such as the samples examined in this thesis) have demonstrated intervention effects on general psychopathology, whereas treatment studies have not.

Taken together, findings from the present thesis are consistent with the view that general psychopathology represents shared vulnerability to experiencing most or all forms of psychopathology. Specifically, the findings suggest that general psychopathology likely represents a substantive mechanism (or mechanisms) relating to negative emotionality and impulsivity during adolescence, such as emotion dysregulation.

6.4.3 Research implications and future directions

The study of hierarchical-dimensional models of psychopathology has grown rapidly over the last decade but the field has only recently shifted its attention towards understanding these broad psychopathology dimensions from a functional perspective. The studies in this thesis present some of the first work in this next wave of research and provide three key implications for future research.

First, the convergence on the bifactor model may have been premature. In response to concerns about the limitations of bifactor models, recommendations were put forward to better adjudicate between different structural models of psychopathology data (Forbes, Greene, et al., 2021). As reported in Chapter 3, when additional, more rigorous methods are considered, a higher-order model performed better than a bifactor model. Indeed, other recent studies using some of the same metrics have also found that bifactor model is inadequate (e.g., Lees et al., 2021; Mann et al., 2020; Sunderland et al., 2020). Although the need for a consistent approach to modelling psychopathology has not yet been realised, and future research should continue to explore alternative structural models and evaluate against rigorous criteria, the empirical studies in this thesis collectively demonstrate the robustness and utility of a higher-order model of psychopathology.

Second, much of the research to date examining associations between personality and psychopathology from a hierarchical-dimensional perspective has focused on broad personality traits. However, the findings from Chapter 4 imply that narrower aspects of personality domains show nuanced associations with psychopathology that are masked when only the broader domains are examined. It is also possible that these more nuanced associations were uncovered by the separation of between-person and within-person changes. As the theories around associations between personality and psychopathology are inherently theories of within-person change, future research should prioritise methods that allow for the examination of within-person change. Future research that considers associations with more fine-grained aspects of personality will no doubt be beneficial for understanding the origins of psychopathology while also identifying modifiable prevention targets.

Third, Chapter 5 was the first study to examine the intervention effects of a brief school-based, personality-targeted intervention on psychopathology in a hierarchical-dimensional framework. The study in some ways serves as a 'proof of concept' that general psychopathology can be modified through intervention and should encourage further research on the prevention of general psychopathology as well as the upscaling of effective programs.

6.5 Conclusions

The findings from this thesis substantiate the role of personality in the development of general psychopathology and demonstrate the potential for personalised approaches to the prevention of broad dimensions of psychopathology. The evidence for concurrent and prospective associations between different aspects of personality and different dimensions of psychopathology demonstrates the utility of personality in the early detection of young people more likely to experience psychopathology. Importantly, findings from this thesis indicate that growth in general psychopathology can be reduced through an intervention targeting personality-based risk factors. The effects of the intervention appear to have a herd immunity type response, suggesting that protecting more vulnerable individuals can have widespread benefits for broader communities. This thesis contributes to the ongoing efforts to advance our understanding of the structure and development of psychopathology and to reduce the symptoms and consequences of psychopathology for young people. Given the increasing rates of psychopathology among young people, and the substantial burden of disease and economic and social costs associated with mental disorders, novel and efficient prevention and early intervention is crucial for reducing the consequences for individuals and the wider community.

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Appendix A

Candidate contribution statement

The empirical chapters in this thesis are new analyses using data from the 'Climate and Preventure' (CAP) and 'Climate Schools Combined' (CSC) trials conducted at the Matilda Centre at the University of Sydney. As part of my candidature, I harmonised the baseline data from the CAP and CSC trials (analysed in Chapter 3) and contributed to the harmonisation of longitudinal data from the CAP and CSC trials (up to year 3; analysed in Chapter 4).
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Appendix B

A systematic review of transdiagnostic risk and protective factors for general and specific psychopathology in young people

This paper has been published as:

SJL conceptualised and led the study. All authors (SJL, MS, NN and CC) contributed to the design of the study. SJL wrote the manuscript and CC, MS and NN provided advice, reviewed, and contributed to revisions of the manuscript. SJL conducted all searches. SJL screened 100% of the titles and abstracts, and CC, MS and NN screened 25%. SJL and MS reviewed 100% of the studies eligible for full text review. Quality assessments were completed by SJL (100%) and MS and CC (50%). SJL is the corresponding author
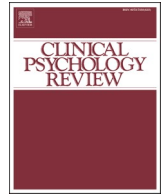
Review

A systematic review of transdiagnostic risk and protective factors for general and specific psychopathology in young people

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ABSTRACT

A large body of research has emerged over the last decade examining empirical models of general and specific psychopathology, which take into account comorbidity among psychiatric disorders and enable investigation of risk and protective factors that are common across disorders. This systematic review presents findings from studies of empirical models of psychopathology and transdiagnostic risk and protective factors for psychopathology among young people (10–24 years). PsycInfo, Medline and EMBASE were searched from inception to November 2020, and 41 studies were identified that examined at least one risk or protective factor in relation to broad, empirically derived, psychopathology outcomes. Results revealed several biological (executive functioning deficits, earlier pubertal timing, genetic risk for ADHD and schizophrenia, reduced gray matter volume), socio-environmental (stressful life events, maternal depression) and psychological (low effortful control, high neuroticism, negative affectivity) transdiagnostic risk factors for broad psychopathology outcomes, including general psychopathology, internalising and externalising. Methodological complexities are discussed and recommendations for future studies of empirical models of psychopathology are presented. These results contribute to a growing body of support for transdiagnostic approaches to prevention and intervention for psychiatric disorders and highlight several promising avenues for future research.

1. Introduction

Mental and substance use disorders often emerge between the ages of 13 and 24 years, and are among the leading causes of burden of disease worldwide (Costello, Copeland, & Angold, 2011; Kessler et al., 2011; Whiteford, Ferrari, Degenhardt, Feigin, & Vos, 2015). It is estimated that up to two-thirds of young people who have one mental or substance use disorder, have at least one additional comorbid disorder (Kessler et al., 2011; Leadbeater, Thompson, & Gruppuso, 2012). Comorbidity is associated with greater symptom severity and chronicity, and poorer treatment outcomes (Kessler et al., 2011). Comorbidity between mental disorders can undermine the validity of discrete diagnostic classifications and hinder or complicate etiological research. Research that fails to account for additional disorders may demonstrate support for putative risk and protective factors of a given disorder that are in fact due to the compounding nature of psychopathology rather than a specific, direct association (Dalgleish, Black, Johnston, & Bevan, 2020). Thus, relying on case-control research designs that exclude cases with multiple diagnoses leads to a loss of ecological validity and may not reflect actual clinical populations where comorbidity is common (Ofrat & Krueger, 2012). Furthermore, focusing on specific disorders alone may result in a loss of power to detect associations between risk and protective factors and psychopathology due to unaccounted similarities between interrelated conditions. In light of the challenges and limitations associated with discrete diagnostic entities, alternative approaches for conceptualising psychopathology have emerged to better understand and study the nature of psychiatric comorbidity (Eaton, 2015). The resulting empirically based models of psychopathology provide an important framework for investigating, identifying, and delineating specific versus transdiagnostic risk and protective factors.

1.1. Empirical models of psychopathology

Empirical models of psychopathology apply statistical techniques, such as latent variable (e.g., factor analysis and latent class analysis) or network approaches, to generate coherent structures of interrelated psychiatric conditions and symptoms, rather than relying on clinical consensus to form discrete diagnoses from traditional classification

systems. As a result, newer empirical models accommodate psychiatric comorbidity which in turn enhances ecological validity (Carragher, Krueger, Eaton, & Slade, 2015; Ofrat & Krueger, 2012). Two fundamental conceptualisations of psychopathology and comorbidity have emerged from two alternative statistical approaches.

Latent variable approaches conceptualise psychopathology as a hierarchical-dimensional structure comprised of a few, broad transdiagnostic dimensions (Kotov et al., 2017). For example, early comorbidity research among children and adolescents revealed the presence of two higher-order groupings: internalising and externalising (Achenbach, 1966). *Internalising* captures comorbidity among mood and anxiety disorders, whereas *externalising* reflects comorbidity among substance use, antisocial, oppositional and impulse related disorders. There is also consistent evidence that internalising and externalising are positively correlated, and there is mounting support for a higher-order, *general factor of psychopathology* (Caspi et al., 2014; Kotov et al., 2017). The general factor of psychopathology (sometimes referred to as 'p-factor' or 'p') may reflect a shared vulnerability to mental disorders (Kotov et al., 2017). More specifically, dispositional negative emotionality, impulsive responsivity to emotion, low cognitive functioning and thought dysfunction are all leading interpretations of what the general factor of psychopathology may reflect (Smith, Atkinson, Davis, Riley, & Oltmanns, 2020). However, it has also been suggested the general factor of psychopathology may reflect an index of overall impairment.

variety of statistical methods have been used in studies of latent variable structures of psychopathology, however there are three particularly common statistical models: the correlated actor, higher-order and bifactor models (Forbes et al., 2021). Although, these three models are closely related, each offer a different substantive interpretation of the structure of psychopathology. For example, a bifactor model's general psychopathology directly reflects the shared variance among all indicators, whereas a higher-order model's general factor reflects the shared variance among first-order factors, such as internalising and externalising. Further in correlated factors and higher-order models, the narrow latent variables reflect shared variance among a set of indicators, whereas specific factors in a bifactor model are uncorrelated and reflect the variance unique to a factor (after the shared variance among indicators has been attributed to the general factor). The differences between statistical models presents a challenge when interpreting evidence relating to key constructs derived from different methods. For example, the strength and direction of the relationship between latent variables and external criteria has sometimes differed as a function of the statistical model used (Watts, Poore, & Waldman, 2019).

Network modelling approaches however propose that disorders are comprised of networks of causally related symptoms, and comorbidity is the result of some symptoms causing symptoms in other disorder networks resulting in a broad network of associations among disorders (Borsboom, 2017; Eaton, 2015). Transdiagnostic groupings identified through latent variable modelling and found in hierarchical-dimensional models, such as internalising and externalising, have also been replicated in network models (Boschloo, Schoevers, van Borkulo, Borsboom, & Oldehinkel, 2016; McElroy, Shevlin, Murphy, & McBride, 2018). Both hierarchical (latent variable) dimensional and network models accommodate comorbidity (network models through the analysis of associations among pairs of symptoms and latent variable models through the analysis of shared and unique variance among symptoms and or diagnoses) among mental disorders and facilitate the investigation of transdiagnostic (vs disorder-specific) risk and protective factors that is not achievable with traditional classification systems (Forbes, Rapee, & Krueger, 2019; Fried et al., 2017; Krueger & Markon, 2011).

1.2. Transdiagnostic risk and protective factors

Previous research on risk and protective factors for mental disorders among young people has heavily relied on studies focussing on associations with single disorders. Some previous reviews have defined transdiagnostic risk/protective factors as factors associated with four or more disorders (Harvey, Watkins, Mansell, & Shafran, 2004). However, as described above, relying on studies of specific disorders has lower ecological validity and may also have less power to detect associations (Ofrat & Krueger, 2012). Transdiagnostic psychopathology constructs, such as internalising, externalising, and general psychopathology factors offer an alternative approach. While three previous systematic reviews have examined risk and protective factors in relation to internalising and externalising dimensions among children and adolescents, to our knowledge, no previous systematic reviews have synthesised evidence from studies of other broadband dimensions or constructs such as thought disorder or general psychopathology (Crews et al., 2007; McMahon, Grant, Compas, Thurm, & Ey, 2003). Furthermore, these reviews have tended to focus on narrow risk factor groups, particularly trauma and stress. Crews et al. (2007) conducted a systematic review of meta-analyses looking at child, family, school, community and cultural factors correlated with either internalising behaviours, externalising behaviours, or both. The review reported that six risk factors and three protective factors were common to both internalising and externalising, however it is unclear from the review whether internalising and externalising were examined simultaneously in the studies included. As such, it is not possible to conclude whether the identified risk and protective factors were transdiagnostic across internalising and externalising disorders. McMahon et al. (2003) conducted a systematic review of studies examining the relationship between several domains of stressors and internalising and externalising psychopathology in children and adolescents. The review reported that most stressors, such as exposure to violence, poverty and parental divorce were transdiagnostic across internalising and externalising. A more recent systematic review and meta-analysis also found that stressful life events during adolescence increase risk for both internalising and externalising (March-Llanes, Marqués-Feixa, Mezquita, Fañanás, & Moya-Higueras, 2017). However, it is unclear from these reviews whether the transdiagnostic nature of stressors holds across other domains of psychopathology, such as thought disorders, or whether these specific associations remain when multiple transdiagnostic psychopathology groupings are examined simultaneously. Additionally, while stressors may increase risk across disorders and are useful for identifying young people at risk of developing mental disorders, a broader synthesis is needed to identify modifiable factors (e.g., coping skills, emotion processing and regulation, maladaptive thinking styles and beliefs) that can be targeted through intervention (Forbes et al., 2019).

The advent of empirical models in recent decades has generated a sizeable body of literature on factors associated with transdiagnostic constructs in young people, particularly in relation to the internalising and externalising dimensions and more recently general psychopathology. However, to date, no systematic review has brought together the findings from this body of research. The present review addresses this gap via the synthesis and critical evaluation of studies with empirically based models of psychopathology to identify transdiagnostic risk and protective factors for psychopathology among young people. Insights drawn from this review may provide a foundation upon which interventions can be developed to reduce or prevent mental health problems earlier in life, and thus disrupt the cascade of psychopathology sequelae into adulthood.

2. Method

2.1. Search strategy and selection criteria

This systematic review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement (Moher et al., 2015). The protocol was registered with PROSPERO (CRD42020161368) and was previously published (Lynch, Sunderland, Newton, & Chapman, 2020). Medline, EMBASE and PsycINFO databases were searched systematically for studies published from inception to *November 2020* that examined

empirically based models of psychopathology in young people and at least one potential transdiagnostic risk or protective factor. Search strings for each database can be found in Appendix A.

An initial search in December 2019 yielded a total of 2676 studies, and 2016 remained after removing duplicates. Searches were re-run in *November 2020* (and limited to publication between 2019 to 'current'). A further 839 studies were returned, and 393 remained after deduplication. Search results were imported into Covidence for screening (Veritas Health Innovation, 2020). After removal of duplicates, all titles and abstracts were screened by one reviewer (SJL). The other reviewers (CC, NCN, MS) screened 25% of the titles and abstracts, which were randomly selected. Full-text articles were screened by SJL and MS. Disagreements at each stage of screening were resolved through discussion between the two screening authors or by a third reviewer.

2.2. Inclusion and exclusion criteria

The eligibility criteria were developed using the Population Exposure Comparator Outcome (PECO) framework. Empirical studies were included if they met the following criteria:

1. Participants mean age was between 10 and 24 years, in accordance with the World Health Organization definition of 'young person' (World Health Organization, 2014).
2. Examined any risk/protective factor variable, such as genetic, neurobiological, cognitive, social and environmental characteristics, and their association with an empirically based model of psychopathology.
3. Studies were not required to have a comparison group as the dimensional nature of psychopathology implicit within contemporary knowledge precludes the need for control groups.
4. Psychopathology outcomes derived from empirically based models of at least two broad groups of signs or symptoms, such as internalising, externalising, or thought disorder.
5. Written in English.
6. Peer-reviewed.

Articles were excluded if they did not report peer-reviewed, original

Fig. 1. PRISMA flow diagram depicting study selection process.

empirical findings, such as reviews, opinion pieces and conferences abstracts.

2.3. Quality assessment

Study quality was assessed independently by two reviewers using checklists from the Joanna Briggs Institute (Moola et al., 2019). Cross-sectional studies were evaluated using the Checklist for Analytical Cross-Sectional Studies, and longitudinal studies were evaluated using the Checklist for Cohort Studies (Moola et al., 2019). Uncertainty around interpretation of items on either checklist or application to studies included in the review was resolved through discussion between authors. In order to compare the quality of studies, a percentage score was calculated using the method described by Hoppen and Chalder (2018). That is, the number of items rated 'yes' were summed and then dividing by the number of maximum possible number of 'yes' ratings (and multiplied by 100). The maximum possible score was the total number of applicable items only as not all items were applicable to each study.

3. Results

3.1. Selection of studies

After screening titles and abstracts, 160 studies remained for inclusion, of which 119 were excluded following full-text review (see Fig. 1). Inter-rater reliability was high for title and abstract screening (92% agreement) and full-text screening (82% agreement).

3.2. Characteristics of included studies

A summary of the included studies is shown in Table 1. Of the 41 included studies, 26 were cross-sectional and 15 were longitudinal, and 54% were published in the last 2 years ($n = 22$). The vast majority of studies were from the United States of America (USA), the remaining studies were from Australia, Europe (Romania, Sweden, Netherlands and Italy), the United Kingdom (UK) and South Korea.

3.2.1. Overall quality

The overall quality of included studies was high with a mean rating of 90% across all studies. Cross-sectional studies demonstrated slightly higher quality with an average score of 93%, compared to 84% for longitudinal studies (See Appendix B and C for details). Lower quality ratings were largely due to studies not identifying confounding factors, and/or not stating strategies for dealing with confounds. Many longitudinal studies did not report follow up details, such as completion rate or reasons for loss to follow up, however generally strategies for addressing incomplete follow up were described in these studies. Agreement between independent raters was high (84%).

3.2.2. Models of psychopathology

In total, 50 structural models of psychopathology from 41 studies were examined in the papers. A summary of the models is presented in Table 2, and more detailed information is provided in Appendix D. As shown in Table 2, latent variable models were the most common. The most commonly used method was a bifactor model ($n = 25$, including one modified bifactor model), followed by confirmatory factor analysis ($n = 8$). None of the included studies examined a network model of psychopathology. In terms of transdiagnostic psychopathology groupings, a 3-group model comprised of general psychopathology, internalising and externalising was the most common structure examined in the included studies. Five studies examined relationships with a general psychopathology latent variable only, and six studies focussed on internalising and externalising latent variables only. Over 60 different measures of psychopathology were used across the included studies, of which only 16 were used in more than one study. The two most common

measures were the Youth Self Report and the Child Behaviour Checklist (Achenbach & Rescorla, 2001).

3.3. Risk and protective factors

Of the 41 included studies, 31 analysed biological (average QS = 90%), 15 analysed socio-environmental (average QS = 93%) and 19 analysed psychological (average QS = 91%) risk/protective factors. Included studies examined more than 130 unique risk and protective factors. Transdiagnostic risk and protective factors supported by evidence from two or more studies (or where two or more studies found no association) are summarised in Table 3, and a visual summary is presented in Fig. 2. A longer summary of findings from the included studies can be found in Appendix E, and detailed information about the findings, including effect sizes where available, can be found in Appendix F. What follows is a summary of findings relating to variables examined in more than one study, and notable trends within some sub-domains.

3.3.1. Biological risk and protective factors

Only *birth weight, executive functioning, genetic variance, non-shared environment, genetic risk for schizophrenia and ADHD, and sex/gender* were examined in more than one study (see Appendix E). Evidence from biological studies indicated that *earlier pubertal timing, executive functioning deficits, connectivity between regions in the default mode network, heteromodal frontoparietal network, visual association cortex and somatosensory network, less cerebellar gray matter, reduced white matter integrity of the pontine pathways and lower rates myeline maturation in dorsal cingulum and uncinate fasciculus* were associated with increased general psychopathology. The two studies that examined *birth weight* reported mixed findings. One study found that lower birth weight was associated with higher general psychopathology, while the other found no significant associations between general psychopathology, internalising, or externalising. *Executive functioning deficits* and *early pubertal timing* were also associated with greater levels of internalising and externalising. Regarding *functional connectivity* involving the dorsal anterior cingulate cortex (dACC) there were conflicting results. One study reported no significant associations with general psychopathology and resting-state functional connectivity of dACC and amygdala and with amygdala–medial frontal connectivity (van Hoof et al., 2019). In contrast, Kaczkurkin et al. (2018) found that general psychopathology was associated ith reduced connectivity between dACC and bilateral caudate, right thalamus, supramarginal gyrus and right putamen, and increased connectivity between dACC and dorso-medial frontal cortex.

Findings from genetic studies indicated that variance in general psychopathology, internalising, externalising, thought disorder, and depression and anxiety related latent variables were in part explained by *genetic influences*, and *non-shared environmental influences* were unique to specific disorder dimensions. *Additive genetic influences (i.e., heritable genetic factors) on negative emotionality and daring* were positively associated with general psychopathology, while *additive genetic influences on prosociality* were negatively associated with general psychopathology. *Additive genetic influences on prosociality and daring* were also related to externalising, such that prosociality reduced and daring increased externalising scores. There was also evidence that *earlier onset of menarche* was associated with greater externalising, distress and fear.

Regarding *sex/gender*, it was typically reported that *males/boys* were higher on general psychopathology and externalising, whereas *females/girls* were higher on internalising, however three studies found no significant associations with *sex/gender*. Furthermore, there were some inconsistencies among the significant findings. For example, Hamlat, Snyder, Young, and Hankin (2019) reported that girls were higher on both externalising and internalising, and boys were higher on general psychopathology in a bifactor model, whereas in a correlated factors model using the same sample there were no gender differences for externalising. These results differ from other studies reporting on bifactor models, which found that males/boys were higher on

Table 1

Characteristics of included studies.

Study	Country	Design	Sample	Risk/protective factors	Risk/protective factors measures	Measures of psychopathology	Respondent	Model: outcome variables examined	Quality score
Brikell et al. (2020)	Sweden	C	6603 A-TAC sub-sample, 6854 SCARED sub-sample (9 or 12 years, 50% male)	Genetic risk for ADHD, sex/gender	PRS for ADHD using GWAS summary statistics	A-TAC, SMFQ, SCARED	SR	*Correlated factors A-TAC:* IA, H/I, ASD, LD, ODD, CD, DEP, ANX *Correlated factors SCARED:* IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP *Bifactor A-TAC:* general psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, ANX *Bifactor SCARED:* general psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP	86%
Buzzell et al. (2020)	Romania	L	124 (40 institutionalised, 40 foster care, 44 never institutionalised; assessed at 12 and 16 years; 45% male	Cognitive control, mediofrontal theta oscillations	Go/No-Go task, EEG	MHBQ	PR, TR	*Bifactor:* general psychopathology, internalising, externalising	60%
Carragher et al. (2016)	Australia	C	2175 (mean age = 13.3 years, 57.4% male)	Sex/gender, anxiety sensitivity, impulsivity, negative thinking sensation seeking	SURPS	SDQ, BSI, RAPI, Hallucinatory experiences	SR	*Modified bifactor (correlated factors):* general psychopathology, internalising, externalising and thought disorder	71%
Deutz et al. (2020)	USA	L	1073 (assessed at age 14; 51.2% male)	Birth weight, attachment, temperament, cognitive ability, EF, self-control, positive maternal caregiving, harsh control, maternal depression, home environment	Refer to Deutz 2020 for measurement details	CBCL, YSR	SR, PR	*Bifactor:* general psychopathology, internalising, externalising	100%
Elliott et al. (2018)	USA	C	605 (university students, mean age = 20.23, 44% male)	Connectome wide intrinsic functional connectivity	fMRI	e-MINI, SCID-I	SR	*Bifactor:* general psychopathology	100%
Frenkel et al. (2015)	USA	L	116 (18–21 years, 43.7% male,	Adolescent social involvement LCA: 1. high social involvement and large network size 2. low social involvement and small network size Childhood BI (assessed 14 months through 7 years) latent class analysis: 1. Stable High BI 2. Stable Low BI	H-SAS, NRI POS, TBAQ, CCTI-SS	SCID-I, ASR, LSAS	SR	*LCA:* healthy, internalising (primarily anxiety), externalising (primarily substance use)	90%
Hamlat et al. (2019)	USA	C	567 (9–17 years, mean age = 13.58 years, 44.5% male)	Pubertal timing	PDS	CDI, MASC, CBCL, YSR, EATQ-R, SNAP-IV	SR, PR	*Bifactor:* general psychopathology, internalising, externalising *CFA (correlated factors):* internalising, externalising	100%
	USA	C					SR, PR		71%

Table 1 (*continued*)

Study	Country	Design	Sample	Risk/protective factors	Risk/protective factors measures	Measures of psychopathology	Respondent	Model: outcome variables examined	Quality score
Hankin et al. (2017)			571 youth parent pairs (youth age 9.3–17.5 years, mean age = 13.58, 45% male)	Effortful control, negative affectivity, positive affectivity	EATQ-R; PANAS-C	CDI, MASC, CBCL, YSR, EATQ-R, SNAP-IV		general psychopathology, internalising, externalising	
Harden et al. (2019)	USA	C	1913 twins and multiples (7.8–20.1 years, mean age = 13.1 years; 51% male, 35% MZ, 65% DZ; 1007 pairs)	Overall EF, visuospatial reasoning, verbal ability, general intelligence, genetic correlation, non-Shared environment correlation	WASI-II, Zygosity classified using LCA of twins', parents', and research assistants' ratings of physical similarity and ease of being mistaken for one another, Animal Strong, Stop Signal and Mickey tasks, Trail Making, Local-Global and Plus-Minus tasks, Digit Span Backward, Symmetry Span and Listening Recall tasks, 2-Back, Keeping Tack and Running Memory for Letters tasks	CBCL, CPRS, BFI-N	SR, PR	*Bifactor*: general psychopathology, internalising, externalising, attention problems	100%
Hatoum et al. (2018)	USA	L	885 same sex twins (16.5–20.1 years, mean age 17.3 years, 49% male)	Common EF, updating specific, shifting specific	Computerised executive functioning task battery (9 tasks)	CBCL, TRF	PR, TR	*Parallel process LGM*: internalising, externalising	60%
Jones et al. (2018)	Australia	C	2863 (mean age = 16.5 years)	Genetic risk for neuroticism and schizophrenia	PRS for schizophrenia, MDD, neuroticism and bipolar disorder using GWAS summary statistics	PLIKS-Q, CAPE, MFQ, DAWBA	SR	*Bifactor*: general psychopathology, anxiety, psychotic experiences, depression, negative (symptoms of psychosis) factors *CFA (correlated factors)*: anxiety, psychotic experiences, depression, negative (symptoms of psychosis) factors	86%
Jones et al. (2019)	USA	L	765 (13–14 years, 51% male, recruited through schools)	Family history of psychopathology, family tobacco environment, positive family environment, peer antisocial behaviour, peer substance use, behavioural disinhibition	Refer to Jones 2019 for measurement details	TRF, past month alcohol, cigarette & marijuana use	SR, PR, TR	*CFA (one factor)*: general psychopathology	75%
Jung et al. (2019)	South Korea	C	913 (high school students in South Korea)	Sex/gender, Peer conflict, academic problems, family conflict, violence, number of school counsellors, number of counselling sessions in school, number of counselling	AMPQ-II, school and community characteristics obtained from government information services	AMPQ-II	SR	*Multilevel LPA*: group 1 – high scores on all mental health domains, group 2 – high scores on internalising/ emotional domains, low scores on externalising/ behavioural domains, group 3 – low scores	75%

Table 1 (*continued*)

Study	Country	Design	Sample	Risk/protective factors	Risk/protective factors measures	Measures of psychopathology	Respondent	Model: outcome variables examined	Quality score
				sessions out-of-school, school dropout rate, number of students per teacher, counselling rate, percent of population aged 15–19, suicide rate for teenagers aged 15–19, availability of mental health services, ratio of public assistance recipients, social welfare facilities, percentage of education budget to total budget, percentage of welfare budget to total budget				on all mental health domains	
Kaczkurkin et al. (2018)	USA	C	1042 (11–23 years, mean age = 16.12 years; 45% males)	Functional connectivity of the dorsal ACC and regions associated with general psychopathology, cerebral blood flow	fMRI, arterial spin labeled (ASL) MRI	GOASSESS	SR, PR	*Bifactor*: general psychopathology, anxious-misery, psychosis, behavioural (externalising), fear	100%
Kaczkurkin et al. (2019)	USA	C	1394 (mean age = 14.98, 48% male)	Gray matter volume, cortical thickness	fMRI	GOASSESS	SR, PR	*Bifactor*: general psychopathology, anxious-misery, psychosis, behavioural (externalising), fear	100%
Lahey et al. (2011)	USA	C	1571 twin pairs (9–17 years)	Genetic variance, non-shared environment	Biometric modelling	CAPS	SR, PR	*Bifactor*: general psychopathology, internalising, externalising	100%
Lee et al. (2012)	South Korea	L	2844 (10–13 years, 54% male)	Sex/gender, level of attachment, parental knowledge of whereabouts, delinquent peers, externalising (initial level), internalising (initial level), parental violence	Refer to Lee 2012 for measurement details	YSR, JHDS, SDQ + others	SR	*Parallel process LGM*: internalising, Externalising	90%
Levin-Aspenson et al. (2019)	USA	C	1798 (20–29 years old, young adult sub-sample); 806 (15–19 years old, adolescent sub-sample)	Extroversion, neuroticism, openness	GL-NEO-S	UMCIDI	SR	*Bass-ackwards young adults*: general psychopathology, internalising, externalising, fear, distress and thought disorder *Bass-ackwards adolescents*: general psychopathology, internalising, externalising, fear and distress	71%
Liu et al. (2017)	USA	C	592 (13–19 years, mean age = 15.9 years, 49% male, 100% African American, raised in high-poverty neighbourhood)	Exposure to violence, racial discrimination, stressful life events, collective efficacy	EVI-Q, SRE, TSI, TCES	YSR	SR	*Bifactor*: general psychopathology, internalising, externalising	100%
Mann et al. (2020)	USA	L	646 (50% female, Mexican origin,	Agreeableness, neuroticism,	TIPI	DISC-IV	SR	*Parallel process LGM*: general	90%

Table 1 (*continued*)

Study	Country	Design	Sample	Risk/protective factors	Risk/protective factors measures	Measures of psychopathology	Respondent	Model: outcome variables examined	Quality score
			assessed annually from age 12–17 years)	openness/ intellect, extraversion, conscientiousness				psychopathology, internalising, externalising, ADHD	
McCutcheon et al. (2013)	USA	C	831 (offspring of male-male twin pairs who served in the military during the Vietnam era, mean age = 22.7 years, 51.5% male)	Sex/gender, genetic x environment risk, childhood physical/sexual abuse, mother inconsistent with rules, maternal depression, sibling substance use	Refer to McCutcheon 2013 for measurement details	SSAGA	SR	*LCA:* AUD, AUD-ANX-MDD & SUD-CD classes	100%
Olino et al. (2019)	USA	L	567 (14–18 years at wave 1, mean age = 16.6 years, excluded participants with lifetime history of psychosis or bipolar spectrum disorders, and adolescents with a history of MDD and/or dysthymia)	Sex/gender, parental education, paternal history of MDD, paternal SUD, early/ childhood psychopathology	Refer to Olino 2019 for measurement details	K-SADS, LIFE, SCID-I	SR	*LCA:* thriving functioning, average functioning, externalising vulnerability and family stress, internalising vulnerability	100%
Platt et al. (2017)	USA	C	4925 (13–17 years, 100% female)	Onset of menarche	Self-reported age at first period	CIDI-A	SR	*EFA (correlated factors):* Distress, fear, externalising and eating pathology	100%
Riglin et al. (2020)	UK	L	5518 (assessed at birth, age 7/8 and 13 years)	Genetic risk for schizophrenia, ADHD, autism spectrum disorder and depression	PRS from weighted mean number of disorder risk alleles in approximate linkage equilibrium	DAWBA	PR	*Bifactor:* general psychopathology, emotional problems, behavioural problems, neurodevelopmental problems	50%
Romer et al. (2018)	USA	C	1246 (mean age = 19.69, 42% male)	White matter integrity of pontine pathways, cerebellar gray matter volume	fMRI	e-MINI, MASQ-SD, STAI-T, CESD, SRP-SF, SRD, AUDIT, RDUS	SR	*Bifactor:* general psychopathology	100%
Schweizer et al. (2020)	USA	C	571 youth parent pairs (youth age 9.3–17.5 years, mean age = 13.58, 45% male)	Common cognitive risk, self-criticism, rumination (brooding), dysfunctional attitudes, negative inferential style, and dependency	CDAS, ACSQ, CRSQ-RS, CDEQ	CDI, MASC, CBCL, YSR, EATQ-R, SNAP-IV	SR, PR	*Bifactor:* general psychopathology, internalising, externalising	100%
Shanmugan et al. (2016)	USA	C	1129 (mean age = 15.5 years, 46% male)	Executive system activation	fMRI, T1, and B0 images, fractal version of n-back task	GOASSESS	SR, PR	*Bifactor:* general psychopathology, anxious-misery, psychosis, behavioural (externalising), fear	100%
Shields et al. (2019)	USA	C	895 (aged 8–18 years, mean age = 11.54, 48% male)	Effortful control, EF	EATQ-R, TMCQ, digit span forward, digit span backward, Go/No-Go, Trail-Making Test Part B, Iowa Gambling Task or Hungry Donkey	CBCL, C-DISC	PR	*Bifactor:* general psychopathology, internalising, externalising *CFA (correlated factors):* internalising, externalising	100%
Silveira et al. (2019)	USA	C	6127 (aged 15–17 years)	Tobacco, alcohol and drug use	Past 12-month tobacco, alcohol and drug use, refer to Silveira 2019 for details	GAIN-SS	SR	*LCA (entered as covariates):* internalising, externalising	86%
	USA	C					SR		86%

Table 1 (*continued*)

Study	Country	Design	Sample	Risk/protective factors	Risk/protective factors measures	Measures of psychopathology	Respondent	Model: outcome variables examined	Quality score
Snyder et al. (2019)			292 (13–22 years, mean age = 16.2 years, 44% male)	Common EF, stressful life events, rumination	ALEQ-R, CRSQ-RS, Anti-cascade, Stroop, Stop Signal, Keep Track, Letter Memory, Spatial 2-back, Category Switch, Color-Shape, Letter-Number	CDI, PSWQ-C, MASC, CBCL, YSR, SDQ, SNAP-IV		*Bifactor:* general psychopathology, internalising, externalising	
Sunderland et al. (2020)	Australia	C	2002 (aged 14–17 years, mean age = 15.5 years, 51.4% male)	Suicide attempt, suicidal ideation, self-harm, self-esteem, poor sleep (weekend/weeknight), multiple sexual partners, condom use	self-reports of health and behavioural factors, ASQ	DISC-IV, substance use items, psychotic-like experiences items	SR	*CFA (higher order):* general psychopathology, internalising, externalising and psychotic-like experiences	100%
Tackett et al. (2013)	USA	C	1569 twin pairs (ages 9–17; monozygotic twin pairs ($n = 316$ female pairs; $n = 283$ male pairs), same-sex dizygotic twin pairs ($n = 256$ female pairs; $n = 258$ male pairs), and opposite-sex dizygotic twin pairs ($n = 456$ pairs))	Genetic influences, disposition (negative emotionality, prosociality (empathy and remorse), and daring (sensation seeking and risk taking))	Biometric modelling, CADS	CAPS	SR, PR	*Bifactor:* general psychopathology, internalising, externalising	100%
Terrone et al. (2018)	Italy	C	91 (17–22 years, mean age = 17.77 years, 67% male, recruited through schools in Rome)	Attachment style	TRQ	YSR	SR	*CFA (correlated factors):* internalising, externalising	88%
Vanes et al. (2020)	UK	L	293 (aged 14–24 years, selected to ensure sex, age and ethnicity distribution representative of London and Cambridgeshire)	Myeline maturation	magnetisation transfer imaging	R-CMAS, MFQ, SPQ, r-LOI, ABQ, RSE, WB	SR	*Bifactor:* general psychopathology	75%
van Hoof et al. (2019)	Netherlands	C	74 (12–20 years, mean age = 15.42, 14.90% male)	Resting state functional connectivity (whole brain and region of interest), unresolved-disorganised attachment	fMRI, AAI	YSR, CBCL, RCADS, TSCC, CDI, A-DES	SR, PR	*PCA:* general psychopathology	100%
Vella et al. (2019)	Australia	L	3717 (12–13 years at wave 5, mean age at wave 5 = 12.41, 51.75% male, representative sample of Australian children)	Sex/gender, household income, parental warmth, sociability, sports participation	Primary parent report, STS	SDQ	SR, PR	*Growth mixture modelling:* mental health trajectory from 4 to 12 years of age: low difficulty, improvers, decliners, early decliners/late improvers, early improvers/late decliners, high difficulty	88%
Wade et al. (2018)	Romania	L	220 (119 ever institutionalised, 50% male, assessed at ages 6, 12 & 16 years)	Sex/gender, history of institutional rearing (foster care, institutionalised, never institutionalised)	Institutional rearing groups randomly assigned as part of an RCT, a matched sample of never-institutionalised	MHBQ	PR, TR	*Bifactor:* general psychopathology, internalising, externalising	100%

Table 1 (*continued*)

Study	Country	Design	Sample	Risk/protective factors	Risk/protective factors measures	Measures of psychopathology	Respondent	Model: outcome variables examined	Quality score
					children were recruited for comparison				
Wade et al. (2019)	Romania	L	188 (children in foster/institutional care, assessed at ages 6, 12 & 16 years)	Common executive functioning, early/childhood psychopathology, history of institutional rearing (foster care, institutionalised, never institutionalised)	CANT, MHBQ	MHBQ	PR, TR	*Bifactor*: general psychopathology, internalising, externalising	100%
Wang et al. (2020)	USA	L	515 (14 years, 50% male)	Behavioural inhibition, inhibitory control, negative affect, aggression and internalising PRS	observational measures at age 2 and 3, CBQ, RACS, PRS	CBCL, TRF	PR, TR	*LCA*: low problems, internalising problems only, externalising problems only, co-occurring problems *Bifactor*: general psychopathology, internalising, externalising	88%
Wilson et al. (2015)	USA	L	177 (14–22 years at wave 6, mean age = 17.72, 100% female, 100% African American, sought services from outpatient mental health clinics in low-income areas in Chicago)	Childhood abuse and neglect	Self-reports, reports from maternal caregiver, LTVH, CEQ	YSR, AIDS-RBA	SR	*Parallel process LGM*: internalising, externalising	100%
Xia et al. (2018)	USA	C	999 (8–22 years, mean age = 15.76, 45%)	Brain region functional connectivity	fMRI	GOASSESS	SR, PR	*Sparse canonical correlation analysis*: mood, psychosis, fear, externalising behaviour	100%

Abbreviations: C = cross-sectional design, L = longitudinal design, RCT = Randomised Control Trial; *Respondent:* SR = self-report, PR = parent/caregiver-report, TR = teacher-report; *Models:* CFA = Confirmatory Factor Analysis, EFA = Exploratory Factor Analysis, LCA = Latent Class Analysis, PCA = Principial Component Analysis; *Risk Factors:* BI = Behavioural inhibition, EF = Executive functioning; *Outcome variables:* AUD = Alcohol Use Disorder Class, AUD-ANX-MDD = Alcohol Use Disorder, Anxiety Disorder and Major Depression Disorder Class, SUD-CD = Substance Use Disorder and Conduct Disorder Class, IA = inattention, H/I = hyperactivity/impulsivity, ASD = autism spectrum disorder, LD = learning difficulties, ODD = oppositional defiant disorder, CD = conduct disorder, DEP = depression, ANX = anxiety, PD = panic disorder, GAD = generalized anxiety disorder, SAD = separation anxiety, SA = school anxiety, SP = social phobia; *Risk/Protective Factors Measures:* AAI = Adult Attachment Interview, ACSQ = Adolescent Cognitive Style Questionnaires, ASQ = Adolescent Self-esteem Questionnaire, ALEQ-R = Adolescent Life Events Questionnaire Revised, CANT = Cambridge Automated Neuropsychological Test Battery, CCTI-SS = Colorado Children's Temperament Inventory Shyness/Sociability subscale, CDAS = Children's Dysfunctional Attitudes Scale, CEQ = Childhood Experiences Questionnaire, CDEQ = Children's Depressive Experiences Questionnaire, CRSQ-RS = Child Response Styles Questionnaire-Rumination subscale, CSHQ = Child Sleep Habits Questionnaire, EEG = Electroencephalogram, EVI-Q = Exposure to Violence Interview – Questionnaire version, fMRI = functional magnetic resonance imaging, GL-NEO-S = Goldberg lexical neuroticism, extraversion, and openness scales, GWAS = Genome Wide Association Study, H-SAS = Hetero-Social Activities Scale Social Involvement subscale, LTVH = Lifetime Trauma and Victimization History, NRI = Networks Relationships Inventory, PANAS-C = Positive and Negative Affect Scale for Children, PDS = Pubertal Development Scale, POS = Play Observation Scale, PRS = Polygenic Risk Score, RACS = Relationship Affect Coding System, SRE = Schedule of Racist Events, STS = Short Temperament Scale, SURPS = Substance Use Risk Profiles Scale, TBAQ = Toddler Behaviour Assessment Questionnaire, TCES = The Collective Efficacy Scale, TIPI = Ten Item Personality Inventory, TMCQ = Temperament in Middle Childhood Questionnaire, TRQ = The Relationship Questionnaire, TSI = The Stress Index, WASI-II = Wechsler Abbreviated Scale of Intelligence-II; *Measures of Psychopathology:* A-DES = Adolescent Dissociative Experiences Scale, A-TAC = Autism-Tics, ADHD, and Other Comorbidities inventory, ABQ = Antisocial Behaviour Questionnaire, AIDS-RBA = AIDS-Risk Behaviour Assessment (substance use & sexual risk behaviours), AMPQ-II = Adolescents Mental Health and Problem Behaviour Screening Questionnaire-II, ASR = Adult Self Report questionnaire, AUDIT = Alcohol Use Disorders Identification Test, BFI-N = Neuroticism subscale of Big Five Inventory, BSI = Brief Symptom Inventory, C-DISC = Computer Assisted Diagnostic Interview Schedule for Children, CAPE = Community Assessment of Psychic Experiences, CAPS = Child and Adolescent Psychopathology Scale, CBCL = Child Behaviour Checklist, CDI = Children's Depression Inventory, CESD = Center for Epidemiological Studies on Depression scale, CIDI-A = Composite International Diagnostic Interview - Adolescent Version, CIDI-UM = Composite International Diagnostic Interview - University of Michigan version, CPRS = Conners 3 parent rating scales, DAWBA = Development and Well-being Assessment, DIS = Diagnostic Interview Schedule, DISC = Diagnostic Interview Schedule for Children, DISC-IV = Diagnostic Interview Schedule for Children, e-MINI = Mini International Neuropsychiatric Interview - electronic version, EATQ-R = Early Adolescent Temperament Questionnaire, GAIN-SS = Global Appraisal of Individual Needs - Short Screener, GOASSESS = modified version of K-SADS, JHDS = John's Hopkins Depression Scale, K-SADS = Schedule for Affective Disorders and Schizophrenia for School Age Children, LIFE = Longitudinal Interval Follow-Up Evaluation, LSAS = Liebowitz Social Anxiety Scale, MASC = Manifest Anxiety Scale for Children, MASQ-SF = Mood and Anxiety Symptom Questionnaire—Short Form, MFQ = Mood and Feelings Questionnaire, MHBQ = MacArthur Health and Behaviour Questionnaire, PLIKS-Q = Psychosis-Like Symptom Questionnaire, PSWQ-C = Penn State Worry Questionnaire for Children, R-CMAS = Revised Children's Manifest Anxiety Scale, r-LOI = Revised Leyton Obsessional Inventory, RAPI = Rutgers Alcohol Problem Index, RCADS = Revised Child Anxiety and Depression Scale, RDUS = Recreational Drug Use Scale, RSE = Rosenberg Self-Esteem Scale, SCARED = Screen for Child Anxiety Related Emotional Disorders, SCID-I = Structured Clinical

Interview for DSM-IV Axis 1 Disorders, SCID-I: MAS = Structured Clinical Interview for DSM-IV Axis 1 Disorders: Mood, Anxiety and Substance Use modules, SDQ = Strengths and Difficulties Questionnaire, SMFQ = Short Mood and Feelings Questionnaire, SNAP-IV = Swanson, Nolan, and Pelham scale, SPQ = Schizotypal Personality Questionnaire, SRD = Self Report of Delinquency Scale, SRP-SF = Self Report of Psychopathy Short Form Scale, SSAGA = Semi-Structured Assessment for the Genetics of Alcoholism, STAI-T = State-Trait Anxiety Inventory—Trait, TRF = Teacher's Rating Form, TSCC = Trauma Symptom Checklist for Children, WB = Warwick-Edinburgh Mental Well-Being Scale, YSR = Youth Self Report.

externalising (Carragher et al., 2016; Wade, Fox, Zeanah, & Nelson, 2018).

3.3.2. Socio-environmental risk and protective factors

As shown in Table 3, *stressful life events* were positively associated with general psychopathology and externalising in two studies, one of which found that the association was moderated by *collective efficacy*, which is a measure of environment reflecting a neighbourhood broadly characterised by social cohesion, shared values among neighbours and a willingness to improve safety and order (Liu, Mustanski, Dick, Bolland, & Kertes, 2017; Snyder, Friedman, & Hankin, 2019). A similar trend emerged in the remaining childhood trauma and stress factors, such that most were typically related to general psychopathology and externalising (see Appendix E). Only *childhood abuse and neglect* was associated with internalising and externalising, however this study did not examine general psychopathology (Wilson, Samuelson, Staudenmeyer, & Widom, 2015). Interestingly, *exposure to violence* was associated with externalising, but not internalising or general psychopathology (Liu et al., 2017).

Family and home environment factors were also reported to increase transdiagnostic risk for psychopathology in young people. *Institutional rearing* was examined in one sample across two studies, which reported that history of institutional rearing predicted greater levels of general psychopathology at ages 12 and 16, and greater levels of externalising at age 12. Children who remained institutionalised demonstrated sustained high levels of general psychopathology from ages 8 to 16 years, whereas children who were placed in foster care demonstrated significant declines in externalising and modest declines in general psychopathology.

Paternal substance use disorder increased the likelihood of being in an internalising vulnerability latent class (Olino, Klein, & Seeley, 2019), and *family tobacco environment* was associated with increased general psychopathology (Jones, Epstein, Hill, Bailey, & Hawkins, 2019). *Sibling substance use* increased the likelihood of being in multiple classes (co-morbid Alcohol Use Disorder-Anxiety Disorder-Major Depressive Disorder (AUD-ANX-MDD), Alcohol Use Disorder only (AUD), comorbid Substance Use Disorder-Conduct Disorder class (SUD-CD)), such that different classes were associated with different substances used by siblings (McCutcheon et al., 2013), for example sibling alcohol problems were associated with an increased likelihood of being in the AUD-ANX-MDD class, whereas sibling marijuana or other drug use was associated with increased likelihood of being in the AUD class.

In general, *parental psychopathology* increased likelihood of being placed in a poor mental health class, though one study found no relationship with general psychopathology (Deutz et al., 2020; Jones et al., 2019; McCutcheon et al., 2013; Olino et al., 2019). *Paternal history of Major Depressive Disorder (MDD)* was associated with increased risk for internalising and externalising (Olino et al., 2019), and *maternal history of MDD* was associated with increased general psychopathology and internalising, and increased likelihood of being placed in an AUD-MDD-ANX class (Deutz et al., 2020; McCutcheon et al., 2013).

Three socio-environmental protective factors were identified, however only two of these were found to act transdiagnostically. *Parental warmth* was associated with reduced risk for moderate to high mental health difficulty trajectories (Vella, Gardner, Swann, & Allen, 2019). In contrast, *positive family environment* was negatively associated with an anxiety indicator but was not associated with general psychopathology. *Collective efficacy*, acted as a protective factor for general psychopathology and externalising among African-American young people living in economically disadvantaged areas (Liu et al., 2017). The study also

reported that *collective efficacy* moderated the effects of *stressful life events* and *racial discrimination* on general psychopathology and externalising.

Lifestyle and peer and friendship problems also appeared to increase risk transdiagnostically. Findings from a growth mixture model revealed that *sociability* was associated with a reduced likelihood of being placed in a poorer mental health trajectory (Vella et al., 2019). *Adolescent social involvement* was reported to moderate the relationship between childhood behavioural inhibition and young adult anxiety. *Delinquent/anti-social peer behaviour* was associated with internalising and externalising like latent factors longitudinally (Jones et al., 2019; Lee & Bukowski, 2012). However only one study examined a general factor variable and did not find evidence for an association between general psychopathology and *delinquent peers*. *Poor sleep, risky sexual behaviour* (multiple sexual partners and not using condom at least once) and *academic performance* were all related to general psychopathology (or comorbid psychopathology like classes). While controlling for general psychopathology, *poor sleep and academic problems* were also associated with increased levels of internalising, and *risky sexual behaviours* was associated increased levels of externalising (Sunderland et al., 2020). *Substance use* was associated with increased levels of internalising and externalising (Silveira, Green, Iannaccone, Kimmel, & Conway, 2019).

3.3.3. Psychological risk and protective factors

Personality and temperament factors were the most widely studied psychological variables, many of which were found to be associated with general and specific factors of psychopathology across multiple studies and methods of modelling psychopathology, as shown in Table 3. Levin-Aspenson, Khoo, and Kotelnikova (2019) examined *neuroticism, extroversion* and *openness* among two sub samples of the National Comorbidity Survey in the United States in relation to a bass-ackwards derived model of psychopathology. Among adolescents (15–19 years) and young adults (20–29 years), *extroversion* was negatively correlated with general psychopathology, internalising, fear and distress components. The relationship was strongest at lower levels of the hierarchical model (i.e., internalising and fear), compared to higher levels (i.e., general psychopathology). *Neuroticism* was positively correlated with all psychopathology dimensions (general psychopathology, internalising, externalising, fear and distress factors and thought disorder). Associations with *neuroticism* were strongest with a general psychopathology factor compared to other dimensions, and stronger for internalising (vs externalising) among both samples. Similar cross-sectional results were reported be Mann, Atherton, DeYoung, Krueger, and Robins (2020), who also found that increases in *neuroticism* were associated with increases in general psychopathology, externalising and an Attention Deficit Hyperactivity Disorder (ADHD) specific factor, but not internalising. Furthermore, increases in *extroversion* were associated with increases in general psychopathology and externalising overtime. It was also found that *conscientiousness* and *agreeableness* were related to initial levels of general psychopathology and specific factors, but not changes in psychopathology over time. No association was found between *openness* and psychopathology among either samples.

Additional temperament factors were also found to be related to broad psychopathology outcomes. *High negative affectivity* was related to higher levels of general psychopathology in three studies (using both bifactor and latent class analysis), and internalising in one study (Deutz et al., 2020; Hankin et al., 2017; Wang, Galán, Lemery-Chalfant, Wilson, & Shaw, 2020). *High behavioural inhibition* in early childhood was positively associated with internalising in two studies (Frenkel et al., 2015; Wang et al., 2020). *High rumination* was positively associated with

Table 2

Summary of empirical models of psychopathology from included studies.

Statistics family	Modelling approach	Description	Outcome variables	Number of models
Factor analytic	Bifactor	A bifactor model is comprised of a general factor (e.g., general psychopathology) that reflects shared variance among all indicators (i.e. observed variables), and two or more uncorrelated specific factors (e.g. internalising, externalising) that explain the remaining shared variance among selected indicators not accounted for by the general factor (Gibbons & Hedeker, 1992; Holzinger & Swineford, 1937; Markon, 2019).	General psychopathology	3
			General psychopathology, anxiety, psychotic experiences, depression, negative (symptoms of psychosis) factors	1
			General psychopathology, emotional problems, behavioural problems, neurodevelopmental problems	1
			General psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, ANX	1
			General psychopathology, IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP	1
			General psychopathology, internalising, externalising	14
			General psychopathology, internalising, externalising, attention problems	2
			General psychopathology, anxious-misery, psychosis, behavioural (externalising), fear	1
	Modified bifactor (correlated factors)	As above, except in this model the specific factors are allowed to correlate (see Carragher et al., 2016 for details).	General psychopathology, internalising, externalising and thought disorder	1
	Bifactor subtotal			25
	CFA (correlated factors)	Uses confirmatory factor analysis (CFA) to generate a model comprised of two or more latent variables (e.g., internalising, externalising) that reflect the shared variance among selected indicators. The latent factors are allowed to correlate; however, a general or underlying factor is not extracted. Details of the model, such as number of factors, and which indicators relate to which factors are prespecified by researcher (Brown, 2014; Thurstone, 1944).	Internalising, externalising	3
			Anxiety, psychotic experiences, depression, negative (symptoms of psychosis) dimensions	1
			IA, H/I, ASD, LD, ODD, CD, DEP, ANX	1
			IA, H/I, ASD, LD, ODD, CD, DEP, PD, GAD, SAD, SA, SP	1
	CFA (one factor)	Uses CFA to extract a single latent factor that explains the shared variance across all observed variables (Brown, 2014).	General psychopathology	1
	CFA (higher order)	Similar to CFA with correlated factors, however a higher-order latent variable (e.g., general psychopathology) is also extracted which reflects the shared variance among lower-order latent variables (e.g., internalising, externalising and thought disorder).	General psychopathology, internalising, externalising and psychotic-like experiences	1
	CFA Subtotal			8
	EFA (correlated factors)	Similar to CFA with correlated factors, except in exploratory factor analysis (EFA) does not require details of a model to be prespecified, such as the number of factors or which indicators should be loaded onto which factors (Brown, 2014; Fabrigar, Wegener, MacCallum, & Strahan, 1999).	Distress, fear, externalising and eating pathology	1
Factor analytic subtotal				34
Growth curve analysis	Growth Mixture Modelling	Models change in latent classes overtime and allows for variation in trajectories within classes as well as estimating mean growth curves for each class (T. Jung & Wickrama, 2008; Muthén, 2006).	Mental health trajectory from 4 to 12 years of age: low difficulty, improvers, decliners, early decliners/late improvers, early improvers/late decliners, high difficulty	1
	Parallel Process Latent Growth Model	Models the change in latent factors over time, such as internalising and externalising. Latent variables in growth models are the initial status internalising and externalising (known as the intercepts) and change in internalising and externalising (known as the slopes; Duncan & Duncan, 2004; Preacher, Wichman, MacCallum, & Briggs, 2008).	General psychopathology, internalising, externalising, ADHD	1
			Internalising, externalising	3
Growth curve subtotal				5
Class-based	Latent class analysis	Latent class analysis (LCA) identifies groups of cases where individuals are most similar to each other and distinct from individuals in other groups. These groups are known as 'latent classes' and are categorical, rather than dimensional (Collins & Lanza, 2009). LCA is typically applied to categorical variables, however the term LCA is also sometimes used to describe models based on both categorical and continuous variables.	AUD, AUD-ANX-MDD & SUD-CD classes	1
			Healthy, internalising (primarily anxiety), externalising (primarily substance use)	1
			Internalising, externalising	1
			Low problems, internalising problems only, externalising problems only, co-occurring problems	2
	Latent profile analysis	Similar to LCA in that it identifies discrete groups of individuals, except analysis is applied to continuous variables (Collins & Lanza, 2009).	Thriving functioning, average functioning, externalising vulnerability and family stress, internalising vulnerability	1
	Multilevel latent profile analysis	Similar to latent profile analysis, except that it accommodates hierarchical data sets where individuals are nested within groups, such as schools (Henry & Muthen, 2010)	Group 1 - high scores on all mental health domains, group 2 - high scores on internalising/emotional domains, low scores on externalising/behavioural domains, group 3 - low scores on all mental health domains	1
Class-based subtotal				7
Principal component	Bass-ackwards	Similar to PCA, however correlations between component scores across levels (i.e. sequence) of extraction are calculated and used to generate a hierarchical structure (	General psychopathology, internalising, externalising, fear, distress and thought disorder	1
				1

Table 2 (*continued*)

Statistics family	Modelling approach	Description	Outcome variables	Number of models
		Goldberg, 2006). Sometimes referred to as sequential principal components.	General psychopathology, internalising, externalising, fear and distress	
	Principal Component Analysis	Generates a series of uncorrelated components that reflect the maximum amount of variance from each observed variable, including error variance and unique variance. The first factor extracted accounts for the most amount of variance shared among included variables, each subsequent factor is the next largest factor after accounting for/removing the influence of the preceding factors. As such, the sequence that components are extracted reflects a decreasing order of importance in terms of how much variance is accounted for. Differs from factor analytic approaches which focus on the analysis of covariance, rather than all variance (Abdi & Williams, 2010; Everitt & Dunn, 2001; Tabachnick, 2014)	General psychopathology	1
Principal component subtotal				3
Machine Learning	Sparse canonical correlation analysis	Sparse canonical correlation analysis aims to reduce multidimensional data (e.g., neuroimaging or genomic data and psychopathology symptoms) to a smaller set of projected variables (i.e., canonical correlation vectors) that reflect the maximum correlation between two sets of multidimensional variables (Hardoon & Shawe-Taylor, 2011; Witten, Tibshirani, & Hastie, 2009).	Mood, psychosis, fear, externalising behaviour	1
Total number of models from included studies				50

IA = inattention, H/I = hyperactivity/impulsivity, ASD = autism spectrum disorder, LD = learning difficulties, ODD = oppositional defiant disorder, CD = conduct disorder, DEP = depression, ANX = anxiety, PD = panic disorder, GAD = generalized anxiety disorder, SAD = separation anxiety, SA = school anxiety, SP = social phobia.

Table 3

Summary of replicated transdiagnostic risk and protective factors by psychopathology outcome and modelling approach.

	Psychopathology outcome			Modelling approach				
	General psychopathology	Internalising	Externalising	Bifactor	CFA (Correlated factors)	Growth model	LC/PA	Bass-ackwards
Biological								
Genetic risk for ADHD	+++			✓				
Genetic risk for schizophrenia	++			✓				
Being female	+/− − −	+++	+ +/− − −/~	✓	✓			
Being male	+++/− −	++/− − −	++/−	✓	✓			
Earlier pubertal timing/onset of menarche	++	++	++	✓	✓			
Executive functioning deficits	+++	++/−	++/− −	✓	✓	✓		
Reduced gray matter volume	++			✓	✓			
Socio-environmental								
Maternal depression	++	+	−	✓			✓	
Stressful life events	++	+/−	++	✓				
Psychological								
Low extroversion	++/−	++/−	+/−			✓		✓
High negative affectivity	+++	++/−	− − −	✓			✓	
High neuroticism	+++	+++	+++	✓		✓		✓
High behavioural inhibition	++	++/−	+/− −	✓	✓		✓	
Low effortful control	+++	+/−	+++	✓	✓			
High rumination	+++	++/− −	++/~	✓				
Openness	− − −	− − −	− − −			✓		✓

'+' = evidence, but no replication, '++' = some replication (two samples), '+++' = consistent replication (3 or more samples), '~' = mixed evidence for direction of association,
'−' = no association (one sample), '− −' = no association (two samples), '− − −' = no association (3 or more samples),
✓ = modelling approach used, CFA = confirmatory factor analysis, LC/PA = latent class or latent profile analysis.

general psychopathology and internalising in two studies (Schweizer, Snyder, Young, & Hankin, 2020; Snyder et al., 2019). However, as shown in Table 4, one study reported a negative association with externalising (ß = −0.47), while the other reported a positive association (ß = 0.42). *Low effortful control* was associated with higher general psychopathology across three studies, and externalising across four studies, however only two studies reported significant associations with internalising (one using a bifactor model, and the other a correlated

factors model), however inspection of effects sizes revealed that this association was weaker in longitudinal studies (see Table 4; Deutz et al., 2020; Hankin et al., 2017; Shields, Reardon, Brandes, & Tackett, 2019).

Four studies (average QS = 95%) reported mixed findings for associations between *attachment style* and general psychopathology. Two of these studies found no significant association between general psychopathology, internalising or externalising and attachment style (Deutz et al., 2020; van Hoof et al., 2019), while another study found that *lower*
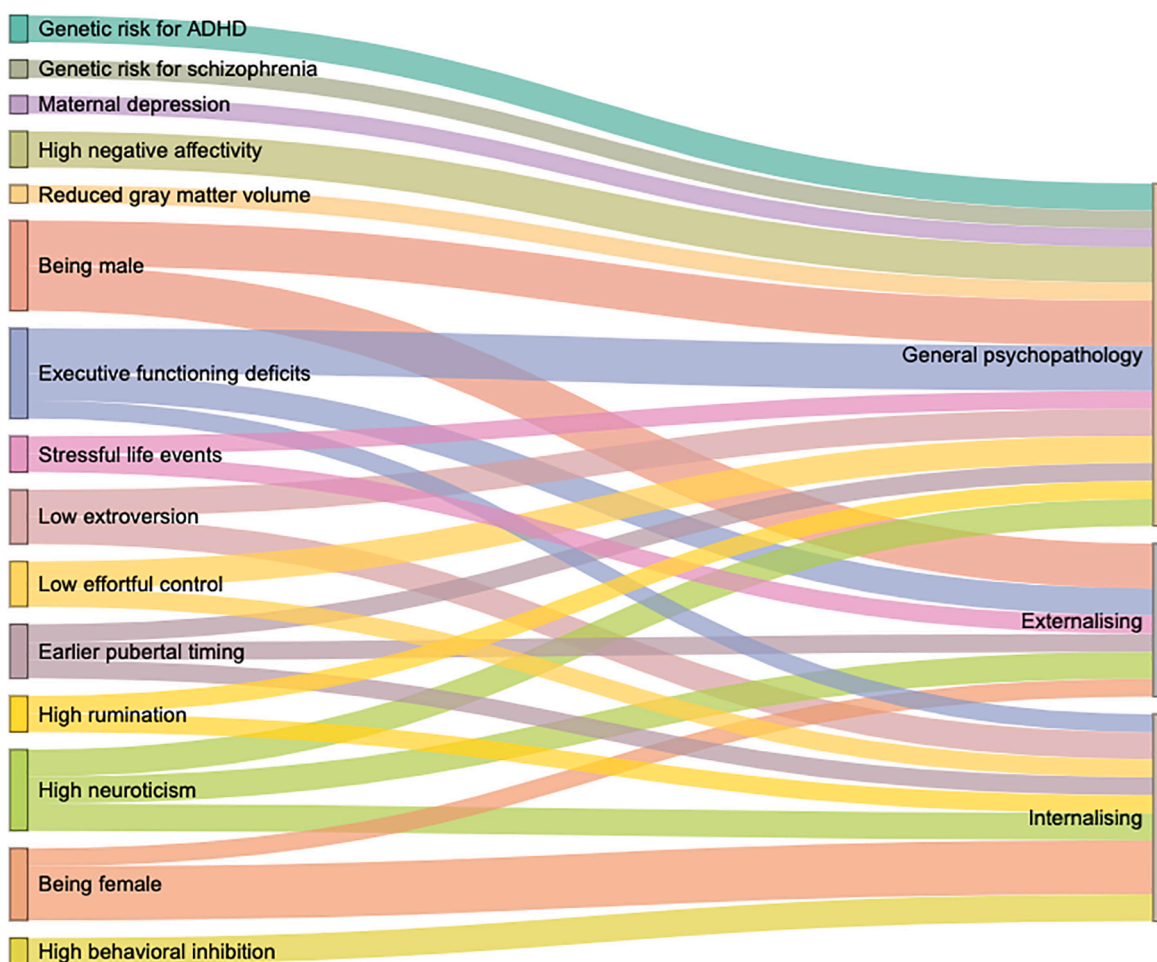
Fig. 2. Sankey diagram visualising relationship between transdiagnostic risk and protective factors supported by evidence from two or more studies and psychopathology outcomes. The thickness of lines indicates the number of studies supporting the association.

levels of attachment were associated with high levels of internalising at age 10 (Lee & Bukowski, 2012). A fourth study found that *attachment style* moderated the relationship between gambling and internalising and externalising (Terrone et al., 2018).

3.4. Longitudinal vs. cross-sectional studies

Findings from longitudinal studies identified several important risk factors for general psychopathology. A summary of effect sizes for replicated findings grouped by design and type of effect size is provided Table 4. High behavioural inhibition, high negative affectivity and executive functioning deficits were reported to be predictive (or longitudinally associated with) of general psychopathology (Deutz et al., 2020; Frenkel et al., 2015; Hatoum, Rhee, Corley, Hewitt, & Friedman, 2018; Jones et al., 2019; Wade, Zeanah, Fox, & Nelson, 2019; Wang et al., 2020). Cross-sectional studies examining genetic, biological or historical influences found that genetic risk for ADHD and schizophrenia, stressful life events and earlier pubertal timing were also found to be associated with increased general psychopathology (Brikell et al., 2020; Hamlat et al., 2019; Jones et al., 2018; Liu et al., 2017; Platt, Colich, McLaughlin, Gary, & Keyes, 2017; Riglin et al., 2020; Snyder et al., 2019).

There was also evidence for risk factors for internalising and externalising psychopathology supported by longitudinal studies and cross-sectional studies where biological or historical influences were examined. Behavioural inhibition was found to have a stronger, more

consistent association with internalising than externalising (Frenkel et al., 2015; Jones et al., 2019; Wang et al., 2020). High negative affectivity was reported to be uniquely associated with internalising and consistently not associated with externalising (Deutz et al., 2020; Hankin et al., 2017; Wang et al., 2020). Stressful life-events were found to have a small to non-significant association with internalising, and small to medium association with externalising (Liu et al., 2017; Snyder et al., 2019). Pubertal timing associated with both internalising and externalising (Hamlat et al., 2019; Platt et al., 2017).

Comparison of effect sizes reported by longitudinal and cross-sectional studies generally revealed effects to be weaker longitudinally (i.e., generally small to medium effect size) than cross-sectionally. For example, high negative affectivity was found to have a small or not significant longitudinal association ($\beta = 0.07$) and large cross-sectional association with internalising ($\beta = 0.81$). Similarly, effortful control was associated with greater levels of general psychopathology and externalising in one longitudinal study (Deutz et al., 2020) and two cross-sectional studies (Hankin et al., 2017; Shields et al., 2019). An association with internalising was only found cross-sectionally, and in one instance the association was non-significant. As shown in Table 4, the effect sizes were larger in the cross-sectional studies.

4. Discussion

A dizzying constellation of biological, psychological and socio-environmental factors emerged from the reviewed studies that appear

Table 4

Summary of effect sizes for replicated findings of transdiagnostic risk and protective factors for general psychopathology, internalising and externalising.

	Design	Sample size	Effect size type	General psychopathology	Internalising	Externalising	Study
Biological							
Genetic risk for ADHD	L (1)	5518	ß	0.087			Riglin et al. (2020)
	C (2)	13,457	ß	0.09 to 0.10			Brikell et al. (2020)
Genetic risk for schizophrenia	L (1)	5518	ß	0.055			Jones et al. (2018)
	C (1)	2863	ß	0.056			Riglin et al. (2020)
Being female	C (3)	16,199	ß	ns to −0.17	0.31 to 0.40	−0.14 to 0.16	Carragher et al. (2016), Hamlat et al. (2019), Brikell et al. (2020)
	L (1)	646	r	Intercept: 0.22 Slope: 0.49	Intercept: 0.30 Slope: 0.66	Intercept: 0.29 Slope: ns	Mann et al. (2020)
	L (1)	5518	ß	−0.11			Riglin et al. (2020)
Being male	L (1)	220	r	0.16 to 0.21	ns	0.18 to 0.24	Wade et al. (2018)
	L (1)	515	ß	ns	0.24	ns	Wang et al. (2020)
	L (1)	3717	Odds Ratio	1.81 to 6.34			Vella et al. (2019)
	C (3)	15,201	B	ns to −1.41	0.83		Brikell et al. (2020), Jung et al. (2019), McCutcheon et al., 2013)
Earlier pubertal timing/onset of menarche	C (2)	5492	ß	0.69	0.51 to 0.52	0.33 to 0.42	Hamlat et al. (2019), Platt et al. (2017)
Executive functioning deficits	C (2)	1187	r	−0.16	ns to −0.23	ns to −0.19	Snyder et al. (2019), Shields et al. (2019)
	C (1)	292	ß	−0.24	ns	ns	Snyder et al. (2019)
	L (1)	188	ß	−0.17			Wade et al. (2019)
	L (1)	885	r	−0.56 (males only)	Intercept: −0.25 (females only) Slope: ns	Intercept: ns Slope: −0.28 (teacher rating only)	Hatoum et al. (2018)
	L (1)	885	ß		Intercept: −0.17 to −0.26 Slope: 0.22 (parent rating only)	Intercept: −0.50 (males only) Slope: ns	Hatoum et al. (2018)
Reduced gray matter volume	C (1)	1246	ß	Bifactor model: Pons FA = −0.134; Cerebellum GMV = −0.066; Occipital GMV = −0.77	Corr factors model: Pons FA = −0.137; Cerebellum GMV = −0.085; Occipital GMV = −0.064	Corr factors model: Pons FA = −0.32 (ns); Cerebellum GMV = −0.044; Occipital GMV = −0.038 (ns)	Romer et al. (2018)
	C (1)	1394	Partial r	≤ −0.14			Kaczkurkin et al. (2019)
Socio-environmental							
Maternal depression	L (1)	1073	ß	0.18	0.06	ns	Deutz et al. (2020)
	C (1)	831	Odds Ratio	3.33			McCutcheon et al. (2013)
Stressful life events	C (2)	884	ß	0.20 to 0.32	ns to 0.23	0.23 to 0.42	Liu et al. (2017), Snyder et al. (2019)
Psychological							
Low extroversion	C (2)	2604	r	−0.11 to −0.13	−0.15 to −0.16	ns	Levin-Aspenson et al. (2019)
	L (1)	646	r	Intercept: ns Slope: −0.29	ns	Intercept: 0.13 Slope: −0.28	Mann et al. (2020)
High negative affectivity	C (1)	571	ß	0.61	0.81	ns	Hankin et al. (2017)
	L (2)	1588	ß	0.10 to 0.21	0.07	ns	Deutz et al. (2020), Wang et al. (2020)
	L (1)	515	Odds Ratio	1.72 to 2.15	ns	ns	Wang et al. (2020)
High neuroticism	C (2)	2604	r	0.40 to 0.41	0.36 to 0.37	0.17 to 0.19	Levin-Aspenson et al. (2019)
	L (1)	646	r	Intercept: 0.46 Slope: 0.29	Intercept: 0.43 Slope: ns	Intercept: 0.42 Slope: 0.25	Mann et al. (2020)
High behavioural inhibition	L (2)	1280	ß	0.16 to 0.21	0.12–0.37	ns to 0.11	Frenkel et al. (2015), Jones et al. (2019)
	L (1)	515	Odds Ratio	1.51 to 1.73	ns to 1.4	ns	Wang et al. (2020)
Low effortful control	L (1)	1073)	ß	−0.17	ns	−0.13	Deutz et al. (2020)
	C (1)	1466	ß	−0.48	−0.14	−0.65	Hankin et al. (2017)
	C (1)	895	r	−0.38 to −0.89	ns to −0.48	−0.35 to −0.71	Shields et al. (2019)
High rumination/ brooding	C (2)	863	ß	0.33 to 0.61	0.19 to 0.86	−0.47 to 0.42	Schweizer et al. (2020), Snyder et al. (2019)
Openness	C (2)	2604	r	ns	ns	ns	Levin-Aspenson et al. (2019)
	L (1)	646	r	ns	ns	ns	Mann et al. (2020)

to be transdiagnostically relevant among young people aged between 10 and 24 years. Among these, 14 factors were replicated in two or more samples and generally replicated across multiple models of psychopathology. The results of the review highlight a number of factors that may serve as salient markers of risk or targets for transdiagnostic prevention and intervention efforts and revealed promising avenues for future investigation to better understand the many varied transdiagnostic risk and protective factors for psychopathology among young people.

4.1. Transdiagnostic risk and protective factors

4.1.1. Risk factors for internalising psychopathology

The review identified seven risk factors for the development of internalising psychopathology among young people. These included three biological factors (*being female, earlier pubertal timing (including early onset of menarche)* and *executive functioning deficits*), one socio-environmental factor (*maternal depression*), and four psychological factors (*high neuroticism, low extroversion, high behavioural inhibition*). Four additional risk factors for internalising that demonstrated some replication were also identified but require further investigation to clarify inconsistent results. *Low effortful control* and *stressful life events* were only associated with increased internalising in some studies, while other studies found no relationship. Both significant and non-significant associations were identified using bifactor models of psychopathology, which suggests that there may have been inconsistencies in study design, such as measurement, indicators or specification of the internalising variable across studies. Furthermore, *high rumination* was positively associated with internalising in two studies, and negatively in one study. As such, further research is needed to determine whether *low effortful control, stressful life events and rumination* are reliable risk factors for internalising psychopathology.

4.1.2. Risk factors for externalising psychopathology

There were six risk factors found to increase risk for the development of externalising psychopathology among young people in the present review. Three biological factors (*executive functioning deficits, earlier pubertal timing, being male*), one socio-environmental factor (*stressful life events*), two psychological factors (*high neuroticism and low effortful control*). Additionally, although *being male* was fairly consistently found to be associated with increased externalising, there were also three studies that did not find any gender differences, and one study that reported *being female* increased risk for externalising (all studies with non-significant results used a bifactor model).

4.1.3. Risk factors for general psychopathology

Eleven risk factors for general psychopathology were identified. Four biological factors (*executive functioning deficits, genetic risk for ADHD, genetic risk for schizophrenia, earlier pubertal timing*), two socio-environmental (*stressful life events and maternal depression*) and five psychological factors (*high negative affectivity, high neuroticism, low effortful control, high rumination and low extroversion*). Although *being male* was typically associated with greater levels of general psychopathology, there were studies that also found no association with sex/gender.

Findings from twin studies indicated that variance in general psychopathology appears to be partly genetic in nature, while environmental influences tended to explain more variance among individual disorders. This is consistent with the 'generalist genes, specialist environments' hypothesis, which posits that co-occurring characteristics, such as internalising and externalising, tend to be influenced by common sets of genes, while the differences in internalising and externalising, are explained by environmental influences (Kovas & Plomin, 2007). However, there was also some evidence for genetic influences on more specific sub-factors (e.g., social phobia, hyperactivity/impulsivity, neurodevelopmental, and negative (symptoms of psychosis) specific factors), via genetic risk for schizophrenia and ADHD, which suggests

that some genes may have more specific influences. There was also evidence for genetic and non-shared environmental influences on the association between psychopathology and other risk factors, including executive functioning and some psychological factors (e.g., prosociality and intelligence). In summary, the evidence indicates that genetic factors may increase risk for psychopathology transdiagnostically, however specific genetic markers and mechanisms have not yet been identified.

4.1.4. General summary of transdiagnostic risk and protective factors

Evidence from the present review indicates that *high negative affectivity, low effortful control,* and *executive functioning deficits* are well supported transdiagnostic markers of risk for psychopathology among young people. *Rumination, neuroticism* and *extroversion* also appear to be important markers, however further longitudinal research is needed to determine whether they are true risk factors. Altogether, this is consistent with other recent reviews which have found evidence that the related over-arching constructs of *self-regulation* and *emotion regulation* may contribute to the development of a broad range of psychiatric disorders (Aldao, Gee, De Los Reyes, & Seager, 2016; Nigg, 2017; Santens, Claes, Dierckx, & Dom, 2020; Sloan et al., 2017).

Similarly, results from studies of *childhood trauma and stress* in the present review generally found consistent relationships with a variety of broad psychopathology outcomes, which is consistent with previous research which has indicated that stressors are associated with increased risk for both internalising and externalising psychopathology in adolescence (March-Llanes et al., 2017; McMahon et al., 2003). However, there were some inconsistent findings for the relationship between internalising and *childhood stress and trauma* in the present review. While the inconsistencies may be due to differences in methodology, it is also possible the consistent relationship between *childhood stress and trauma* and general psychopathology may indicate that previous reported associations with internalising were due to an unmeasured shared variability across internalising and externalising dimensions.

Despite consistencies with previous reviews, a number of limitations and methodological concerns were also identified that should be taken into account when interpreting the results and addressed in future research. There were also some areas of research that have so far been relatively underexplored that warrant investigation in future research.

4.2. Methodological considerations

It is important to stress that findings from this review must be interpreted with caution due to a number of methodological complexities and uncertainties. First, the studies varied considerably in terms of measures/indicators of psychopathology, statistical approaches and the outcomes examined. Many studies modelled general psychopathology, internalising and externalising as latent variables. However, the inconsistency of indicators and measures included in models across studies means that the extracted factors likely reflect different forms of psychopathology (Watts et al., 2019). While this may explain some of the inconsistent findings in the present review, it also suggests that factors that were replicated across multiple studies and models are likely very robust contributing factors for psychopathology. Overall, however, the diversity in the measures of psychopathology included across studies makes it difficult to draw unifying conclusions.

Second, over half of the studies used a bifactor model, which tend to show superior goodness of fit over other models because they are more flexible and accommodate complexities, such as random noise (Watts et al., 2019). However, model fit indices are increasingly considered an insufficient indicator of structural validity, and a number of additional tests are now recommended in adjudicating between structural models (Forbes et al., 2021). In particular, there are increasing calls for the interpretability of models to be considered more carefully as well as the inclusion of more theoretically, rather than statistically, driven models. For example, higher-order latent variable models tend to show superior reliability and interpretability over bifactor models, particularly in

relation to specific factors such as internalising, externalising and thought disorder (Lees et al., 2020; Sunderland et al., 2020). The convergence on a particular modelling approach, such as the bifactor model, may be premature given that there are multiple plausible models and explanations for the onset and maintenance of individual and co-occurring mental disorders (van Bork, Epskamp, Rhemtulla, Borsboom, & van der Maas, 2017). Network models of psychopathology in particular have been gaining momentum in the literature over the last decade, but as yet no studies have examined risk or protective factors using a network approach among young people. This presents an important opportunity to better understand the influence of risk and protective factors on the development of mental disorders at the symptom level and would complement existing knowledge from factor analytic studies.

Third, it also worth noting that the majority of studies were based on cross-sectional data from the USA, thus making it difficult to determine causality and generalisability. Furthermore, most of the studies were from non-clinical samples which are more likely to have low-to-moderate levels of psychopathology. As such, it is possible that some studies may have detected 'false negatives' due to low levels of psychopathology.

Finally, the inclusion criteria applied in this review adopted the World Health Organisations definition of a young person and specified that participants mean age needed to between 10 and 24 years (World Health Organization, 2014). This unfortunately meant that studies from some new well-known cohorts, such as the Adolescent Brain Cognitive Development (ABCD) Study where the mean age is below 10 years, could not be included (e.g., Lees et al., 2020; Michelini et al., 2019). However, findings from relevant studies of the ABCD cohort generally corroborated findings from studies in the present review. For example, Lees et al. (2020) reported a number of common and dissociable patterns of functional connectivity relating to the frontoparietal, default mode and salience networks, which aligns with other studies of functional connectivity which did meet the criteria for inclusion in the present review (Elliott, Romer, Knodt, & Hariri, 2018; Kaczkurkin et al., 2018; Xia et al., 2018).

4.3. Future directions

Within the context of the methodological concerns surrounding bifactor models, it is recommended that future research explore multiple models of psychopathology by examining reliability metrics and relationships with external variables across multiple models. Furthermore, exploration of multiple models may help resolve some of the inconsistent findings identified in the review, such as the uncertain relationship between childhood trauma and stress and internalising psychopathology.

Among the factors investigated by studies in the present review, there were some gaps and underexplored factors that warrant further investigation. In particular, very few studies explicitly examined protective factors, and none were examined in more than one study. Public health prevention policies and interventions could significantly benefit from the identification of reliable transdiagnostic protective factors. Neurobiological factors were also relatively underexplored in the present review. Advances in understanding the complexity of neurobiological mechanisms underlying the development of psychopathology on young people has important etiological implications.

Future research should also aim to delineate the mechanisms through which key risk factors identified in the present review, particularly *neuroticism, negative affectivity, effortful control* and *executive functioning,* contribute to increased risk for psychopathology. Further, there has been very little research to date that integrates biological, psychological and socio-environmental factors. A multidisciplinary approach that explores multiple factors contributing to the development psychopathology among young people may help identify transdiagnostic mechanisms and processes and foster the development of

comprehensive etiological models of psychopathology. In turn, this may lead to the identification of more salient targets for prevention and intervention.

5. Conclusions

To our knowledge, this is the first systematic review of empirical models of psychopathology and risk and protective factors in young people. Results from the review revealed several key risk factors for psychopathology, in particular executive functioning deficits, stressful life events, high neuroticism, negative affectivity and behavioural inhibition, and low effortful control. These findings have important implications for prevention and intervention. Improving *emotion regulation* and *self-regulation* and reducing environmental conditions that foster *stressful life events* may be particularly salient targets for the prevention and intervention of general and specific dimensions of psychopathology. In addition, this review identified a number of methodological concerns that should be addressed in future research. Specifically, there is a fundamental need for more longitudinal, multidisciplinary, causally driven methods and a clear need for a more consistent approach to modelling of psychopathology. Ultimately, a stronger foundation of knowledge for how best to model psychopathology will drive the identification of robust relationships between transdiagnostic risk and protective factors and mental and substance use disorders to inform our understanding of developmental psychopathology and facilitate empirically supported approaches to prevention and intervention.

Contributors

All authors (SJL, MS, NN and CC) contributed to the design of the study which was led by SJL. SJL wrote the manuscript and CC, MS and NN provided advice, reviewed and contributed to revisions of the manuscript. SJL conducted all searches. SJL screened 100% of the titles and abstracts, and CC, MS and NN screened 25%. SJL and MS reviewed 100% of the studies eligible for full text review. Quality assessments were completed by SJL (100%) and MS and CC (50%).

Declaration of competing interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cpr.2021.102036.

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Appendix C

Protocol paper for Chapter 2

This protocol paper for Chapter 2 has been published as:

SJL conceptualised the paper. SJL, MS, NN and CC developed the study design and protocol. SJL wrote the first draft of the manuscript. All authors read, revised, and approved the final manuscript. SJL is the corresponding author.

<u>Protocol</u>

Transdiagnostic Risk and Protective Factors for Psychopathology in Young People: Systematic Review Protocol

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Abstract

Background: Mental and substance use disorders are among the leading causes of burden of disease worldwide, with risk of onset peaking between the ages of 13 and 24 years. Comorbidity is also common among young people and complicates research, diagnosis and assessment, and clinical decision making. There is increasing support for empirically derived models of psychopathology that overcome issues of comorbidity and provide a transdiagnostic framework for investigating the specificity and generality of risk and protective factors for psychopathology.

Objective: This systematic review aims to identify transdiagnostic risk and protective factors for psychopathology in young people by synthesizing and evaluating findings from research investigating empirically based models of psychopathology.

Methods: Searches will be conducted in Medline, EMBASE, and PsycINFO databases. Reference lists of selected articles will also be hand searched for other relevant publications. All studies will be screened against eligibility criteria designed to identify studies that examined empirical models of psychopathology in relation to risk and/or protective factors in young people with a mean age between 10 and 24 years. Study quality will be assessed using the Joanna Briggs Institute Critical Appraisal Checklists for Cohort Studies and Analytical Cross-Sectional Studies. Findings will be summarized in a narrative synthesis, and a meta-analysis will be conducted if sufficient data are available.

Results: This review is ongoing. At the time of submission, full-text screening was completed, and hand searching of selected articles was underway. Results are expected to be completed by the end of 2020.

Conclusions: This protocol is for a systematic review of evidence for transdiagnostic risk and protective factors associated with empirically based models of psychopathology in young people. To our knowledge, the critical synthesis of this evidence will be the first to date and will provide a better understanding of the factors that contribute to the onset and maintenance of psychopathology in young people. Insights drawn from the review will provide critical new knowledge to improve the targeting of interventions to prevent or reduce mental health problems.

Trial Registration: This systematic review is registered with PROSPERO (CRD42020161368) and is available via Open Science Framework.

International Registered Report Identifier (IRRID): DERR1-10.2196/19779

KEYWORDS

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Introduction

Mental and substance use disorders are among the leading causes of burden of disease worldwide, and the mortality and morbidity of these disorders have not declined since 1990 [1]. These disorders often emerge during adolescence, with risk of onset heightened between the ages of 13 and 24 years [2,3]. A number of factors have been identified that increase (risk factors) or decrease (protective factors) the likelihood of young people experiencing mental health problems. Risk and protective factors help identify young people most at risk of developing mental disorders and guide intervention targets. Many risk and protective factors have been found to be associated with a number of different mental disorders [4]. However, it is unclear whether these associations are specific to certain mental disorders or transdiagnostic in nature.

Comorbidity among mental disorders is common, with estimates that up to two-thirds of adolescents with a mental disorder will also have at least one other mental disorder [3,5]. The prevalence of comorbidity makes diagnostic and treatment decision making complicated, as additional disorders can affect treatment outcome [6,7]. Furthermore, failing to account for comorbid mental disorders when investigating risk and protective factors could mean that relationships with mental disorders might be due to the compounding nature of overall psychopathology rather than any specific associations, hampering research, prevention, and treatment efforts.

Given the ubiquity of comorbidity, understanding risk and protective factors in relation to the development of mental disorders in young people is important for three reasons. First, comorbidity has been associated with greater symptom severity and poorer treatment outcomes [3,8]. Second, risk and protective factors may enhance identification and prediction of individuals with a greater likelihood of developing mental disorders [9]. Third, identification of the characteristics and processes that can be targeted and modified through intervention is critical to the development of efficacious prevention and treatment [10]. Much of the prior research investigating risk and protective factors has typically focused on associations with a single disorder or a single risk or protective factor [4]. As such, the relationships between the breadth of psychopathology and putative risk and protective factors are not clear, heralding the need for a different approach to examining these relationships.

Empirical Models of Psychopathology

The categorical, prototypical approach to organizing mental disorders used in traditional classifications systems, such as the Diagnostic and Statistical Manual of Mental Disorders (DSM; now in its 5th edition) has a number of limitations, such as a lack of specificity as demonstrated by the prevalence of comorbidity [7]. In contrast, empirical models of psychopathology use a broad range of quantitative approaches to generate coherent arrangements of signs and symptoms of psychopathology and capture the high rates of psychiatric comorbidity [11]. What results is a quantitively organized framework that facilitates investigation of the specificity and generality of risk and protective factors for psychopathology that is not achievable with traditional classification systems

[9,12,13]. Two empirical models have emerged in recent years and received increasing attention in the literature.

Hierarchical Dimensional Models

Hierarchical dimensional models, such as the Hierarchical Taxonomy of Psychopathology (HiTOP) model, propose latent factors that capture covariance among commonly comorbid disorders. Early examination of comorbidity among common childhood disorders suggested the presence of two latent factors: internalizing (eg, mood and anxiety disorders) and externalizing (eg, substance abuse and antisocial, oppositional, and impulsive related disorders) factors [3,11,14]. However, internalizing and externalizing have also consistently been found to be positively correlated, suggesting the presence of a higher-order latent factor [3,12,15].

According to the HiTOP model, this association represents a general factor of psychopathology (the "p" factor). The "p" factor sits at the apex of the hierarchical structure and is thought to capture a latent vulnerability to all mental disorders (see Kotov et al [6]). Efforts to expand the internalizing-externalizing model to cover the breadth of psychopathology have flourished over the last two decades. Additional spectra that sit below the "p" factor have also begun to emerge, such as thought disorder (or psychoticism), detachment (eg, histrionic, avoidant, dependent, and schizoid personality disorders), and somatoform dimensions. Beneath each of these spectra sit a number of lower order dimensions, and beneath these sit a number of even more specific components and traits. In this framework, transdiagnostic risk and protective factors may be uniquely associated with the "p" factor or specific spectra, such as internalizing or externalizing.

Network Models

Network theory proposes that disorders arise from dynamic relationships between symptoms, resulting in a network of connected symptoms [13]. Disorders can therefore be seen as systems of causally related symptoms, rather than manifestations of latent vulnerabilities. Factors outside of the psychopathology network form what is referred to as the external field and can influence or activate symptoms, which in turn promotes the activation of other symptoms in a cascading system leading to the onset and maintenance of mental disorders [16]. Transdiagnostic risk and protective factors are therefore components of the network that are external to symptoms but are connected to symptoms from many symptom groupings within the psychopathology network.

Transdiagnostic Risk and Protective Factors

Two previous reviews have examined risk and protective factors in relation to internalizing and externalizing dimensions in children and adolescents; however, to our knowledge, no previous reviews have investigated other broadband dimensions [17,18]. A mega-analytic synthesis of child, family, school, community, and cultural risk and protective factors correlated with internalizing behaviors, externalizing behaviors, or both found 4 risk factors and 3 protective factors common to both internalizing and externalizing disorders [17]. Although this suggests that additional factors examined were specific to either internalizing or externalizing, it is unclear from the review

whether the studies included examined both internalizing and externalizing disorders simultaneously, only one of these, or specific behaviors or disorders within those disorder groupings. Thus, it is not possible to draw any conclusions about whether any of the identified risk and protective factors are transdiagnostic or disorder-specific.

McMahon and colleagues [18] conducted a systematic review of studies examining the relationship between internalizing and externalizing symptoms and a range of stressors, such as exposure to violence, abuse, poverty, and parental divorce, with the aim of evaluating the specificity of stressors. However, the review found little evidence that individual stressors were associated with specific internalizing or externalizing outcomes, with the exception of an association between sexual abuse and internalizing or post-traumatic stress disorder symptoms. This suggests that most stressors examined were transdiagnostic across internalizing and externalizing disorders. However, while stressors may be transdiagnostic risk factors and useful for identifying young people at risk of developing mental health problems, further investigation is needed to identify factors that can be addressed and modified through intervention. Further, it is unknown whether these transdiagnostic associations hold across other domains of psychopathology, such as psychotic-related disorders.

Research that takes into account a broad range of disorders and comorbidity is necessary to identify transdiagnostic risk and protective factors. Identifying the risk and protective factors for psychopathology in young people that occur across traditional diagnostic categories is of great clinical significance. Such factors may be useful for more efficient prediction and early identification of psychopathology, as some may provide useful targets for reducing overall risk for psychopathology, thus preventing a variety of mental disorders from subsequently emerging [19].

Review Aim

The aim of this systematic review is to identify transdiagnostic risk and protective factors for psychopathology in young people. This will be done by synthesizing and critically evaluating studies examining empirically based models of psychopathology.

Methods

This protocol conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement [20], which can be found in Multimedia Appendix 1, and is registered with PROSPERO (CRD42020161368). The protocol is also available via Open Science Framework [21].

Eligibility Criteria

The Population Exposure Comparator Outcome (PECO) framework was used to develop the research question and eligibility criteria for this review [22].

Population

The population of interest will be young people between 10 and 24 years of age, as defined by the World Health Organization [23]. Studies where the mean age of participants falls between 10 and 24 years will be considered for inclusion.

Exposure

Studies that have examined variables such as genetic, neurobiological, cognitive, social, and environmental characteristics and their association with an empirically based model of psychopathology will be considered for inclusion.

Comparison

Studies with or without a comparison group will be considered for inclusion as the dimensional nature of psychopathology implicit within contemporary knowledge precludes the need for control groups.

Outcome

Psychopathology outcomes derived from empirically based models of at least two broad groups of signs or symptoms, such as internalizing, externalizing, or thought disorders, will be included. Quantitative approaches typically used to organize signs and symptoms of psychopathology include factor analytic, class-based, and network approaches. Studies where validated measures of internalizing and externalizing have been used will also be included where findings for both dimensions have been reported.

Studies

Longitudinal and cross-sectional studies examining risk and protective factors associated with psychopathology in young people will be eligible. Although longitudinal studies provide stronger evidence for causation, cross-sectional studies will be included because they may help identify characteristics needing further research.

Studies must be peer-reviewed, be in English, and report original empirical findings. Reviews, opinion pieces, and other publication types that do not report original empirical findings will be excluded.

Search Strategy

Searches will be conducted in Medline, EMBASE, and PsycINFO databases. An example search string developed for Ovid PsycINFO is shown in Table 1, which will be replicated for EMBASE and Medline databases. Reference lists of selected articles will also be hand searched to identify additional relevant articles not captured by the initial search strategy.

Table 1. Sample search strategy developed for Ovid PsycINFO.

Search	Terms
1	SH[a]: Latent Variables/ or Latent Class Analysis/ or Latent Profile Analysis/ or Item Response Theory/ or Principal Component Analysis/
2	(general factor* or p-factor* or transdiagnostic* or psychopathology network* or symptom network* or bridge symptom* or comorbidity network* or latent* or factor mixture model* or multimode* or item response theory).mp[b].
3	1 or 2
4	SH: exp[c] Psychopathology/ or exp Psychiatry/ or exp Dual Diagnosis/ or exp Comorbidity/
5	(psychopatholog* or psychiatr* or comorbid* or co?occur* or dual diagnos*).mp.
6	4 or 5
7	3 AND 6
8	(Child* or adolescen* or teen* or youth* or pediatr* or paediatr* or young or emerging adult* or youth).mp.
9	SH: exp risk factors/ or exp protective factors/
10	((risk or protec* or resilienc* OR underlying or vulnerab*) adj4 (factor* or mechanism* or character*)).mp.
11	9 OR 10
12	7 AND 8 AND 11
13	Limit 12 to English language
14	Limit 13 to peer-reviewed journals

[a]SH: subject heading.

[b]mp: title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms.

[c]exp: explode.

Selection of Studies

All titles and abstracts will be screened by one reviewer (SJL); the other reviewers (CC, NN, MS) will screen 25% of the titles and abstracts, which will be randomly selected. For all studies identified in the initial screen, the full-text articles will be reviewed and assessed against the eligibility criteria by two reviewers (SJL and MS). Disagreements at each stage of screening will be resolved through discussion or by a third reviewer (CC). A PRISMA flow chart will be created to show the results of each stage of the screening process.

Review Procedure and Data Extraction

Citations will be imported into the Covidence systematic review software [24], which will be used to remove duplicates and screen tittles, abstracts, and full texts. The following information will be extracted by the primary reviewer (SJL): publication details (authors, year of publication, country), study design (eg, cross-sectional, longitudinal), sample characteristics (sample size, mean age, ethnicity, sex), psychopathology measures (measures used), informant type (parent, self, other), risk or protective factor measures, data analysis strategy (techniques used, model specification, indicator type), outcome statistics (eg, test statistics, *P* values, effect size, model fit statistics, network centrality statistics). For longitudinal studies, additional information will be extracted regarding follow-up intervals and frequency. A summary of main findings will also be recorded.

Assessment of Quality

Following data extraction, study quality will be assessed independently by two reviewers. Cross-sectional studies will be evaluated using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies, and longitudinal studies will be evaluated using the Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies [25].

Results

This systematic review is ongoing. At the time of submission, full-text screening was completed, and hand searching of articles for additional studies to be included was underway. Findings will be summarized in a narrative synthesis and grouped by research domain, such as genetic, neurobiological, cognitive, social, environmental, or any other broad themes that emerge from the review. Studies will also be summarized by statistical approach. Analysis of subgroups or subsets will be determined based on results of the review and availability of sufficient data. Results are expected to be completed by the end of 2020.

Discussion

Understanding how risk and protective factors are associated with empirical models of psychopathology is critically important to determining which factors will be most useful to target when developing treatment and preventative interventions. It may be that some transdiagnostic risk factors are associated with a general vulnerability to all mental disorders, while others may be more specific to certain dimensions or spectra (eg, internalizing, externalizing). Factors associated with a general liability may serve as fruitful targets for preventative interventions, whereas specific factors may be more useful in developing selective or indicated interventions.

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The results of this systematic review will provide a much-needed critical analysis of the risk and protective factors for mental and substance use disorders in young people derived from empirically based models of psychopathology. Findings will help guide and accelerate the development of transdiagnostic prevention programs. To our knowledge, this will be the first systematic review of the risk and protective factors associated with empirically based models of psychopathology in young people. The critical synthesis of this evidence provides an opportunity to better understand the factors that contribute to the onset and maintenance of psychopathology in young people. This information can provide a foundation upon which interventions can be designed that are better able to prevent or reduce mental health problems and in turn disrupt the cascade of psychopathological sequelae into adulthood.

Acknowledgments

Conflicts of Interest

None declared.

Multimedia Appendix 1

PRSIMA-P Checklist 2015.
[PDF File (Adobe PDF File), 153 KB-Multimedia Appendix 1]

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Abbreviations

HiTOP: Hierarchical Taxonomy of Psychopathology
PECO: Population Exposure Comparator Outcome
PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols

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Appendix D

Structure of psychopathology in adolescents and its association with high-risk personality traits

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Regular Article

Structure of psychopathology in adolescents and its association with high-risk personality traits

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Abstract

The present study examined high-risk personality traits and associations with psychopathology across multiple levels of a hierarchical-dimensional model of psychopathology in a large adolescent, general population sample. Confirmatory factor analyses were run using data from two randomized controlled trials of Australian adolescents ($N = 8,654$, mean age = 13.01 years, 52% female). A higher-order model – comprised of general psychopathology, fear, distress, alcohol use/harms, and conduct/inattention dimensions – was selected based on model fit, reliability, and replicability. Indirect-effects models were estimated to examine the unique associations between high-risk personality traits (anxiety sensitivity, negative thinking, impulsivity, and sensation seeking) and general and specific dimensions and symptoms of psychopathology. All personality traits were positively associated with general psychopathology. After accounting for general psychopathology, anxiety sensitivity was positively associated with fear; negative thinking was positively associated with distress; impulsivity was positively associated with conduct/inattention; and sensation seeking was positively associated with alcohol use/harms and conduct/inattention, and negatively associated with fear. Several significant associations between personality traits and individual symptoms remained after accounting for general and specific psychopathology. These findings contribute to our understanding of the underlying structure of psychopathology among adolescents and have implications for the development of personality-based prevention and early intervention programs.

Keywords: adolescents; higher-order model; personality; psychopathology

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Introduction

Personality is a well-established risk factor for psychopathology, with evidence for links with a variety of mental and substance use disorders (Kotov et al., 2010; Tackett, 2006; Watson et al., 2005, 2019; Widiger et al., 2019; den Akker et al., 2013). However, there are high rates of comorbidity among disorders, making it difficult to identify reliable links between personality traits and mental disorders. Recent advances in the study of the underlying structure of psychopathology supports a data-driven, hierarchical-dimensional model of psychopathology which accounts for comorbidity among disorders and enables the study of relations with external variables at various levels of specificity. Yet, only a small number of studies have examined the associations between personality traits and psychopathology within this framework among adolescents to date (Lynch et al., 2021). Further, past research has primarily focused on associations between normal-range trait domains (e.g., "the Big 5" or five factor model traits) and distinct disorders (Sellbom et al., 2020). Examining established high-risk personality traits (e.g., lower-order facets of neuroticism

or sub-dimensions of disinhibition) may be informative in terms of refining our understanding of the underlying structure of psychopathology and for advancing knowledge of personality-related risk for psychopathology. Focusing on these associations in a hierarchical-dimensional model of psychopathology, for example, may be particularly useful for clarifying the role personality may play in the development of general and specific forms of psychopathology, from individual symptoms up to broad transdiagnostic dimensions.

Hierarchical-dimensional models of psychopathology

Psychopathology has historically been conceptualized in terms of discrete diagnostic categories. However, categorical approaches to conceptualizing psychopathology tend to have poor reliability and low specificity, as evidenced by the high rates of comorbidity between disorders and heterogeneity within disorders (Kotov et al., 2017; Ofrat & Krueger, 2012). In response to these issues, there has been a renaissance of empirical studies examining the underlying structure of psychopathology. This work has generated a wealth of evidence for conceptualizing psychopathology in a hierarchical-dimensional framework, such as the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017, 2021). At the apex of hierarchical-dimensional models sits a general factor of psychopathology, which captures shared variance

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among mental and substance use disorders. Beneath the general factor sit more specific factors that reflect shared variance among closely related disorders, such as internalizing and externalizing dimensions. Internalizing captures comorbidity among, for example, phobias, eating, obsessive-compulsive, and mood and anxiety-related disorders, whereas externalizing reflects shared variance among, for example, substance use, conduct, antisocial and impulse related disorders. There is also evidence that these dimensions may be partitioned into even narrower dimensions (Krueger et al., 2021; Watson et al., 2022). For example, internalizing includes sub-dimensions of fear and distress, and externalizing includes sub-dimensions of substance use and antisocial behavior.

Personality and psychopathology

Previous research has consistently shown that there are strong associations between certain personality traits and certain forms of psychopathology (Brandes & Tackett, 2019; Haltigan et al., 2018; Kotov et al., 2010; Widiger et al., 2019). For example, neuroticism has been established as an important risk factor for internalizing and general psychopathology dimensions (Brandes et al., 2019; Castellanos-Ryan et al., 2016; Etkin et al., 2021; Kotov et al., 2010). Similarly, antagonism and impulsivity traits are both associated with externalizing and substance misuse problems (Castellanos-Ryan et al., 2016; Etkin et al., 2022; Kotov et al., 2010; Lynam & Miller, 2019). However, currently very little is known about associations at the subfactor (e.g., fear and distress) and symptom levels of hierarchical-dimensional models of psychopathology (Brandes & Tackett, 2019; Kotov et al., 2010). Similarly, although personality can also be conceptualized hierarchically, most research thus far has focused on broad personality traits, rather than the underlying facets or aspects of these traits (Brandes & Tackett, 2019; Tackett, 2006; Watts et al., 2019). Amid renewed calls for research on the integration of and differentiation between personality and psychopathology (Hopwood et al., 2022; Wright & Hopwood, 2022), exploration of associations between narrower components of personality and subfactor and symptom levels of psychopathology could help clarify the structure of lower levels of a hierarchical model of psychopathology or point to shared or distinguishable elements of personality and psychopathology.

The four-factor model of vulnerability integrates and distills previous research linking neuroticism as well as inhibited and disinhibited personality traits to substance misuse and comorbid psychopathology via distinct cognitive and motivational pathways (Castellanos-Ryan et al., 2016; Castellanos-Ryan & Conrod, 2012). Although this model was initially conceptualized as a model of personality-based risk for substance use, there is considerable evidence that the traits are also associated with higher levels of and increased risk for other forms of psychopathology (Carragher et al., 2016; Castellanos-Ryan et al., 2016). In contrast to comprehensive models of personality, such as the Big Five, the four-factor model of vulnerability is comprised of four particularly compelling personality-based risk factors for substance use problems, and psychopathology more broadly (Castellanos-Ryan & Conrod, 2012). Inhibited/neurotic traits of *negative thinking* (tendency to experience hopelessness and low positive affect) and *anxiety sensitivity* (fear of anxiety-related physical sensations relating to beliefs that such sensation could lead to harmful consequences) are associated with mood and anxiety-related problems, as well as increased substance use problems (to manage or relieve symptoms of anxiety/depression). Disinhibition is partitioned into two

sub-domains: *impulsivity*, which broadly reflects a failure to inhibit behaviors likely to result in negative consequences, and *sensation seeking*, which reflects a willingness to take risks for the sake of novel experiences. Individuals high in impulsivity have difficulties with emotion and behavioral regulation, tend **to** experience more conduct related problems and are at increased risk for substance misuse through enhancement, coping and conformity motives. Whereas individuals high in sensation seeking are more likely to develop substance use problems due to a heightened susceptibility to the rewarding properties of alcohol and other substances. Sensation seeking appears to be more directly related to substance misuse problems than other externalizing related problems (Castellanos-Ryan & Conrod, 2011).

Prior research on the four-factor model of vulnerability and hierarchical-dimensional model of psychopathology have revealed theoretically aligned patterns of association with transdiagnostic dimensions (though there are some exceptions). For example, *negative thinking* and *anxiety sensitivity* appear to be prospectively and concurrently associated with greater internalizing and general psychopathology (Carragher et al., 2016; Castellanos-Ryan et al., 2016), and either unrelated or inversely related to externalizing (although one study reported a positive association between negative thinking and externalizing, but internalizing symptoms were not included in the model (e.g., Castellanos-Ryan & Conrod, 2011). Similarly, impulsivity and sensation seeking appear to be more closely related to externalizing related dimensions, with impulsivity more closely related to conduct/general externalizing and sensation seeking more closely aligned with substance misuse and related harms. One study also reported a negative association between sensation seeking and negative thinking (Carragher et al., 2016). Exploration of unique associations with sub-dimensions of internalizing and externalizing, or indeed individual symptoms, may help clarify some of the inconsistent findings from previous studies. To our knowledge, no studies have examined associations between these high-risk personality traits and lower levels of a hierarchical-dimensional model of psychopathology.

Methodological considerations

Despite strong empirical support for hierarchical-dimensional models of psychopathology, there are some outstanding conceptual and methodological issues. Critically, there is currently no clear consensus on which statistical model is most appropriate for studying the structure of psychopathology. Correlated factors, bifactor and higher-order models appear most frequently in the literature (Forbes, Greene, et al., 2021; Lahey et al., 2021). These models are closely related yet offer different interpretations of the underlying structure of psychopathology. For example, a higher-order model's general factor reflects the shared variance among the lower-order specific factors, whereas a bifactor model's general factor directly reflects shared variance among all indicators. Further, in correlated factors and higher-order models, the specific factors reflect shared variance among a set of observed variables, whereas in a bifactor model the specific factors are uncorrelated and reflect variance unique to the factor (after the shared variance among indicators is accounted for by the general factor). When these models are directly compared using traditional goodness-of-fit statistics, the bifactor model typically outperforms the others (e.g., Greene et al., 2019). However, there are increasing concerns about relying on goodness-of-fit statistics to adjudicate between models, as bifactor models tend to overfit data which can result in inflated goodness-of-fit statistics and consequently

lead to the premature dismissal of other plausible structures (Bonifay et al., 2017). As such, there have been calls to consider additional metrics for model reliability and replicability when studying the underlying structure of psychopathology (Forbes, Greene, et al., 2021; Rodriguez et al., 2016b). Although very few studies have reported on these additional metrics to date, two previous studies have found a higher-order model to outperform a bifactor model of psychopathology in young people (Lees et al., 2020; Sunderland et al., 2020).

Another important methodological issue that requires further attention is the unit of measurement used for observed variables. Much of the past research on hierarchical-dimensional models has been based on diagnostic level indicators (Forbes, Sunderland, et al., 2021). This may inadvertently constrain models to the framework of the prevailing diagnostic taxonomies. Symptom-level approaches are theorized to be better able to capture the underlying structure of psychopathology because they are not bound by the constraints of existing diagnostic categories. Further, symptom-level approaches may be more sensitive to detecting emerging forms of psychopathology (e.g., cases in which symptoms are present, but the individual does not meet full diagnostic criteria; Forbes, Sunderland, et al., 2021). Given that many mental disorders first emerge during adolescence (Costello et al., 2011; Kessler et al., 2011), it is likely that symptom-level analyses may be more appropriate for studying psychopathology in adolescents. Another advantage of symptom-level analysis is that it enables the identification of important symptoms with unique links to risk or vulnerability factors. These symptoms may highlight potential etiological mechanisms and therefore could be salient intervention targets. In summary, symptom-level analyses are important both for advancing our understanding of the underlying causes of mental and substance use disorders and ultimately, for facilitating the identification of better intervention targets.

The present study

The aim of the present research was to conduct a more thorough exploration of the structure of psychopathology and associations with high-risk personality traits among adolescents than previously available. We aimed to examine a variety of hierarchical-dimensional structures of psychopathology using a symptom-level approach and evaluate the models using more rigorous methods of model evaluation and selection. Specifically, we assessed four alternative models of adolescent psychopathology: bifactor, higher-order, four-correlated factors and a one-factor unidimensional model. As we planned to evaluate the structural validity through additional metrics beyond traditional fit indices which not been commonly examined in previous research, we did not have any specific expectations about which model would perform the best.

Extending previous research, we also aimed to examine the direct and indirect effects of high-risk personality traits on psychopathology across three hierarchical levels: general psychopathology, specific factors, and symptoms. To our knowledge, this is the first study to examine symptom-level associations with high-risk personality traits among adolescents. As such, we did not have any specific expectations about associations between the high-risk personality traits and individual symptoms. We did, however, expect that all high-risk personality traits would be positively associated with general psychopathology; impulsivity and sensation seeking would be positively associated with externalizing related specific dimensions; and anxiety sensitivity and negative thinking would be associated with internalizing related specific dimensions.

Methods

Participants

The sample was derived from two large cluster randomized controlled trials investigating the effectiveness of eHealth prevention programs in Australia – the Climate and Preventure (CAP) and Climate Schools Combined (CSC) studies (Newton et al., 2012; Teesson et al., 2014). The present study examined baseline data from these cohorts. The CAP cohort comprises 2,268 students with a mean age of 12.96 years (SD = 0.46) recruited through 27 schools in 2012. Within the CAP cohort, 972 were female (42.89%) and 1,941 were born in Australia (86.84%). The CSC cohort comprises 6,386 students with a mean age of 13.03 years (SD = 0.61) from 71 schools in 2014. Within the CSC cohort, 3,502 were female (54.83%) and 5,147 were born in Australia (84.17%). The combined sample contained 8,654 students, 53 of which were missing on all variables and were excluded from analyses, resulting in a final sample size of 8,601 (mean age 13.01 years, SD = 0.57) from 98 schools, of which 4,474 were female (51.71%) and 7,088 were born in Australia (84.88%).

Measures

Psychopathology

Item-level responses from measures of psychopathology used in both CAP and CSC baseline assessments were used in the present study. Due to the low prevalence of substance use and psychopathology in this general population sample, all items were recoded into binary indicators to reduce the number of sparse cells and improve the stability of the models and overall precision of the estimates. Cut points were determined based on inspection of the distribution of responses (further details provided below). The measures used to assess psychopathology are described below and a summary of the items, proportions and counts is provided in Supplementary Table S1.

Strengths and Difficulties Questionnaire (SDQ). The SDQ is a brief, 25-item questionnaire that measures emotional and behavioral difficulties over the past 6 months and is comprised of four subscales: conduct problems, emotional symptoms, hyperactivity, peer problems and prosocial behavior (Goodman, 2001). Items were selected to load onto the fear, distress and conduct dimensions as informed by previous analyses (Carragher et al., 2016; Goodman et al., 2010). Reverse-scored items were removed due to poor performance and previously documented problems (Van De Looij-Jansen et al., 2011). Items from the SDQ were recoded into binary indicators with levels representing "not true" or "true" (i.e., "somewhat true" or "certainly true").

Kessler Psychological Distress Scale (K6). The K6 is a 6-item screening tool for psychological distress due to symptoms of depression and anxiety over the past 4 weeks (Kessler et al., 2002, 2003), and has been found to be a valid and reliable measure of psychological distress among adolescents (Ferro, 2019; Mewton et al., 2016). Two items were loaded onto the fear dimension, and the remaining four items loaded onto the distress dimension. Items were recoded as "none of the time" or "any time" (i.e., "a little of the time," "some of the time," "most of the time," "all of the time").

Rutgers Alcohol Problem Index. The Rutgers Alcohol Problem Index measures alcohol-related consequences experienced over the past 6 months and has been validated amongst high-school aged people as a measure of alcohol-related problems (Neal et al., 2006; White & Labouvie, 1989). A shortened 8-item version that had previously demonstrated adequate validity and reliability for

assessing alcohol-related problems among young people was administered to the CAP cohort (Topper et al., 2011). As such, only these items have been used in the present study. Items were recoded as "did not experience in the last 6 months" and "experienced at least one time in the last 6 months."

Patterns of Alcohol Use. Patterns of alcohol use over the past 6 months were assessed using three items adapted from the School Health and Alcohol Harm Reduction Project's "Patterns of Alcohol Use" index (McBride et al., 2004). Specifically, there were three items measuring frequency of alcohol use in the past 6 months, quantity of alcohol consumed in the past 6 months and frequency of drinking above low risk levels in the past 6 months. Items were recoded into "none or less than monthly" and "once a month or more."

High-risk personality traits

Substance Use Personality Risk Profile Scale (SURPS) is a 23-item measure of personality risk for substance misuse, comprised of four distinct subscales: hopelessness/negative thinking, anxiety sensitivity, sensation seeking and impulsivity (Woicik et al., 2009). The SURPS asks participants to indicate the extent to which they agree with each item on a 4-point scale (1 = strongly disagree, 2 = disagree, 3 = agree, 4 = strongly agree). Total scores were calculated for each subscale and used in subsequent analyses. The SURPS has demonstrated good validity and reliability as a measure of personality-related risk for substance use and co-occurring psychopathology among young people across multiple cohorts (Castellanos-Ryan et al., 2013; Newton et al., 2016; Woicik et al., 2009).

Analytic plan

Analyses in the present study were conducted in the following broad steps: 1) model estimation, 2) model evaluation via traditional goodness-of-fit and contemporary model reliability and replicability indices, 3) measurement invariance testing, and 4) finally the associations between personality traits and psychopathology dimensions were assessed via regression and indirect-effects models. Further details of each step are provided below.

First, we estimated four alternative structural models of psychopathology using confirmatory factor analysis: 1) a *one-factor* model with all items loading on a single latent variable representing general psychopathology; 2) a *four-correlated factors* model with four latent variables representing fear, distress, alcohol use/harms and conduct/inattention; 3) a *bifactor* model with all indicators loading onto a single latent variable representing general psychopathology as well as four orthogonal (i.e., uncorrelated) latent variables representing fear, distress, alcohol use/harms and conduct/inattention, and 4) a *higher-order model* comprising four lower-order factors representing fear, distress, alcohol use/harms and conduct/inattention and a higher-order general psychopathology latent variable that accounts for the correlations among the lower-order factors.

The structural models were based on prior symptom-level studies among adolescents, which have consistently found evidence for a general psychopathology factor, and at least two specific or correlated factors representing externalizing and internalizing symptoms (Afzali et al., 2017; Carragher et al., 2016; Haltigan et al., 2018; Levin-Aspenson et al., 2019). Notably, one study found that internalizing bifurcated into fear and distress sub-dimensions (Levin-Aspenson et al., 2019), and another study found evidence for separate attention and externalizing factors (Haltigan et al., 2018).

All models accounted for school-level clustering and were estimated in Mplus version 8.4 using robust weighted least squares and robust maximum likelihood estimation methods to generate a range of fit statistics.

Second, the structural validity of each model was evaluated with goodness-of-fit and latent variable reliability indices (Forbes, Greene, et al., 2021; Rodriguez et al., 2016a). Incremental fit indices, including root mean square error of approximation (RMSEA) comparative fit index (CFI, values >0.95) and Tucker–Lewis index (TLI) were used to assess model fit, where RMSEA values <0.6, and CFI and TLI values >0.95 indicate close fit (Brown, 2014). Models were also compared using the information criteria, including the Akaike information criterion, Bayesian information criterion, and the sample size-adjusted Bayesian information criterion, for which lower values indicate superior fit (Raftery, 1995).

Given the tendency for goodness-of-fit statistics to be biased towards selecting bifactor models, additional reliability and replicability indices were calculated (Forbes, Greene, et al., 2021; Rodriguez et al., 2016a). Specifically, the H coefficient, which gives an indication of the construct replicability (H, ideally >0.8), omega (ideally >0.75), which represents the proportion of variance accounted for by a single latent variable, omega hierarchical (OmegaH, ideally >0.8), indicates the proportion of variance accounted for by the general factor, and omega hierarchal subscale (OmegaHS, ideally >0.75) which represents the variance accounted for by a specific factor after removing variance accounted for by the general factor. Additionally, we calculated the explained common variance which provides an indication of the importance of the general factor relative to the specific factors (Explained Common Variance, ideally >0.7), and the explained common variance of specific factors which gives an indication of the uniqueness of a specific factor (ECV_S = Explained Common Variance of specific factors, ideally >0.7). Unidimensionality was examined by calculating the percent of uncontaminated correlations (Percent of Uncontaminated Correlations, values >0.7 indicate unidimensionality) and absolute relative parameter bias (Absolute Relative Parameter Bias; 10–15% is acceptable). Percent of Uncontaminated Correlations indicates the proportion of unique correlations among indicators (i.e., parameter estimates) that can be explained by a general factor alone, thus high Percent of Uncontaminated Correlations indicates that the parameter estimates are relatively unbiased by multidimensionality and supports a unidimensional structure (Reise et al., 2013). Absolute Relative Parameter Bias compares the absolute difference between parameter estimates between a unidimensional model and a bifactor (or other multidimensional) model. For the higher-order model, these indices were calculated following a Schmid–Leiman transformation (SLT), which orthogonalizes the latent variables. Following a SLT, the lower-order factors in a higher-order model are like the specific factors in a bifactor model. Whereas the latent variables from a correlated factors model are like the lower-order factors *prior* to SLT and are useful for understanding their reliability as standalone constructs. Models found to have acceptable structural validity according to the goodness-of-fit, reliability and replicability indices progressed to the next step.

Third, to examine the robustness of the models selected in the previous step and ensure that it was appropriate to combine data from both samples, measurement invariance was tested across the CAP and CSC groups within a multigroup confirmatory factor analysis framework. Specifically, we tested invariance in the following sequence as recommended by Brown (2014): 0) test the model

Table 1. Fit indices for different structural models of adolescent psychopathology (*n* = 8,589)

Model	No. of parameters	WLSMV					MLR		
		χ^2	df	CFI	TLI	RMSEA (90% CI)	AIC	BIC	SSABIC
One-factor	58	10859.603	377	0.807	0.793	0.057 (0.056–0.058)	171456.65	171863.03	171678.72
Four-correlated factors	64	2564.967	371	0.960	0.956	0.026 (0.025–0.027)	161016.20	161467.90	161264.50
Higher-order	62	2944.731	373	0.953	0.949	0.028 (0.027–0.029)	161203.80	161641.41	161444.38
Bifactor	87	2586.392	348	0.959	0.952	0.027 (0.026–0.028)	159600.40	160214.50	159938.00

Note. χ^2 = Chi-square statistic; df = degree of freedom; CFI = comparative fit index; TLI = Tucker–Lewis index; RMSEA = root mean square error of approximation; CI = confidence interval; AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; SSABIC = sample size-adjusted BIC; WLSMV = weighted least square mean and variance adjusted. The bifactor could not be estimated using the default integration methods for MLR in Mplus. In order to compare the models, the MLR models were then estimated using the INTEGRATIONS = montecarlo(5000) command in Mplus.

separately in each group 1) test invariance of the overall factor structure simultaneously (i.e., configural invariance); 2) test the invariance of the factor loadings (i.e., metric or weak factorial invariance); 3) test the invariance of item intercepts/thresholds (i.e., scalar or strong factorial invariance); and 4) test the invariance of item residual variances (i.e., residual or strict invariance). For higher-order models, we assessed invariance using the procedure described by Rudnev et al. (2018), which assess invariance of the first-order factor alone, and the invariance of the first and higher-order factors simultaneously at each level of invariance.

As the chi-square difference test is too sensitive to be informative in the context of large sample sizes, invariance was evaluated by comparing changes in CFI and RMSEA (Brown, 2014; Chen, 2007; Kline, 2015). Factor structures with changes in CFI less than 0.01 and RMSEA less than 0.015 (from the previous model in the sequence) were considered to demonstrate invariance across groups. Structures demonstrating adequate invariance progressed to the next step. If there was evidence for non-invariance, which would suggest that factor structures or that the interpretation of the latent variables differed across the groups, then alternative tests of measurement invariance would be considered, such as partial measurement invariance, and we conducted additional post hoc analyses to determine whether there are cohort-specific associations between the personality traits and psychopathology dimensions.

Finally, associations with the personality traits were added to the model(s) found to have adequate structural validity. Regression analyses were conducted to obtain total effect estimates for the association between each trait and general psychopathology. Indirect-effects models were estimated to obtain total, direct, and indirect effect sizes at the specific factor and symptom levels. This approach enabled us to test associations between personality traits and psychopathology across three levels of the structural model, and to disentangle unique associations from those that are accounted for by broader dimensions of psychopathology (Conway et al., 2021).

Availability of data and analysis code

The Mplus output files for these analyses are publicly available and can be accessed online (https://osf.io/cq2rz/). Data may be shared with other researchers upon reasonable request.

Results

Structure of adolescent psychopathology

Goodness-of-fit indices are presented in Table 1 and standardized factor loadings for each of the latent variable models using

weighted least square mean and variance adjusted are shown in Table 2. All models, except the one-factor model, were found to have acceptable fit according to traditional fit indices (i.e., CFI and TLI > 0.95). Based on the information criteria (Akaike information criterion, Bayesian information criterion, sample size-adjusted Bayesian information criterion), the bifactor model was the best fitting model, followed by the correlated factors and higher-order models. However, standardized factor loadings in the bifactor model were generally weak for the specific factors and some loadings were negative. In particular, standardized factor loadings on the fear, distress and conduct/inattention specific factors were weak, and the alcohol use/harms related indicators mostly loaded poorly onto the general factor. Further, a Heywood case (i.e., negative residual variance) was detected in the bifactor model on the fear factor (item "restless or fidgety"). Thus, the bifactor model was not considered for further analysis. Standardized factor loadings in the one-factor, four-correlated factors and higher-order models were all positive and reasonably strong (>0.4). In the higher-order model, standardized factor loadings indicate that the general psychopathology factor was more reflective of fear ($b = 0.948$) and distress ($b = 0.876$) dimensions followed by conduct/inattention ($b = 0.744$) and alcohol use/harms ($b = 0.388$) dimensions.

Model reliability indices are shown in Table 3. Overall, the general psychopathology factor showed good internal reliability (omega range 0.96–0.97) and construct reliability (*H* range 0.93–0.97) across the one-factor and higher-order models. The specific factors (fear, distress, alcohol use/harms and conduct/inattention), also showed good internal reliability (omegaS range 0.72–0.98) across the four-correlated factors and higher-order models. Construct reliability (*H* range 0.73–0.98) in the four-correlated factors model was good. However, in the higher-order model, only the alcohol use/harms specific factor had adequate reliability (i.e., *H* > 0.7).

Omega hierarchical subscale (OmegaHS) indices were low for fear, distress, and conduct/inattention factors, indicating that the majority of variance in these factors may be attributable to the general factor. However, OmegaHS was high for the alcohol use/harms factor in the higher-order model, suggesting that the variance in this specific factor may not be attributable to the general factor.

Overall, the general factor appears to have good reliability across the one-factor and higher-order models and the specific factors appear to have poor reliability, except for the alcohol use/harms factor, across the bifactor and higher-order models. Although the correlated factors model demonstrated better fit and reliability, the lower-order factors of a higher-order model are comparable to the correlated factors model (i.e., the correlated factors model is similar to the lower-order level of the higher-order

Table 2. Standardized factor loadings on general and specific (fear, distress, alcohol use/harms, conduct/inattention) factors using WLSMV estimator and inter-factor correlations

Symptom	Item ID	One factor	Four factors	Higher-order		Bifactor	
		General	Specific	General	Specific	General	Specific
Fear							
Nervous in new situations	SD16	0.559	0.668	–	0.677	0.665	−0.168
Many fears	SD24	0.498	0.640	–	0.637	0.624	−0.216
Nervous	K61R	0.422	0.556	–	0.546	0.498	0.315
Restless or fidgety	K63R	0.513	0.639	–	0.638	0.617	0.802
Distress							
Somatic symptoms	SD3	0.573	0.643	–	0.645	0.665	−0.010
Worries	SD8	0.642	0.721	–	0.721	0.728	0.066
Unhappy	SD13	0.755	0.842	–	0.844	0.812	0.204
Hopeless	K62R	0.754	0.828	–	0.826	0.638	0.590
Depressed	K64R	0.754	0.835	–	0.836	0.673	0.530
Effort	K65R	0.559	0.641	–	0.641	0.557	0.323
Worthless	K66R	0.810	0.881	–	0.881	0.656	0.682
Alcohol use/harms							
Frequency	AUC1	0.712	0.820	–	0.816	0.242	0.791
Binge	AUC2	0.836	0.915	–	0.912	0.235	0.901
Quantity	AUC3	0.709	0.820	–	0.819	0.236	0.796
Acted bad	AH1	0.831	0.942	–	0.942	0.305	0.902
Shame/embarrassment	AH2	0.892	0.952	–	0.952	0.337	0.894
Neglected responsibilities	AH3	0.807	0.933	–	0.935	0.310	0.892
Tolerance	AH4	0.845	0.943	–	0.945	0.405	0.850
Personality change	AH5	0.858	0.927	–	0.926	0.390	0.838
Tried to cut down	AH6	0.808	0.877	–	0.874	0.410	0.767
Memory loss	AH7	0.760	0.845	–	0.844	0.397	0.738
Crazy	AH8	0.857	0.917	–	0.917	0.486	0.772
Conduct/inattention							
Restless	SD2	0.586	0.734	–	0.736	0.496	0.648
Temper	SD5	0.563	0.729	–	0.734	0.609	0.278
Fidgety	SD10	0.633	0.794	–	0.799	0.547	0.673
Fight a lot	SD12	0.535	0.671	–	0.665	0.516	0.393
Easily distracted	SD15	0.602	0.732	–	0.732	0.573	0.410
Lies or cheats	SD18	0.543	0.667	–	0.661	0.535	0.329
Steals	SD22	0.522	0.652	–	0.644	0.511	0.358
First-order factors							
	Fear	–	–	0.948	–	–	–
	Distress	–	–	0.876	–	–	–
	Alcohol use/harms	–	–	0.388	–	–	–
	Conduct/ inattention	–	–	0.744	–	–	–
Inter-factor correlations							
Fear with Distress		–	0.892	–	–	0.00	0.00
Fear with Alcohol Use/harms		–	0.164	–	–	0.00	0.00
Fear with Conduct/inattention		–	0.668	–	–	0.00	0.00
Distress with Alcohol Use/harms		–	0.309	–	–	0.00	0.00

(*Continued*)

Table 2. (*Continued*)

		One factor	Four factors	Higher-order		Bifactor	
Symptom	Item ID	General	Specific	General	Specific	General	Specific
Distress Conduct/inattention		–	**0.624**	–	–	0.00	0.00
Alcohol use with Conduct/inattention		–	**0.431**	–	–	0.00	0.00

Note. SD = items from Strengths and Difficulties Questionnaire; AH = Alcohol Harms, items from Rutgers Alcohol Problem Index (RAPI); K6 = Kessler 6 Plus scale (K6+); AUC = Alcohol use, AUDIT-C items; WLSMV = weighted least square mean and variance adjusted. Factor loadings and correlations with a p value ≤0.05 are shown in bold.

Table 3. Reliability indices alternative models of adolescent psychopathology

Index	Factor	One factor	Four factor	Bifactor	Higher-order (SLT)
H	General Psychopathology	**0.97**	–	**0.93**	**0.93**
	Fear	–	**0.73**	0.67	0.14
	Distress	–	**0.93**	0.66	0.54
	Alcohol use/harms	–	**0.98**	**0.97**	**0.96**
	Conduct/inattention	–	**0.88**	0.70	0.67
Omega	General Psychopathology	**0.96**	–	**0.97**	**0.97**
OmegaS	Fear	–	0.72	**0.79**	0.72
	Distress	–	**0.91**	**0.92**	**0.91**
	Alcohol use/harms	–	**0.98**	**0.98**	**0.98**
	Conduct/inattention	–	**0.88**	**0.87**	**0.88**
OmegaH	General Psychopathology	–	–	0.66	0.66
OmegaHS	Fear	–	–	*0.07*	*0.07*
	Distress	–	–	*0.19*	*0.21*
	Alcohol use/harms	–	–	**0.84**	**0.83**
	Conduct/inattention	–	–	*0.35*	*0.39*
ECV	General Psychopathology	–	–	0.42	0.44
ECV_S	Fear	–	–	0.04	0.01
	Distress	–	–	0.06	0.05
	Alcohol use/harms	–	–	0.40	0.41
	Conduct/inattention	–	–	0.08	0.09
ECV_S_NEW	Fear	–	–	0.36	0.10
	Distress	–	–	0.28	0.23
	Alcohol use/harms	–	–	**0.85**	**0.85**
	Conduct/inattention	–	–	0.42	0.45
PUC		–	–	**0.75**	**0.75**
ARPB		–	–	*0.64*	*0.55*

Note. Results in bold indicate acceptable reliability. Indices for Higher-Order model cannot be calculated, indices presented are based on Schmid–Leiman transformed (SLT) model. ECV = Explained Common Variance, ARPB = Absolute Relative Parameter Bias, ECV_S = Explained Common Variance of specific factors, H = measure of construct replicability, Omega = internal reliability of general factor/s, OmegaS = internal reliability of specific factor/s, OmegaH = Omega Hierarchical, OmegaHS = Omega Hierarchical subscale, PUC = Percent of Uncontaminated Correlations, SLT = Schmid–Leiman transformation.

model). Thus, support for the reliability of the factors in the correlated factors model also suggests there is evidence for the lower-order factors of a higher-order model. Furthermore, the reliability indices for the lower-order factors are based on residualized factors (i.e., the Schmid–Leiman transformation is applied before the indices are calculated). As such, the lower-order factors following the SLT are very similar to the specific factors in a bifactor model whereas the correlated factors model gives a closer approximation to the lower-order factors (prior to the SLT) as standalone constructs. An advantage of the higher-order model is that it allows inclusion of both the narrower constructs and a general psychopathology factor. We therefore selected the higher-order model on the basis that there was evidence for the general factor having good reliability, along with the evidence for the reliability of the correlated/lower-order factors. However, model fit indices suggest that perhaps the higher-order general factor may not be required to

Figure 1. Higher-order structural model of adolescent psychopathology with standardized parameter estimates. Note. All estimates statistically significant ($p \leq 0.05$). Standardized factor loadings for indicators of psychopathology are presented in Table 2.

Table 4. Results of measurement invariances tests of a higher-order model of psychopathology

Model	χ^2	df	Comparison	χ^2 D	df	CFI	CFI Δ	RMSEA	RMSEA Δ
0. CAP participants ($n = 2260$)	894.422*	346	NA	–	–	0.986	–	0.026 (0.024–0.029)	–
0. CSC participants ($n = 6329$)	1926.085*	346	NA	–	–	0.952	–	0.027 (0.026–0.028)	–
1. Configural model	2664.86*	693	NA	–	–	0.973	–	0.026 (0.025–0.027)	–
2. First-order metric	2728.503*	717	1 vs 2	252.347	24	0.972	−0.001	0.026 (0.025–0.027)	0
3. First- & second-order metric	2634.176*	719	2 vs 3	6.562	2	0.974	0.002	0.025 (0.024–0.026)	−0.001
4. First-order scalar	2680.26*	743	3 vs 4	151.608	24	0.974	0	0.025 (0.024–0.026)	0
5. First- & second-order scalar	2654.42*	747	4 vs 5	24.551	4	0.974	0	0.024 (0.023–0.025)	−0.001
6a. Residual variances free	2687.871*	719	NA	–	–	0.973		0.025 (0.024–0.026)	–
6b. Residual variances fixed	2654.42*	747	6a vs 6b	183.005	28	0.974	0.001	0.024 (0.023–0.025)	−0.001

*Note. * p < 0.001. χ²Δ computed using Mplus DIFFTEST function; CFI Δ = difference in CFI from previous model; RMSEA Δ = difference in RMSEA from previous model. Initial baseline model in the CAP cohort revealed a correlation between AH1 & AH3 of 0.987. The AH1 item was removed from subsequent analyses, and the above table shows the results of measurement invariance tests with AH1 removed.*

account for the associations between factors over and above use of correlations. Therefore, additional external validity was assessed for the correlated factors model (See Supplementary Table S7). A diagram showing the higher-order model and standardized factor loadings is shown in Figure 1.

Following inspection of factor loadings, model fit and reliability indices, additional models were examined including bifactor and higher-order models comprised of general internalizing and general externalizing factors (rather than a single general psychopathology factor). However, these models were found to have inadequate structural validity (see supplementary materials for further details).

The reliability of the higher-order model was further corroborated by measurement invariance tests, as shown in Table 4. The baseline model fit the data well in both the CAP and CSC cohorts. However, a high correlation (0.987) between two items (AH1, "Acted bad" and AH3, "Neglected responsibilities") was found in the CAP cohort. One of the items was removed (AH1,

"Acted bad") from the model in subsequent analyses and this higher-order model demonstrated invariance across the CAP and CSC cohorts.

High-risk personality risk traits and associations with psychopathology dimensions and symptoms

The standardized total and direct effects are available in the supplementary material (Tables S3 to S6). Figure 2 shows the standardized direct effect estimates and 99% confidence intervals for each of the personality traits and general and specific factors of psychopathology. Anxiety sensitivity, negative thinking, impulsivity, and sensation seeking all had significant, positive total effects with general psychopathology. Differential patterns of association emerged with specific factors of psychopathology (Figure 2) and in symptom-level analyses (Figure 3).

Anxiety Sensitivity: Anxiety sensitivity had a significant positive direct effect with fear and distress, with only 58 and 65% of the
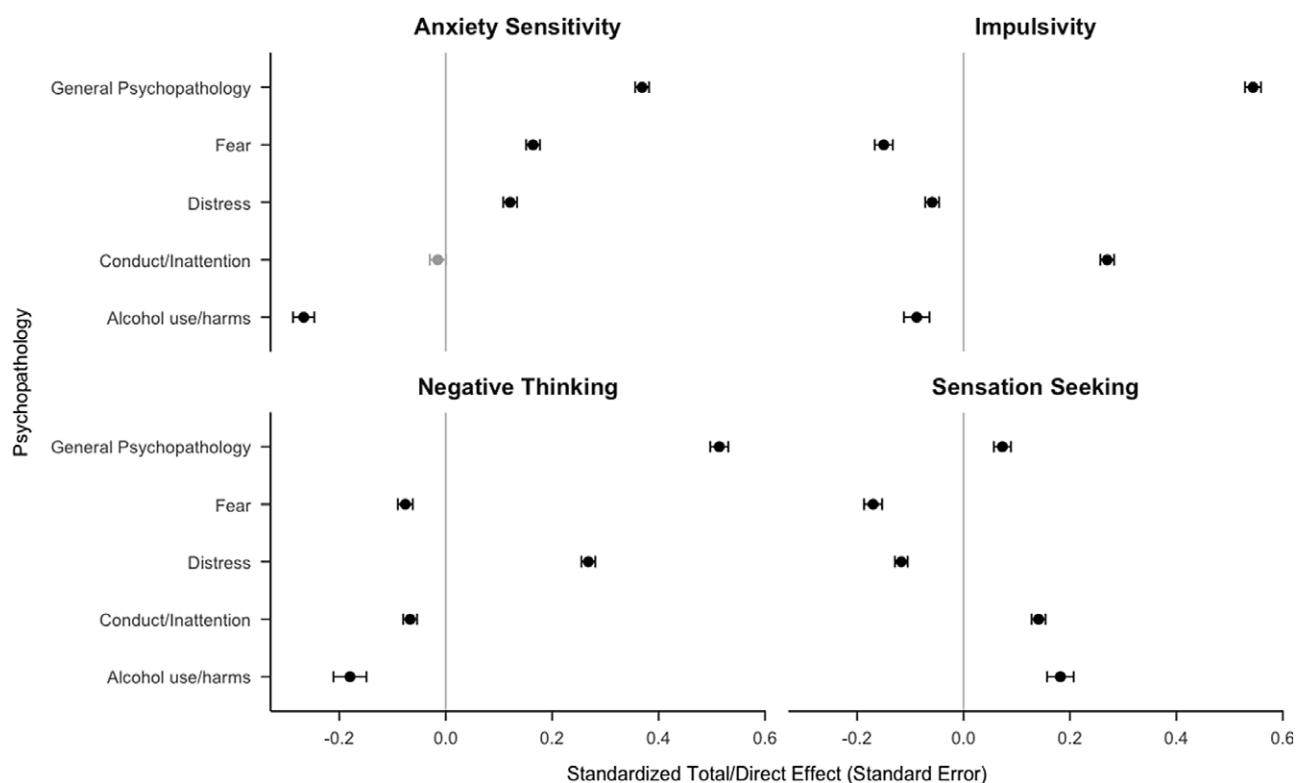
Figure 2. Effect sizes and standard errors for standardized direct effect of each personality trait on first-order psychopathology factors (fear, distress, conduct/inattention, and alcohol use/harms) and total effect on general psychopathology. Note. Significant effects ($p < 0.001$) shown in black, non-significant ($p > 0.001$) effect shown in gray. Vertical gray solid lines show 0.0 effect size.

variance accounted for by for general psychopathology (Table S3). There was also a significant negative direct effect of anxiety sensitivity with alcohol use/harms, which represents a change in direction from the total effect (i.e., the direct effect reversed in sign compared to the total effect). This may be due to a suppressor effect, and it is likely that the association between alcohol use/harms and anxiety sensitivity was accounted for by general psychopathology (Watson et al., 2013). The direct effect with conduct/inattention was not statistically significant, indicating general psychopathology also accounted for the association between anxiety sensitivity and conduct/inattention symptoms. Overall, these results indicate that the adolescents with greater levels of anxiety sensitivity had significantly higher fear and distress levels (but not alcohol use/harms or conduct/inattention) than adolescents with lower levels of anxiety sensitivity.

Symptom-level indirect-effects models revealed that 24 of 28 associations between symptoms and personality risk traits were accounted by higher-order factors (i.e., general psychopathology, and the specific dimension that the symptom is loaded on). For the remaining direct effects, between 53 and 79% of the variance a large proportion of variance accounted for by the higher-order factors. There were significant direct effects for anxiety sensitivity and "nervous in new situations" and "many fears" with small direct effects ($b = 0.139$ and 0.185, $p < 0.001$, respectively), over and above levels of fear and general psychopathology. Similarly, there was a significant and small direct effect for anxiety sensitivity with "worries," over and above levels of distress and general psychopathology ($b = 0.165$, $p < 0.001$). Finally, the direct effect between "easily distracted" and anxiety sensitivity had a small effect size ($b = 0.048$, $p < 0.001$), over and above conduct/inattention and

general psychopathology. All other symptom-level associations were either non-significant or the association was fully accounted for by the higher-order factors.

Negative thinking: Negative thinking, had a *positive* direct effect with distress, with only 50% of variance accounted for by general psychopathology ($b = 0.268$, $p < 0.001$; Table S4). There were *negative* direct effects of negative thinking with fear, conduct/inattention, and alcohol use/harms specific factors ($b = 0.076$, 0.067, 0.180, respectively, $ps < .001$), representing a reversal of their total effects, indicating that the association was accounted for by general psychopathology. Overall, this indicates that adolescents with greater levels of negative thinking had significantly higher distress levels (but not fear, alcohol use/harms or conduct/inattention) than adolescents with lower levels of negative thinking.

At the symptom level, the associations with 21 of 28 symptoms were accounted for by higher-order factors. Of the remaining symptoms, the effects were small and between 75 and 88% of the variance was accounted for by the higher-order factors. Notably, there were significant direct effects for negative thinking and "unhappy," "depressed," and "worthless" ($b = 0.095$, 0.063 and 0.063, $ps < 0.001$, respectively), over and above distress and general psychopathology. The remaining symptom-level associations were either non-significant or the association was fully accounted for by the higher-order factors.

Impulsivity: Impulsivity had a small, positive direct effect with conduct/inattention, with only 53% of variance accounted for by general psychopathology ($b = 0.270$, $p < 0.001$). There were negative direct effects with alcohol use/harms, distress, and fear, which represented a reversal of their total effects, indicating that the association was accounted for by general psychopathology
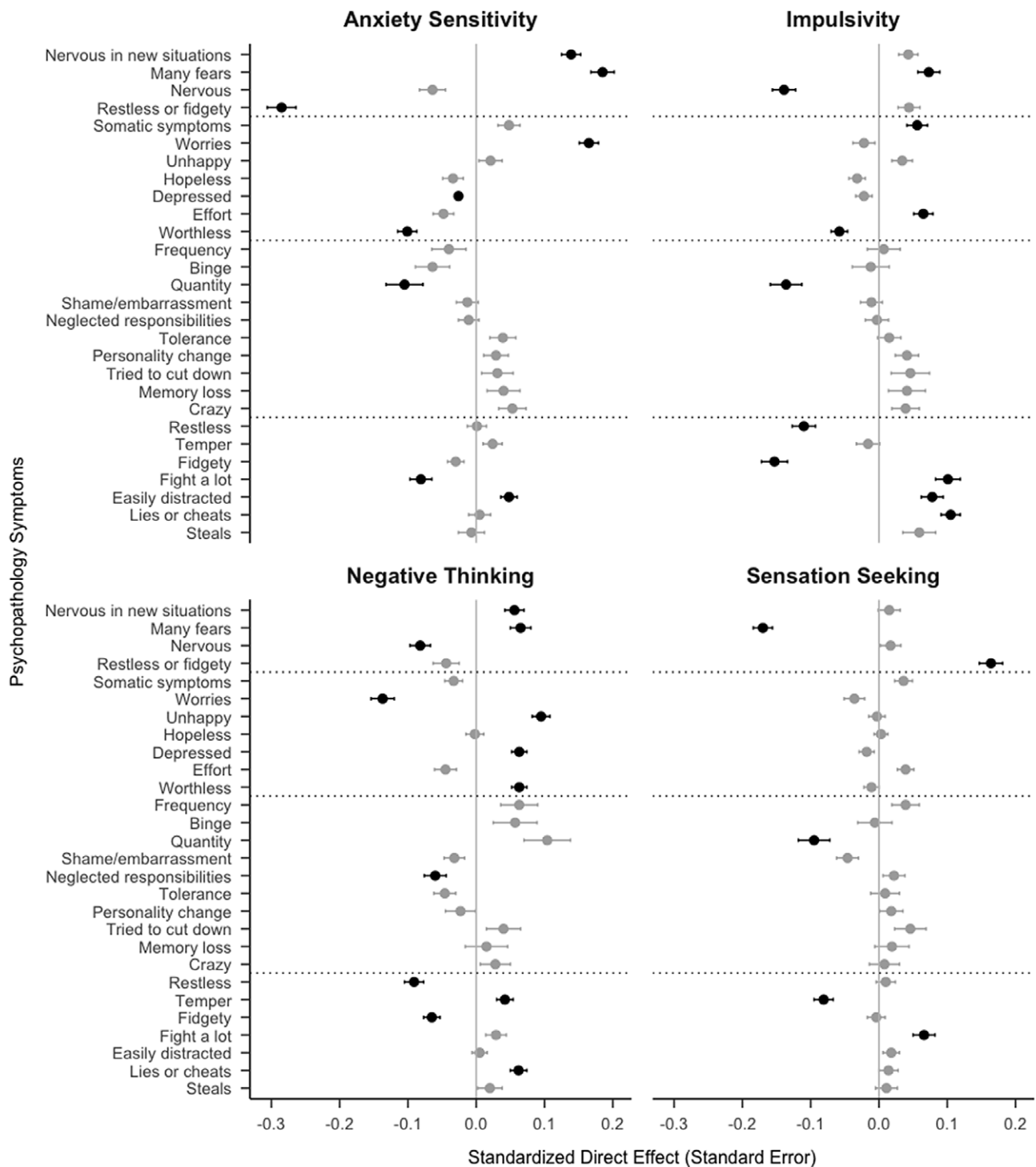
Figure 3. Effect sizes and standard errors for standardized direct effects of each personality profile on symptoms of psychopathology. Note. Significant effects (*p* < 0.001) shown in black, non-significant (*p* > 0.001) effect shown in gray. Black dotted lines mark boundaries between first-order factors, vertical gray solid lines show 0.0 effect size.

($b = −0.088, −0.059, −0.150, p < 0.001$). Overall, this indicates that adolescents with greater levels of impulsivity had significantly higher conduct/inattention levels (but not fear, distress, or alcohol use/harms) than adolescents with lower levels of impulsivity.

At the symptom level, the associations between impulsivity and 22 of 28 symptoms were accounted by the higher-order factors. The remaining direct effects were small, with a large proportion of variance accounted for by the higher-order factors (72 to 83%). Notably, there were significant, positive direct effects with the symptoms "fight a lot," "easily distracted" and "lies or cheats," over and above the conduct/inattention and general psychopathology factors ($b = 0.101, 0.078, 0.105, p < 0.001$, respectively). Direct effects with alcohol use/harms were either fully accounted for by general psychopathology or were not significant, suggesting that the effects of impulsivity with alcohol use/harms were accounted for by the higher-order factors.

Sensation seeking: Sensation seeking had small, positive direct effects with alcohol use/harms and conduct/inattention factors with only 10 and 13% of variance accounted for by general psychopathology, respectively ($b = 0.182$, 0.141, $ps < 0.001$, respectively, see Table S6). There were also small negative direct effects with distress and fear ($b = -0.117$, -0.170, $ps < 0.001$, respectively), and the association was mostly accounted for by general psychopathology (100 and 93%, respectively). Overall, this indicates that adolescents with greater levels of sensation seeking had significantly higher alcohol use/harms and conduct/inattention levels, and significantly lower levels of fear than adolescents with lower levels of impulsivity.

At the symptom level, the associations between sensation seeking and 26 of 28 indicators of psychopathology were accounted for by the higher-order factors. There was a small negative direct effect with "many fears" ($b = -0.170$, $p < 0.001$), and a small positive direct effect with "fight a lot" ($b = 0.066$, $p < 0.001$).

Discussion

The current study extends prior work on the underlying structure of psychopathology by using a symptom-level approach and more rigorous methods of assessing the structural validity, reliability, and replicability of different statistical models. Our results align with previous research on the structure of psychopathology in adolescents and extend this work by illuminating important patterns of association with four high-risk personality traits that have implications for the development of targeted prevention and early intervention programs and our understanding of the underlying structure of psychopathology.

High-risk personality traits and psychopathology

Overall, the results indicate that personality measures could be used to identify adolescents at risk of developing general psychopathology, as well as certain specific forms of psychopathology. Findings showed that all four personality traits were associated with general and specific dimensions of psychopathology in theoretically expected ways and consistent with previous research. Consistent with the four-factor model of vulnerability, our results broadly indicated that inhibited traits (i.e., negative thinking and anxiety sensitivity) were more closely related to internalizing forms of psychopathology (i.e., fear and distress), and disinhibited traits (i.e., impulsivity and sensation seeking) were associated with externalizing forms of psychopathology (i.e., alcohol use/harms and conduct/inattention (Castellanos-Ryan & Conrod, 2012). These findings also align with prior research with young people indicating that neuroticism is positively associated with fear, distress and broad externalizing dimensions (Watts et al., 2019), and that different facets of neuroticism are differentially related to internalizing and externalizing dimensions (Brandes et al., 2019).

Given that associations between each of the four personality traits and substance use are well-established, we anticipated that there would be positive associations with the alcohol use/harm factor. However, we found that only sensation seeking was positively associated with alcohol use/harms above and beyond general psychopathology in our sample. Because most research has typically focused on a broad externalizing factor and sensation seeking (Carragher et al., 2016; Castellanos-Ryan et al., 2016), our results are consistent with only one other study which reported on a bifactor model comprised of a general externalizing factor and a substance use and conduct specific factor. Castellanos-Ryan and Conrod (2011) found that sensation seeking was uniquely linked

with substance use and that impulsivity was related to the specific conduct factor (along with general externalizing). This suggests that impulsivity may be related to broader externalizing (i.e., the overlap between substance use and conduct/antisocial problems) and may also have unique links to conduct/behavioral problems, whereas sensation seeking may be more specifically related to substance misuse.

Consistent with previous research, we found that anxiety sensitivity was related to the internalizing dimensions of fear and distress (Carragher et al., 2016; Castellanos-Ryan et al., 2016). However, we also found that anxiety sensitivity was related to lower alcohol use/harms after accounting for general psychopathology. Although this finding was unexpected, literature on the association between anxiety and alcohol use provides important context for interpreting our results. A recent systematic review revealed inconsistent findings for the association between alcohol use and anxiety (Dyer et al., 2019), and general population research has shown that anxiety may not increase alcohol use until after age 14 (Birrell et al., 2015). This is consistent with longitudinal research that has found dynamic associations among anxiety symptoms and alcohol use in early adolescence (Pardee et al., 2014). Specifically, young adolescents with higher initial levels of anxiety demonstrated more rapid increases in alcohol use, compared to peers with low or declining anxiety symptoms. In contrast, there was evidence to suggest that social anxiety specifically had protective effects in early adolescence before later increasing risk for substance misuse.

Within the present study, our finding that greater anxiety sensitivity was related to lower alcohol use/harms may mean that anxiety sensitivity does not have a meaningful unique association with alcohol use/harms, and that the association is better explained by general psychopathology. Alternatively, anxiety sensitivity may protect against alcohol-related harms in early adolescence or delay the onset/escalation of alcohol use until later in adolescence. For example, as the alcohol use/harms factor in the present study is more heavily defined by alcohol-related harms, it is possible that anxiety sensitivity is protective against experiencing alcohol-related harms within this age group. Indeed, at the symptom level we found that anxiety sensitivity, impulsivity and (to a lesser extent) sensation seeking generally had negative direct effects with alcohol use items (i.e., frequency, binge, and quantity), but positive direct effects with most of the alcohol harm items. Furthermore, given that in the present sample the prevalence of alcohol use and related harms was relatively low (which is expected given the mean age was 13 years), it is possible that anxiety sensitivity may delay the onset of alcohol use or slow the escalation of alcohol consumption until later in adolescence. For example, it is possible that once individuals with high anxiety sensitivity have experienced the stress dampening effects of alcohol, their association with alcohol may change such that anxiety sensitivity leads to greater alcohol use (Stapinski et al., 2015). Ultimately, longitudinal research is needed to further unpack the association between anxiety sensitivity, alcohol use, and psychopathology more broadly within the hierarchical-dimensional model of psychopathology.

As expected, negative thinking was associated with greater general psychopathology. Negative thinking was also directly related to distress, whereas associations with fear, alcohol use/harms and conduct/inattention were accounted for by general psychopathology. This suggests that negative thinking may be a broader risk factor for psychopathology and that interventions targeting negative thinking may result in reductions in a wide range of psychiatric symptoms. This is consistent with other research linking related traits, such as neuroticism, emotion regulation and dysregulation,

to general psychopathology (Brandes et al., 2019; Haltigan et al., 2018; Santens et al., 2020). Indeed, it has even been suggested that general psychopathology reflects emotional/behavioral dysregulation broadly, and maps closely with trait neuroticism. Examination of the intersection between neurotic/inhibited traits and psychopathology over the adolescent period would be a valuable avenue for future research.

In the present study, the general psychopathology factor was more heavily defined by fear and distress dimensions, which complicates the conclusions that could be drawn from the associations between symptom dimensions and the personality traits. However, this is consistent with other studies of general psychopathology among adolescents which have shown that general psychopathology is typically defined by either thought disorder or internalizing dimensions, depending on the symptom domains included in the model (Gomez et al., 2019; Watts et al., 2020). Current knowledge of the onset and temporal sequencing of internalizing and externalizing problems during adolescence suggest that it would be reasonable for a general psychopathology factor to be more reflective of internalizing problems in early adolescence, as seen in the present study, compared to later adolescence (Birrell et al., 2015; Slade et al., 2015; Solmi et al., 2021).

Clinical and classification implications

Our findings have important implications for research on the early detection and prevention of mental and substance use disorders. Adolescents characterized by a fear of anxiety-related sensations (anxiety sensitivity); a sense of hopelessness or low positive affect (negative thinking); difficulties regulating behavioral responses (impulsivity); and/or a desire for novel experiences (sensation seeking) may be at greater risk for developing a wide range of psychiatric problems. Individuals with higher levels of fear or distress may benefit most from receiving interventions targeting anxiety sensitivity and negative thinking; and adolescents with greater levels of alcohol misuse/harms or conduct/inattention problems may benefit from interventions targeting impulsivity and sensation seeking. Indeed, this assumption is corroborated by prior research demonstrating the effectiveness of a personality-targeted prevention program reducing substance use and co-occurring emotional problems by addressing these specific personality traits (Lammers et al., 2017; Newton et al., 2020; O'Leary-Barrett et al., 2013). However, further research is needed to determine whether these effects hold when examining substance use and mental health outcomes with a hierarchical-dimensional framework.

From a classification perspective, our findings support the utility of conceptualizing psychopathology in a hierarchical-dimensional framework and align with prior research on the structure of psychopathology among adolescents. We found evidence for a higher-order model of psychopathology comprised of a general psychopathology dimension, and four specific dimensions: fear, distress, alcohol use/harms and conduct/inattention. While most previous research has selected a bifactor model of psychopathology, when considering model reliability and replicability along with traditional fit indices we found that a higher-order model fit the data best. Although this differs from past research, it is consistent with other more recent studies on hierarchical-dimensional models of psychopathology that have considered additional metrics of model reliability and replicability, underscoring the importance of assessing these indices in future research (Lees et al., 2020; Sunderland et al., 2020). Further, the four specific factors are consistent with prior research indicating that internalizing may be

comprised of fear and distress specific sub-dimensions and externalizing may be comprised of substance misuse and conduct/behavioral sub-dimensions factors (Blanco et al., 2015; Levin-Aspenson et al., 2019; Platt et al., 2017; Slade & Watson, 2006). Further studies are needed, particularly longitudinal research, to confirm the validity and reliability of this underlying structure.

Limitations and future directions

There are some limitations that should be considered when interpreting our findings. Importantly, the present study is cross-sectional and cannot determine causality between personality and psychopathology and the generalizability of our findings are limited by the use of a non-representative community sample of Australian adolescents. Self-reported alcohol use/harms and conduct/inattention problems can be affected by self-report biases among, for example, children and young adults with attention-deficit/hyperactivity disorder and young adults following treatment (Hoza et al., 2012; Nirenberg et al., 2013; Sodano et al., 2021). Although the self-reported psychopathology outcomes did not have corroborating information, such as parent or teacher reports, data were collected using structured and validated instruments. Within this context, self-report methods have been shown to be a valid and reliable approach to measuring substance use and mental health outcomes in adolescents (Smith et al., 1995; Smith, 2007; van der Ende et al., 2020). In addition, although our study incorporated a wide variety of mental health symptoms, there are some notable forms of psychopathology that were not included. We were unable include psychosis-related symptoms, for example, as these were only assessed in one the cohorts, and other common youth-onset disorders such as obsessive-compulsive disorder and eating pathology were not assessed. It is also worth noting that six of the seven items in the negative thinking subscale were worded positively (e.g., "I am happy," "I am very enthusiastic about my future") and then reverse-scored. As such, this subscale may be more reflective of low positive thinking, rather than a direct measure of negative thinking. This is akin to evidence that negative and positive affect are independent dimensions, rather than opposite poles of a single dimension (Curran et al., 2014; Jovanović & Gavrilov-Jerković, 2016; Watson & Tellegen, 1985). Ultimately, as this study was a secondary analysis of data from two randomized controlled trial cohorts our data were limited to what was available. Additional evidence using more extensive and robust measures would be of value. Furthermore, longitudinal studies with greater coverage of psychiatric disorders may provide more comprehensive insight into the underlying structure of psychopathology and personality-based causal pathways.

Another potential limitation of this study concerns some of the observed differential patterns of association at the symptom level (i.e., symptom-level negative direct effects, but positive total/higher-order effects), which could reflect potential measurement error or model misspecification. For example, the "restless & fidgety" item from the K6 and the observed negative association with anxiety sensitivity and positive association with sensation seeking (positive direct effect) suggests this item could reasonably serve as an indicator of internalizing/distress or externalizing/conduct/inattention. As such, an individual's interpretation of the question may influence whether "restless & fidgety" is an indicator of distress or conduct/inattention. Similarly, the unique positive association between anxiety sensitivity and "worries" (and negative association with negative thinking), may suggest that "worries" would be a more appropriate indicator for fear rather than distress.

It is also possible that the symptom-level effects may reflect nuances in our sample. Thus, further longitudinal research is needed to confirm the reliability of these effects and clarify the placement of these potentially cross-cutting symptoms.

Conclusions

Although there is extensive evidence linking personality with psychopathology, much of the research has failed to take into account the empirical structure of psychopathology. Findings from the present study describe the complex links between four high-risk personality traits and their associations with a hierarchical-dimensional framework of psychopathology in a large sample of early adolescents. The results support the four-factor model of vulnerability as a useful tool for identifying adolescents at risk of experiencing psychopathology and provide useful information for the development and optimization of prevention and early intervention programs. Consistent with prior research, the present study indicates that a tendency toward low positive affectivity (negative thinking), a fear of anxiety-related sensations (anxiety sensitivity); difficulties regulating behavioral responses (impulsivity) and/or a desire for novel experiences (sensation seeking) may be associated with a greater risk for developing mental health problems. Although further longitudinal research is needed to better understand the complex interactions between personality and psychopathology, the present study highlights the importance of symptom-level analyses in delineating personality-related risk for psychopathology and the role personality may play in the development of individual symptoms through to broad dimensions of psychopathology. More broadly, the findings contribute to the ongoing the debate surrounding the structure and classification of adolescent psychopathology.

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Appendix E

Supplementary materials for Chapter 2

The supplementary materials for Chapter 2 are best viewed as a spreadsheet due to the size of some of the tables. This spreadsheet can be accessed via the original publication, and a download link and description of the of materials contained in the file are provided below.

Download: [Download spreadsheet](#) (84KB)

Supplementary material includes search strings (Appendix A), quality assessment for included studies (Appendix B and C), model details (Appendix D), summary of findings (Appendix E) and detailed findings (Appendix F).

Appendix F

Supplementary materials for Chapter 3

Table S1 Symptom description, proportions and counts

Item ID	Item / description	Values	Value Labels	CAP %	CAP n	CSC %	CSC n	ALL %	ALL n
T1_SD2	I am restless. I cannot stay still for long.	0	Not true	36.4%	591	53.0%	3143	49.5%	3734
T1_SD2		1	Somewhat true or Certainly true	63.6%	1034	47.0%	2783	50.5%	3817
T1_SD3	I get a lot of headaches, stomach-aches, or sickness.	0	Not true	61.2%	994	66.5%	3938	65.3%	4932
T1_SD3		1	Somewhat true or Certainly true	38.8%	631	33.5%	1987	34.7%	2618
T1_SD5	I get very angry and often lose my temper.	0	Not true	52.0%	845	63.2%	3741	60.8%	4586
T1_SD5		1	Somewhat true or Certainly true	48.0%	780	36.8%	2180	39.2%	2960
T1_SD6	I am usually on my own. I generally play alone or keep to myself.	0	Not true	74.8%	1215	71.7%	4246	72.4%	5461
T1_SD6		1	Somewhat true or Certainly true	25.2%	410	28.3%	1675	27.6%	2085
T1_SD8	I worry a lot.	0	Not true	44.7%	726	57.9%	3424	55.1%	4150
T1_SD8		1	Somewhat true or Certainly true	55.3%	899	42.1%	2488	44.9%	3387
T1_SD10	I am constantly fidgeting or squirming.	0	Not true	57.8%	940	64.4%	3806	63.0%	4746
T1_SD10		1	Somewhat true or Certainly true	42.2%	685	35.6%	2106	37.0%	2791
T1_SD12	I fight a lot. I can make other people do what I want.	0	Not true	79.1%	1285	83.8%	4956	82.8%	6241
T1_SD12		1	Somewhat true or Certainly true	20.9%	340	16.2%	957	17.2%	1297
T1_SD13	I am often unhappy, down-hearted, or tearful.	0	Not true	74.8%	1216	76.1%	4498	75.8%	5714
T1_SD13		1	Somewhat true or Certainly true	25.2%	409	23.9%	1415	24.2%	1824
T1_SD15	I am easily distracted. I find it difficult to concentrate.	0	Not true	39.6%	643	45.8%	2707	44.4%	3350
T1_SD15		1	Somewhat true or Certainly true	60.4%	982	54.2%	3207	55.6%	4189
T1_SD16	I am nervous in new situations. I easily lose confidence.	0	Not true	38.2%	620	45.8%	2709	44.2%	3329
T1_SD16		1	Somewhat true or Certainly true	61.8%	1005	54.2%	3206	55.8%	4211
T1_SD18	I am often accused of lying or cheating.	0	Not true	65.7%	1067	71.3%	4208	70.1%	5275
T1_SD18		1	Somewhat true or Certainly true	34.3%	558	28.7%	1697	29.9%	2255
T1_SD19	Often children or young people pick on me or bully me.	0	Not true	81.5%	1324	82.6%	4880	82.4%	6204
T1_SD19		1	Somewhat true or Certainly true	18.5%	301	17.4%	1028	17.6%	1329
T1_SD23	I get on better with adults than with people my own age.	0	Not true	63.3%	1029	58.4%	3448	59.5%	4477
T1_SD23		1	Somewhat true or Certainly true	36.7%	596	41.6%	2452	40.5%	3048
T1_SD24	I have many fears. I am easily scared.	0	Not true	59.4%	965	63.5%	3750	62.6%	4715

Item ID	Item / description	Values	Value Labels	CAP		CSC		ALL	
				%	n	%	n	%	n
T1_SD24		1	Somewhat true or Certainly true	40.6%	660	36.5%	2159	37.4%	2819
T1_SD22	I take things that are not mine from home, school or elsewhere.	0	Not true	82.5%	1341	87.5%	4239	86.3%	5580
T1_SD22		1	Somewhat true or Certainly true	17.5%	284	12.5%	604	13.7%	888
T1_AUC1	How often did you have a std alcoholic drink of any kind in the past 6 mths?	0	Never or less than monthly	98.3%	2222	97.0%	2869	97.6%	5091
T1_AUC1		1	Once a month, 2-3 times a month, Weekly, Daily or almost daily	1.7%	38	3.0%	88	2.4%	126
T1_AUC2	How often do you have 5+ std drinks in the past 6 mths?	0	Never or less than monthly	98.3%	2221	97.8%	2518	98.0%	4739
T1_AUC2		1	Once a month, 2-3 times a month, Weekly, Daily or almost daily	1.7%	39	2.2%	56	2.0%	95
T1_AUC3	In the past 6 mths, how many std drinks on a typical day?	0	None or 1-2	98.6%	2229	98.1%	2901	98.4%	5130
T1_AUC3		1	3-4, 5-6,7-9, 10+	1.4%	31	1.9%	55	1.6%	86
In the past 6 months how many times have you experienced the following as a consequence of drinking alcohol									
T1_AH1	Got into fights, acted bad, or did mean things.	0	Never	56.6%	1275	90.6%	5710	81.6%	6985
T1_AH1		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	43.4%	979	9.4%	592	18.4%	1571
T1_AH2	Caused shame or embarrassment to someone.	0	Never	59.7%	1345	92.4%	5821	83.7%	7166
T1_AH2		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	40.3%	909	7.6%	482	16.3%	1391
T1_AH3	Neglected my responsibilities.	0	Never	56.9%	1282	92.8%	5844	83.3%	7126
T1_AH3		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	43.1%	972	7.2%	455	16.7%	1427
T1_AH4	Felt that I need more alcohol than I used to in order to get the same effect.	0	Never	51.0%	1150	92.3%	5815	81.4%	6965
T1_AH4		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	49.0%	1104	7.7%	487	18.6%	1591
T1_AH5	Noticed a change in my personality.	0	Never	78.5%	1769	96.8%	6100	92.0%	7869
T1_AH5		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	21.5%	485	3.2%	202	8.0%	687
T1_AH6	Tried to cut down or quit drinking.	0	Never	96.6%	2177	98.3%	6199	97.9%	8376
T1_AH6		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	3.4%	77	1.7%	104	2.1%	181
T1_AH7	Suddenly found myself in a place that I could not remember getting to.	0	Never	96.0%	2163	98.2%	6184	97.6%	8347
T1_AH7		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	4.0%	91	1.8%	113	2.4%	204
T1_AH8	Felt I was going crazy.	0	Never	82.7%	1863	95.6%	6025	92.2%	7888
T1_AH8		1	1-2 times, 3-4 times, 5+6 times, More than 6 times	17.3%	391	4.4%	276	7.8%	667
In the last 4 weeks, about how often did you feel									
T1_K61R	…nervous?	0	None of the time	19.3%	422	17.1%	1046	17.7%	1468
T1_K61R		1	A little of the time, some of the time, most of the time, all of the time	80.7%	1761	82.9%	5075	82.3%	6836
T1_K62R	… hopeless?	0	None of the time	49.4%	1079	51.5%	3152	51.0%	4231

Item ID	Item / description	Values	Value Labels	CAP		CSC		ALL	
				%	n	%	n	%	n
T1_K62R		1	A little of the time, some of the time, most of the time, all of the time	50.6%	1104	48.5%	2964	49.0%	4068
T1_K63R	… restless or fidgety?	0	None of the time	29.9%	653	28.2%	1722	28.7%	2375
T1_K63R		1	A little of the time, some of the time, most of the time, all of the time	70.1%	1529	71.8%	4384	71.3%	5913
T1_K64R	… so depressed that nothing could cheer you up?	0	None of the time	66.6%	1453	68.7%	4200	68.1%	5653
T1_K64R		1	A little of the time, some of the time, most of the time, all of the time	33.4%	730	31.3%	1912	31.9%	2642
T1_K65R	… that everything was an effort?	0	None of the time	33.1%	722	35.6%	2177	35.0%	2899
T1_K65R		1	A little of the time, some of the time, most of the time, all of the time	66.9%	1461	64.4%	3930	65.0%	5391
T1_K66R	… worthless?	0	None of the time	64.9%	1416	64.2%	3919	64.3%	5335
T1_K66R		1	A little of the time, some of the time, most of the time, all of the time	35.1%	767	35.8%	2190	35.7%	2957

Note. SD = items from Strengths and Difficulties Questionnaire; AH = Alcohol Harms, items from Rutgers Alcohol Problem Index (RAPI); K6 = Kessler 6 Plus scale (K6+); AUC = Alcohol use, AUDIT-C items. AH items prefaced with "In the past 6 months how many times have you experienced the following as a consequence of drinking alcohol". K6 items prefaced with "In the last 4 weeks, about how often did you feel"

Table S2 Correlation matrix for symptoms of psychopathology

	SD16	SD24	K61R	K63R	SD3	SD8	SD13	K62R	K64R	K65R	K66R	AUC1	AUC2	AUC3	AH1	AH2	AH3	AH4	AH5	AH6	AH7	AH8	SD2	SD5	SD10	SD12	SD15	SD18	SD22
SD16	1.000																												
SD24	0.552	1.000																											
K61R	0.370	0.268	1.000																										
K63R	0.283	0.235	0.578	1.000																									
SD3	0.414	0.429	0.264	0.297	1.000																								
SD8	0.586	0.546	0.419	0.332	0.507	1.000																							
SD13	0.527	0.542	0.250	0.316	0.572	0.659	1.000																						
K62R	0.435	0.397	0.580	0.513	0.396	0.529	0.610	1.000																					
K64R	0.383	0.384	0.440	0.425	0.474	0.504	0.693	0.734	1.000																				
K65R	0.312	0.267	0.490	0.544	0.325	0.344	0.405	0.562	0.570	1.000																			
K66R	0.426	0.392	0.482	0.464	0.422	0.514	0.689	0.822	0.799	0.578	1.000																		
AUC1	0.012	-0.070	-0.010	0.086	0.192	0.090	0.226	0.120	0.287	0.089	0.188	1.000																	
AUC2	-0.070	-0.030	-0.066	0.136	0.184	0.022	0.236	0.107	0.292	0.083	0.222	0.908	1.000																
AUC3	-0.102	-0.085	0.058	0.181	0.213	-0.014	0.243	0.194	0.356	0.191	0.309	0.797	0.898	1.000															
AH1	0.101	0.046	0.022	0.080	0.208	0.083	0.225	0.141	0.216	0.146	0.185	0.675	0.728	0.705	1.000														
AH2	0.112	0.095	0.037	0.112	0.242	0.124	0.268	0.133	0.227	0.201	0.205	0.648	0.762	0.681	0.937	1.000													
AH3	0.106	0.051	0.058	0.120	0.191	0.095	0.231	0.155	0.229	0.172	0.204	0.602	0.703	0.670	0.925	0.924	1.000												
AH4	0.184	0.113	0.146	0.139	0.280	0.203	0.288	0.214	0.292	0.222	0.272	0.675	0.712	0.622	0.881	0.894	0.882	1.000											
AH5	0.097	0.115	0.036	0.139	0.304	0.168	0.271	0.187	0.299	0.158	0.210	0.695	0.771	0.713	0.870	0.872	0.871	0.886	1.000										
AH6	0.162	0.138	-0.005	0.097	0.302	0.224	0.366	0.176	0.251	0.121	0.252	0.738	0.818	0.728	0.775	0.771	0.775	0.796	0.831	1.000									
AH7	0.168	0.094	0.016	0.090	0.255	0.165	0.331	0.191	0.295	0.142	0.282	0.650	0.738	0.648	0.747	0.750	0.723	0.801	0.804	0.850	1.000								
AH8	0.165	0.181	0.110	0.232	0.296	0.205	0.377	0.303	0.384	0.240	0.353	0.611	0.744	0.637	0.808	0.838	0.830	0.894	0.845	0.782	0.766	1.000							
SD2	0.323	0.290	0.167	0.453	0.369	0.369	0.378	0.277	0.288	0.305	0.299	0.189	0.134	0.079	0.195	0.194	0.202	0.227	0.246	0.261	0.193	0.298	1.000						
SD5	0.387	0.360	0.183	0.304	0.423	0.409	0.528	0.358	0.412	0.328	0.392	0.176	0.214	0.223	0.266	0.251	0.213	0.274	0.228	0.307	0.261	0.312	0.423	1.000					
SD10	0.361	0.328	0.156	0.486	0.401	0.415	0.458	0.318	0.340	0.304	0.353	0.244	0.160	0.159	0.199	0.221	0.202	0.237	0.231	0.286	0.286	0.328	0.764	0.437	1.000				
SD12	0.268	0.259	0.023	0.198	0.343	0.300	0.459	0.217	0.295	0.230	0.273	0.404	0.417	0.255	0.340	0.346	0.305	0.337	0.361	0.484	0.399	0.379	0.424	0.558	0.459	1.000			
SD15	0.450	0.375	0.175	0.355	0.402	0.373	0.439	0.348	0.344	0.360	0.376	0.127	0.166	0.051	0.259	0.233	0.257	0.295	0.249	0.263	0.255	0.320	0.568	0.458	0.583	0.425	1.000		
SD18	0.324	0.298	0.084	0.253	0.344	0.288	0.464	0.291	0.356	0.278	0.329	0.240	0.326	0.271	0.315	0.336	0.302	0.344	0.386	0.334	0.339	0.352	0.367	0.476	0.423	0.506	0.454	1.000	

	SD16	SD24	K61R	K63R	SD3	SD8	SD13	K62R	K64R	K65R	K66R	AUC1	AUC2	AUC3	AH1	AH2	AH3	AH4	AH5	AH6	AH7	AH8	SD2	SD5	SD10	SD12	SD15	SD18	SD22
SD22	0.309	0.348	0.002	0.105	0.342	0.270	0.463	0.189	0.259	0.213	0.221	0.300	0.351	0.286	0.357	0.393	0.341	0.334	0.457	0.462	0.440	0.434	0.358	0.394	0.409	0.593	0.407	0.560	1.000

Table S3 Estimates for latent variable indirect effects models for anxiety sensitivity

	Total Effect			Direct Effect			% accounted for by higher order factor(s)
Symptoms	**b**	**se**	**p**	**b**	**se**	**p**	
Nervous in new situations	0.366	0.010	0.000	0.139	0.014	0.000	**62%**
Many fears	0.393	0.014	0.000	0.185	0.017	0.000	**53%**
Nervous	0.189	0.016	0.000	-0.064	0.019	0.001	100%
Restless or fidgety	0.127	0.014	0.000	-0.285	0.021	0.000	100%
Somatic symptoms	0.262	0.015	0.000	0.048	0.016	0.002	82%
Worries	0.368	0.012	0.000	0.165	0.014	0.000	**55%**
Unhappy	0.312	0.017	0.000	0.021	0.017	0.234	93%
Hopeless	0.265	0.016	0.000	-0.034	0.015	0.022	100%
Depressed	0.082	0.005	0.000	-0.026	0.004	0.000	100%
Effort	0.191	0.016	0.000	-0.048	0.015	0.001	100%
Worthless	0.242	0.015	0.000	-0.101	0.014	0.000	100%
Frequency	0.023	0.028	0.416	-0.040	0.025	0.115	100%
Binge	0.009	0.031	0.774	-0.064	0.025	0.011	100%
Quantity	-0.037	0.030	0.221	-0.105	0.027	0.000	100%
Shame/embarrassment	0.061	0.020	0.003	-0.013	0.016	0.417	100%
Neglected responsibilities	0.059	0.020	0.003	-0.011	0.015	0.448	100%
Tolerance	0.105	0.023	0.000	0.039	0.019	0.042	63%
Personality change	0.096	0.025	0.000	0.029	0.018	0.117	70%
Tried to cut down	0.095	0.029	0.001	0.031	0.023	0.167	67%
Memory loss	0.102	0.028	0.000	0.040	0.024	0.097	61%
Crazy	0.119	0.027	0.000	0.053	0.020	0.007	55%
Restless	0.196	0.013	0.000	0.001	0.014	0.964	99%
Temper	0.209	0.013	0.000	0.024	0.014	0.095	89%
Fidgety	0.190	0.015	0.000	-0.030	0.012	0.018	100%
Fight a lot	0.111	0.019	0.000	-0.081	0.016	0.000	100%
Easily distracted	0.229	0.013	0.000	0.048	0.012	0.000	**79%**

Symptoms	Total Effect			Direct Effect			% accounted for by higher order factor(s)
	b	se	p	b	se	p	
Lies or cheats	0.185	0.017	0.000	0.005	0.016	0.736	97%
Steals	0.169	0.021	0.000	-0.007	0.019	0.730	100%
First-order factors							
Alcohol use	0.077	0.020	0.000	-0.267	0.020	0.000	100%
Conduct/Inattention	0.263	0.014	0.000	-0.015	0.015	0.297	100%
Distress	0.347	0.013	0.000	0.121	0.013	0.000	**65%**
Fear	0.392	0.011	0.000	0.164	0.013	0.000	**58%**
Second-order factor							
General psychopathology	0.369	0.013	0.000	-	-	-	-

Notes. Percentages accounted for by higher order factor(s) in bold indicate meaningful direct effects (ie. Statistically significant, percentage below 100% and no evidence of suppression effect).

Table S4 Estimates for latent variable indirect effects models for negative thinking

Symptoms	b	Total Effect		b	Direct Effect		% accounted for by higher order factor(s)
		se	p		se	p	
Nervous in new situations		0.274	0.015	0.000	0.056	0.014	0.000	**80%**
Many fears		0.256	0.016	0.000	0.065	0.015	0.000	**75%**
Nervous		0.147	0.016	0.000	-0.082	0.015	0.000	100%
Restless or fidgety		0.211	0.016	0.000	-0.044	0.019	0.019	100%
Somatic symptoms		0.322	0.015	0.000	-0.033	0.013	0.013	100%
Worries		0.300	0.017	0.000	-0.137	0.017	0.000	100%
Unhappy		0.508	0.015	0.000	0.095	0.013	0.000	**81%**
Hopeless		0.448	0.014	0.000	-0.002	0.013	0.861	100%
Depressed		0.490	0.015	0.000	0.063	0.011	0.000	**87%**
Effort		0.329	0.015	0.000	-0.045	0.016	0.005	100%
Worthless		0.511	0.014	0.000	0.063	0.011	0.000	**88%**
Frequency		0.251	0.028	0.000	0.063	0.027	0.020	75%
Binge		0.276	0.033	0.000	0.057	0.032	0.074	79%
Quantity		0.289	0.030	0.000	0.104	0.034	0.003	64%
Shame/embarrassment		0.212	0.023	0.000	-0.032	0.015	0.034	100%
Neglected responsibilities		0.185	0.021	0.000	-0.060	0.016	0.000	100%
Tolerance		0.203	0.024	0.000	-0.046	0.016	0.005	100%
Personality change		0.216	0.030	0.000	-0.023	0.022	0.302	100%
Tried to cut down		0.255	0.028	0.000	0.040	0.025	0.104	84%
Memory loss		0.228	0.038	0.000	0.015	0.031	0.639	93%
Crazy		0.260	0.027	0.000	0.028	0.022	0.215	89%
Restless		0.191	0.019	0.000	-0.091	0.014	0.000	100%
Temper		0.274	0.015	0.000	0.042	0.012	0.000	**85%**
Fidgety		0.231	0.016	0.000	-0.065	0.012	0.000	100%
Fight a lot		0.249	0.016	0.000	0.029	0.015	0.048	88%

Easily distracted	0.254	0.017	0.000	0.005	0.011	0.642	98%
Lies or cheats	0.276	0.015	0.000	0.062	0.012	0.000	**78%**
Steals	0.237	0.018	0.000	0.020	0.018	0.263	92%
First-order factors							
Alcohol use	0.258	0.021	0.000	-0.180	0.031	0.000	100%
Conduct/Inattention	0.340	0.018	0.000	-0.067	0.013	0.000	100%
Distress	0.538	0.016	0.000	0.268	0.013	0.000	**50%**
Fear	0.319	0.018	0.000	-0.076	0.014	0.000	100%
Second-order factor							
General psychopathology	0.514	0.017	0.000				

Notes. Percentages accounted for by higher order factor(s) in bold indicate meaningful direct effects (ie. Statistically significant, percentage below 100% and no evidence of suppression effect).

Table S5 Estimates for latent variable indirect effects models for impulsivity

Symptoms	b	Total Effect se	p	b	Direct Effect se	p	% accounted for by higher order factor(s)
Nervous in new situations		0.256	0.015	0.000	0.043	0.014	0.002	83%
Many fears		0.253	0.014	0.000	0.073	0.016	0.000	**71%**
Nervous		0.103	0.013	0.000	-0.139	0.017	0.000	100%
Restless or fidgety		0.245	0.014	0.000	0.044	0.016	0.006	82%
Somatic symptoms		0.275	0.014	0.000	0.056	0.015	0.000	**80%**
Worries		0.244	0.014	0.000	-0.022	0.016	0.172	100%
Unhappy		0.336	0.016	0.000	0.034	0.015	0.021	90%
Hopeless		0.286	0.014	0.000	-0.032	0.012	0.009	100%
Depressed		0.298	0.016	0.000	-0.022	0.012	0.071	100%
Effort		0.289	0.015	0.000	0.065	0.014	0.000	**78%**
Worthless		0.291	0.017	0.000	-0.058	0.012	0.000	100%
Frequency		0.269	0.027	0.000	0.007	0.024	0.776	97%
Binge		0.294	0.032	0.000	-0.012	0.027	0.655	100%
Quantity		0.162	0.030	0.000	-0.136	0.023	0.000	100%
Shame/embarrassment		0.305	0.019	0.000	-0.011	0.016	0.483	100%
Neglected responsibilities		0.300	0.022	0.000	-0.003	0.017	0.840	100%
Tolerance		0.327	0.022	0.000	0.015	0.017	0.379	95%
Personality change		0.343	0.027	0.000	0.041	0.017	0.017	88%
Tried to cut down		0.330	0.037	0.000	0.046	0.028	0.099	86%
Memory loss		0.318	0.031	0.000	0.041	0.027	0.121	87%
Crazy		0.343	0.028	0.000	0.039	0.020	0.045	89%
Restless		0.374	0.013	0.000	-0.110	0.017	0.000	100%
Temper		0.402	0.014	0.000	-0.016	0.017	0.342	100%
Fidgety		0.377	0.017	0.000	-0.153	0.019	0.000	100%
Fight a lot		0.443	0.016	0.000	0.101	0.018	0.000	**77%**

Easily distracted	0.464	0.013	0.000	0.078	0.016	0.000	**83%**
Lies or cheats	0.447	0.013	0.000	0.105	0.014	0.000	**77%**
Steals	0.409	0.021	0.000	0.059	0.024	0.012	86%
First-order factors							
Alcohol use	0.341	0.023	0.000	-0.088	0.024	0.000	100%
Conduct/Inattention	0.572	0.013	0.000	0.270	0.013	0.000	**53%**
Distress	0.368	0.013	0.000	-0.059	0.013	0.000	100%
Fear	0.293	0.013	0.000	-0.150	0.017	0.000	100%
Second-order factor							
General psychopathology	0.544	0.015	0.000				

Notes. Percentages accounted for by higher order factor(s) in bold indicate meaningful direct effects (ie. Statistically significant, percentage below 100% and no evidence of suppression effect).

Table S6 Estimates for latent variable indirect effects models for sensation seeking

Symptoms	Total Effect			Direct Effect			Percentage accounted for by higher order factor(s)
	b	se	p	b	se	p	
Nervous in new situations	-0.057	0.018	0.001	0.015	0.016	0.356	100%
Many fears	-0.181	0.014	0.000	-0.170	0.014	0.000	**6%**
Nervous	-0.040	0.015	0.007	0.017	0.015	0.238	100%
Restless or fidgety	0.056	0.016	0.000	0.164	0.017	0.000	100%
Somatic symptoms	0.024	0.014	0.087	0.036	0.013	0.004	50%
Worries	-0.041	0.014	0.003	-0.036	0.015	0.016	12%
Unhappy	-0.014	0.015	0.337	-0.003	0.012	0.781	79%
Hopeless	-0.009	0.013	0.520	0.003	0.010	0.750	100%
Depressed	-0.027	0.014	0.065	-0.018	0.011	0.091	33%
Effort	0.027	0.015	0.080	0.039	0.012	0.002	44%
Worthless	-0.022	0.016	0.170	-0.011	0.011	0.316	50%
Frequency	0.189	0.023	0.000	0.039	0.020	0.048	79%
Binge	0.174	0.027	0.000	-0.006	0.025	0.817	100%
Quantity	0.074	0.028	0.008	-0.095	0.023	0.000	100%
Shame/embarrassment	0.148	0.026	0.000	-0.046	0.016	0.005	100%
Neglected responsibilities	0.197	0.027	0.000	0.022	0.016	0.176	89%
Tolerance	0.194	0.028	0.000	0.009	0.021	0.672	95%
Personality change	0.200	0.030	0.000	0.018	0.017	0.281	91%
Tried to cut down	0.215	0.032	0.000	0.046	0.023	0.043	79%
Memory loss	0.186	0.032	0.000	0.019	0.025	0.455	90%
Crazy	0.192	0.031	0.000	0.008	0.022	0.715	96%
Restless	0.128	0.016	0.000	0.010	0.014	0.474	92%
Temper	0.054	0.016	0.000	-0.081	0.014	0.000	100%
Fidgety	0.127	0.018	0.000	-0.004	0.013	0.770	100%
Fight a lot	0.167	0.020	0.000	0.066	0.016	0.000	**60%**

Easily distracted	0.134	0.016	0.000	0.018	0.012	0.138	87%
Lies or cheats	0.123	0.018	0.000	0.014	0.014	0.325	89%
Steals	0.116	0.020	0.000	0.011	0.016	0.499	91%
First-order factors							
Alcohol use	0.203	0.025	0.000	0.182	0.025	0.000	**10%**
Conduct/Inattention	0.162	0.018	0.000	0.141	0.013	0.000	**13%**
Distress	-0.013	0.013	0.288	-0.117	0.012	0.000	100%
Fear	-0.088	0.015	0.000	-0.170	0.017	0.000	**93%**
Second-order factor							
General psychopathology	0.073	0.016	0.000				

Notes. Percentages accounted for by higher order factor(s) in bold indicate meaningful direct effects (ie. Statistically significant, percentage below 100% and no evidence of suppression effect).

Table S7 Estimates for total effect estimates from the four correlated factor models

Personality	Psychopathology Latent Variable	b	se	p
Anxiety Sensitivity	Alcohol use	0.075	0.019	.000
Anxiety Sensitivity	Conduct/inattention	0.267	0.014	.000
Anxiety Sensitivity	Distress	0.351	0.013	.000
Anxiety Sensitivity	Fear	0.453	0.012	.000
Impulsivity	Alcohol use	0.331	0.022	.000
Impulsivity	Conduct/inattention	0.577	0.013	.000
Impulsivity	Distress	0.374	0.014	.000
Impulsivity	Fear	0.328	0.015	.000
Negative Thinking	Alcohol use	0.251	0.02	.000
Negative Thinking	Conduct/inattention	0.344	0.018	.000
Negative Thinking	Distress	0.553	0.016	.000
Negative Thinking	Fear	0.352	0.019	.000
Sensation Seeking	Alcohol use	0.195	0.024	.000
Sensation Seeking	Conduct/inattention	0.167	0.018	.000
Sensation Seeking	Distress	-0.014	0.013	.275
Sensation Seeking	Fear	-0.100	0.016	.000

Additional structural models of psychopathology

In addition to the models described in the main text, a further four models were examined. Specifically, we explored a modified bifactor model, where the specific factors were permitted to correlate, and three 'mid-tier' models featuring two general factors, one representing internalising and one representing externalising, and four specific factors fear, distress, alcohol use, and conduct/inattention. We estimated a 2-bifactor, 2-higher-order and modified 2-bifactor (where the general factors were permitted to correlate). Path diagrams for each of these models are shown in Figures S1 to S4. The goodness-of-fit indices, standardised factor loadings and inter-factor correlations can be found in Table S7 and S8, respectively. Reliability indices are presented in Table S9.

The structures examining internalising and externalising general factors were proposed based on the observation that the general psychopathology factors in the models described in the main text were more heavily defined by fear and distress, rather than conduct/inattention and alcohol use, suggesting that the data may be better represented by two general/higher-order factors. Ideally, we would have examined the external validity of one of these models, as well as the model reported on in the main text. However, the complexity if these models and associated computational demands led to difficulties with model convergence, making the stability of the estimates unreliable. Furthermore, we encountered identification issues when assessing measurement invariance across the cohorts. Altogether, these convergence and identification issues suggested that the data were not well represented by a model with two general/higher-order factors.

Table S8 Fit indices for additional models of adolescent psychopathology (n=8,589)

Model	No. of parameters	WLSMV					MLR (Default integration)			MLR (Montecarlo(2000) integration)		
		χ^2	df	CFI	TLI	RMSEA (90% CI)	AIC	BIC	SSABIC	AIC	BIC	SSABIC
2-Bifactor (general internalising & general externalising)	87	11142.964	348	0.802	0.769	0.06 (0.059-0.061)		NA		161612.5	162226.6	161950.1
2-Bifactor (correlated general factors)	88	1926.553	347	0.971	0.966	0.023 (0.022-0.024)		NA		159063.5	159684.6	159404.9
2-Higher-Order	63	2633.846	372	0.958	0.955	0.027 (0.026-0.028)	161050.557	161495.226	161295.024	161141.1	161585.8	161385.5
Modified Bifactor	93	1933.024	342	0.971	0.965	0.023 (0.022-0.024)		NA		158945.6	159602.1	159306.5

Figure S1 Path diagrams for 2-bifactor model of adolescent psychopathology
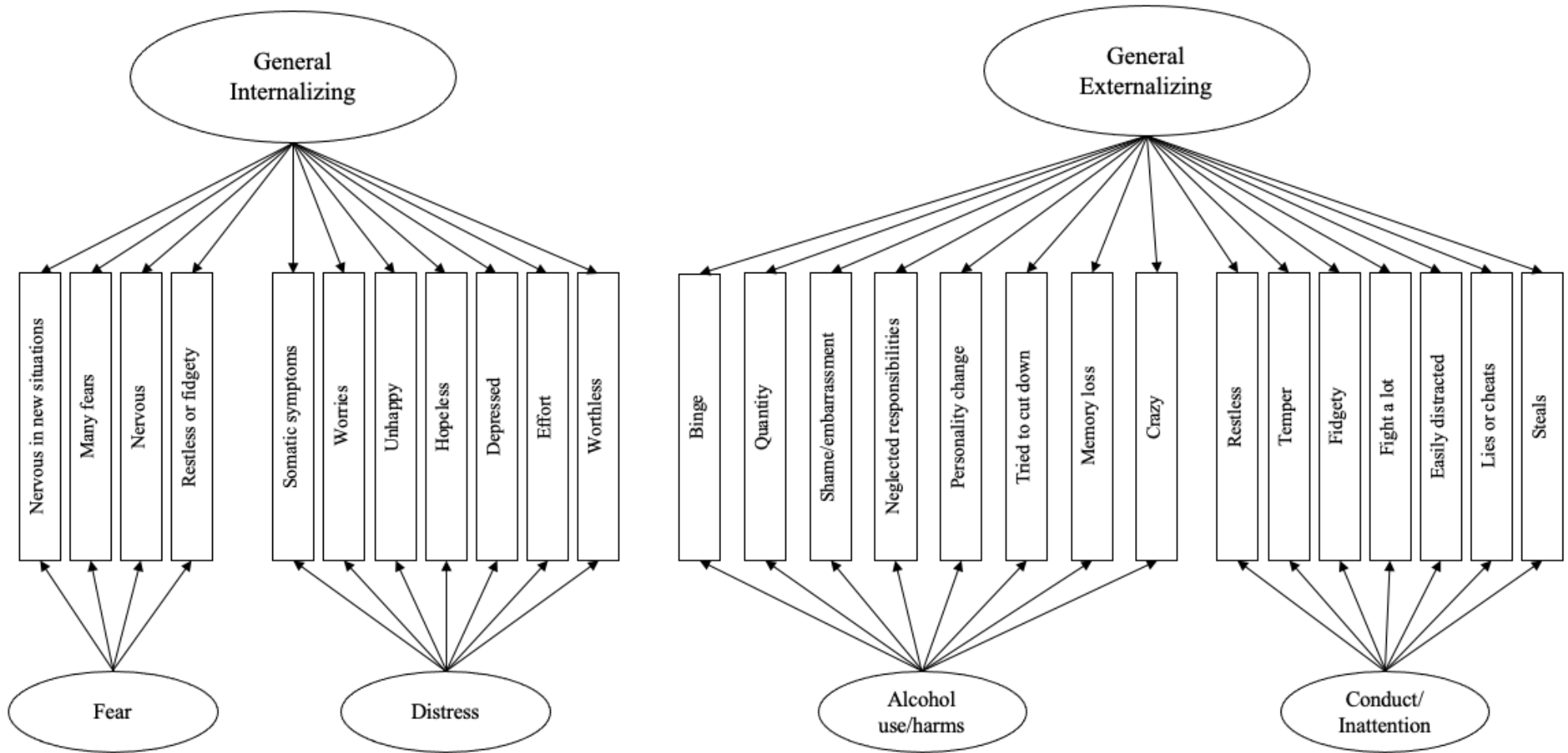
Figure S2 Path diagrams for 2-bifactor model of adolescent psychopathology with correlated general factors
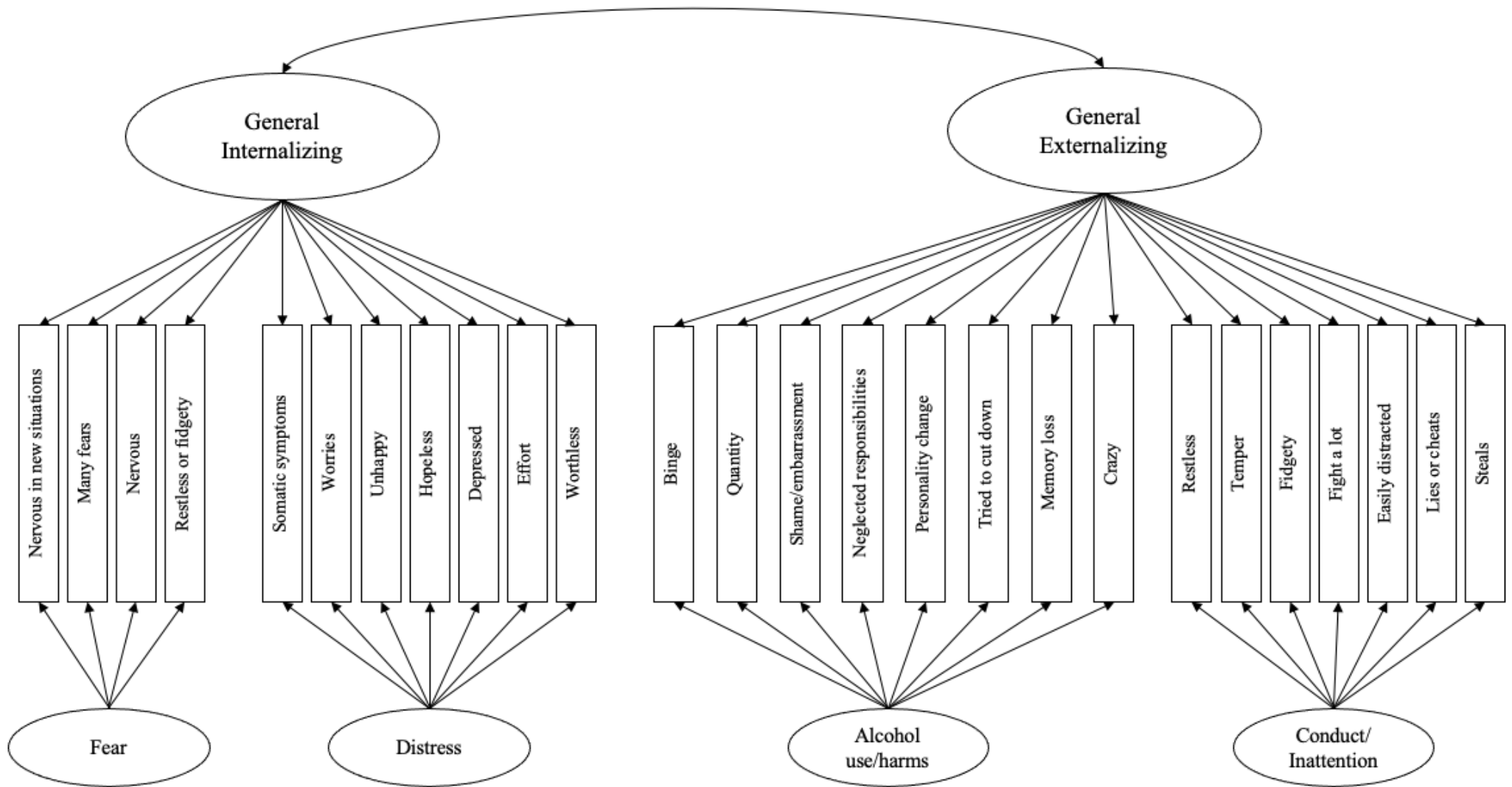
Figure S3 Path diagrams for 2-higher-order model of adolescent psychopathology
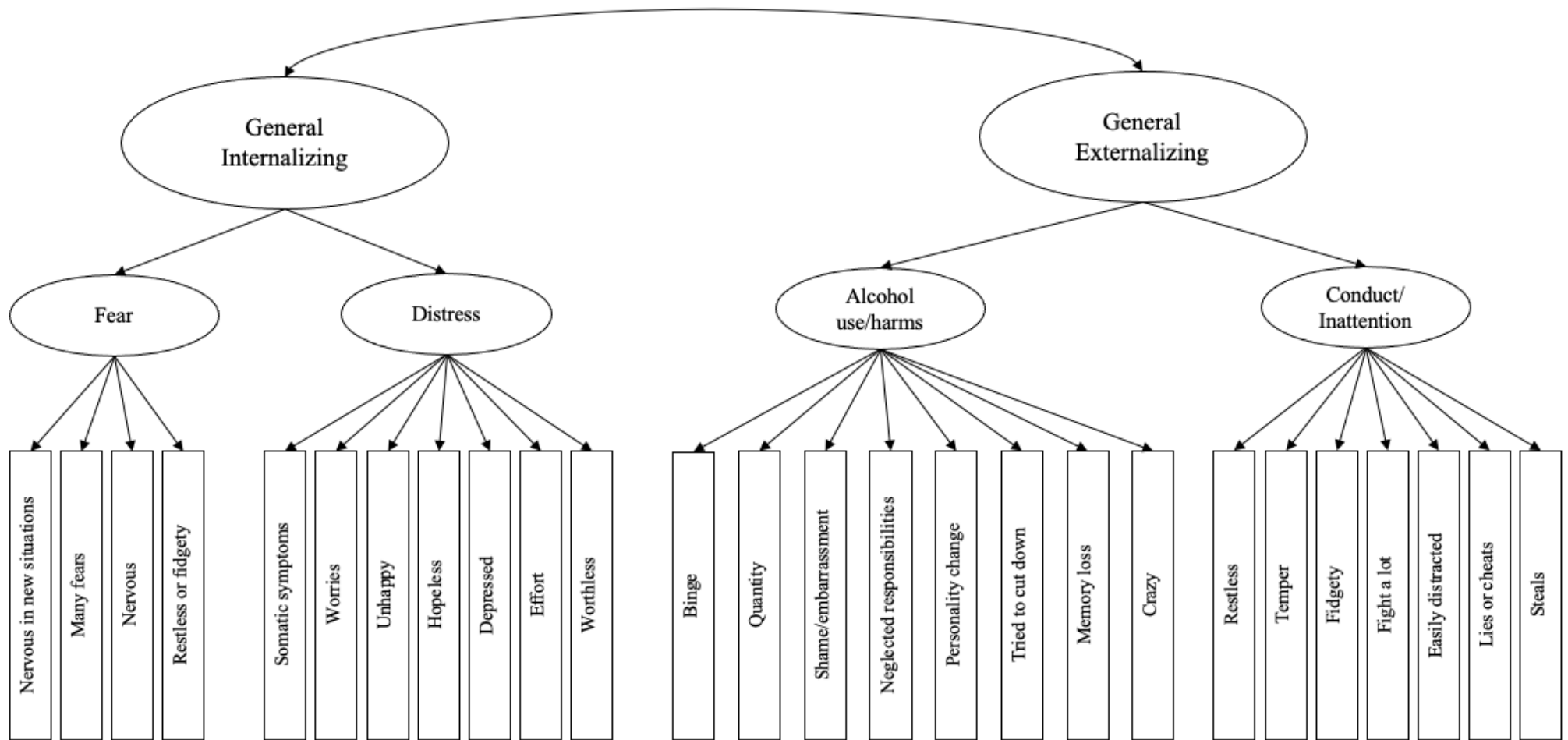
Figure S4 Path diagrams for Modified bifactor model of adolescent psychopathology with correlated specific factors
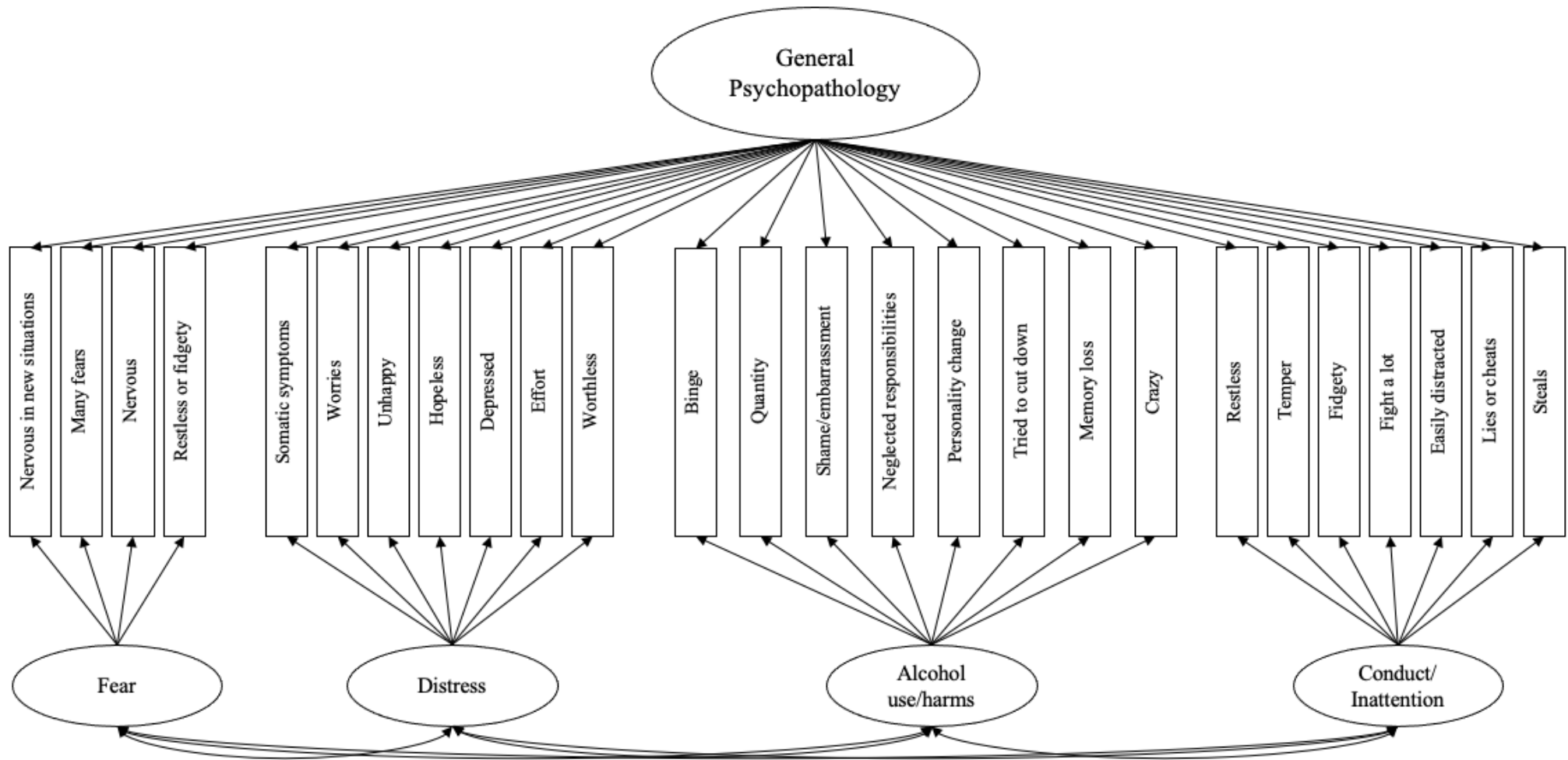
Table S9 Standardised Factor loadings on general and specific (fear, distress, alcohol use/harms, conduct/inattention) factors using WLSMV estimator and inter-factor correlations

Symptom	Item ID	2-Bifactor				Modified 2-Bifactor (correlated general factors)				2-Higher-order				Modified Bifactor	
		General Internalising	General Externalising	Specific Internalising	Specific Externalising	General Internalising	General Externalising	Specific Internalising	Specific Externalising	General Internalising	General Externalising	Specific Internalising	Specific Externalising	General	Specific
Fear															
Nervous in new situations	SD16	0.654		-0.267		0.662		-0.193				0.669		0.538	0.368
Many fears	SD24	0.631		-0.383		0.628		-0.254				0.637		0.504	0.353
Nervous	K61R	0.628		0.361		0.515		0.320				0.557		0.193	0.760
Restless or fidgety	K63R	0.610		0.457		0.627		0.723				0.640		0.436	0.497
Distress															
Somatic symptoms	SD3	0.617		0.005		0.687		-0.114				0.643		0.573	0.266
Worries	SD8	0.811		-0.116		0.759		-0.045				0.721		0.567	0.415
Unhappy	SD13	0.783		0.183		0.847		0.099				0.842		0.690	0.456
Hopeless	K62R	0.721		0.484		0.689		0.527				0.828		0.398	0.793
Depressed	K64R	0.697		0.496		0.720		0.460				0.835		0.482	0.698
Effort	K65R	0.567		0.305		0.583		0.289				0.642		0.393	0.523
Worthless	K66R	0.706		0.634		0.711		0.627				0.881		0.451	0.795
Alcohol use/harms															
Frequency	AUC1		0.354		0.748		0.297		0.771				0.819	0.254	0.787
Binge	AUC2		0.371		0.853		0.292		0.883				0.914	0.250	0.897
Quantity	AUC3		0.274		0.794		0.271		0.785				0.819	0.224	0.803
Acted bad	AH1		0.435		0.846		0.344		0.889				0.942	0.310	0.900
Shame/embarrassment	AH2		0.445		0.846		0.374		0.880				0.952	0.336	0.895
Neglected responsibilities	AH3		0.411		0.852		0.343		0.881				0.934	0.313	0.890
Tolerance	AH4		0.489		0.804		0.443		0.831				0.943	0.405	0.849
Personality change	AH5		0.517		0.767		0.440		0.813				0.927	0.394	0.837

Tried to cut down	AH6		0.570		0.669		0.478		0.731		0.877		0.433		0.758
Memory loss	AH7		0.535		0.652		0.442		0.712		0.844		0.407		0.735
Crazy	AH8		0.561		0.715		0.525		0.747		0.917		0.489		0.770
Conduct/inattention															
Restless	SD2		0.446		0.750		0.678		0.543		0.734		0.747		0.309
Temper	SD5		0.612		0.216		0.742		-0.145		0.729		0.705		-0.152
Fidgety	SD10		0.500		0.717		0.730		0.486		0.794		0.808		0.303
Fight a lot	SD12		0.764		0.110		0.687		-0.131		0.672		0.640		-0.373
Easily distracted	SD15		0.548		0.434		0.716		0.156		0.732		0.731		0.051
Lies or cheats	SD18		0.701		0.099		0.685		-0.186		0.667		0.635		-0.336
Steals	SD22		0.784		-0.005		0.673		-0.218		0.652		0.602		-0.483
First order factors															
Fear		-	-	-	-	-	-	-	-	0.942	-	-	-	-	-
Distress		-	-	-	-	-	-	-	-	0.947	-	-	-	-	-
Alcohol Use		-	-	-	-	-	-	-	-	-	-	0.432	-	-	-
Conduct/inattention		-	-	-	-	-	-	-	-	-	-	0.998	-	-	-
Inter-factor correlations															
Externalising with Internalising		0.000	-	-	-	0.698	-	-	-	0.672	-	-	-	-	-
Internalising with Fear		0.000	-	-	-	0.000	-	-	-	0.942	-	-	-	-	-
Internalising with Distress		0.000	-	-	-	0.000	-	-	-	0.947	-	-	-	-	-
Internalising with Alcohol Use		0.000	-	-	-	0.000	-	-	-	0.291	-	-	-	-	-
Internalising with Conduct/Inattention		0.000	-	-	-	0.000	-	-	-	0.671	-	-	-	-	-
Externalising with Alcohol Use		-	0.000	-	-	-	0.000	-	-	-	-	0.432	-	-	-
Externalising with Conduct/Inattention		-	0.000	-	-	-	0.000	-	-	-	-	0.998	-	-	-
Externalising with Fear		-	0.000	-	-	-	0.000	-	-	-	-	0.634	-	-	-
Externalising with Distress		-	0.000	-	-	-	0.000	-	-	-	-	0.637	-	-	-
Fear with Distress		-	-	0.000	-	-	-	0.000	-	-	-	0.892	-	0.000	0.765
Fear with Alcohol Use		-	-	0.000	-	-	-	0.000	-	-	-	0.274	-	0.000	-0.111

Fear with Conduct/Inattention	-	-	0.000	-	-	-	0.000	-	-	-	**0.633**	-	0.000	**0.207**
Alcohol use with Conduct/Inattention	-	-	-	0.000	-	-	-	0.000	-	-	-	**0.635**	0.000	**-0.327**
Alcohol use with Distress	-	-	-	0.000	-	-	-	0.000	-	-	-	**0.275**	0.000	**0.085**
Conduct/inattention with Distress	-	-	-	0.000	-	-	-	0.000	-	-	-	**0.431**	0.000	**-0.075**

Notes. SD = SDQ, items from Strengths and Difficulties Questionnaire; AH = Alcohol Harms, items from Rutgers Alcohol Problem Index (RAPI); K6 = Kessler 6 Plus scale (K6+); AUC = Alcohol use, AUDIT-C items;

WLSMV = weighted least square mean and variance adjusted. Factor loadings and correlations with a *p* value ≤ 0.05 are shown in bold.

Table S10 Reliability indices for additional structural models of psychopathology

Index	Factor	2-Bifactor	2-Bifactor (correlated general factors)	2-Higher-Order	Modified Bifactor (correlated specific factors)
H	General Psychopathology	-	-	-	**0.93**
	General Internalising	**0.91**	**0.91**	**0.92**	-
	General Externalising	**0.90**	**0.90**	**0.90**	-
	Fear	0.40	0.57	0.16	0.67
	Distress	0.59	0.59	0.32	**0.84**
	Alcohol use	**0.95**	**0.96**	**0.96**	**0.97**
	Conduct/inattention	**0.73**	0.47	0.01	0.45
Omega	General Psychopathology	-	-	-	**0.97**
	General Internalising	**0.93**	**0.93**	**0.92**	-
	General Externalising	**0.97**	**0.97**	**0.97**	-
OmegaS	Fear	**0.78**	**0.78**	0.72	**0.76**
	Distress	**0.92**	**0.92**	**0.91**	**0.91**
	Alcohol use	**0.98**	**0.98**	**0.98**	**0.98**
	Conduct/inattention	**0.90**	**0.89**	**0.88**	**0.89**
OmegaH	General Psychopathology	-	-	-	0.63
	General Internalising	**0.87**	**0.87**	**0.86**	-
	General Externalising	0.51	0.50	0.50	-
OmegaHS	Fear	0.00	0.04	0.08	0.44
	Distress	0.13	0.11	0.09	0.51
	Alcohol use	0.73	**0.80**	**0.80**	**0.83**
	Conduct/inattention	0.20	0.01	0.00	0.02
ECV_NEW	General Psychopathology	-	-	-	0.39
	General Internalising	0.76	0.75	**0.89**	-
	General Externalising	0.39	0.39	0.42	-
ECV_S_NEW	Fear	0.26	0.33	0.11	0.59
	Distress	0.23	0.22	0.10	0.57
	Alcohol use	**0.74**	**0.81**	**0.81**	**0.85**
	Conduct/inattention	0.32	0.16	0.00	0.17

Note. Results in bold indicate acceptable reliability. Indices for 2-higher-Order model cannot be calculated, indices presented are based on Schmid-Leiman transformed

(SLT) model. ECV = Explained Common Variance, ECV_S = Explained Common Variance of specific factors, H = measure of construct replicability, Omega = internal

reliability of general factor/s, OmegaS = internal reliability of specific factor/s, OmegaH = Omega Hierarchical, OmegaHS = Omega Hierarchical subscale, PUC = Percent of Uncontaminated Correlations, SLT = Schmid-Leiman transformation

Appendix G

Supplementary materials for Chapter 4

Supplementary methods

Measures

Table M1 Item wording and corresponding lower-order factors for indicators of psychopathology.

Lower-order factor	Item	Description
Alcohol use/harms	AUC2	How often do you have 5+ std drinks in the past 6 mths?
Alcohol use/harms	AUC3	In the past 6 mths, how many std drinks on a typical day?
Alcohol use/harms	AH2	Caused shame or embarrassment to someone.
Alcohol use/harms	AH3	Neglected my responsibilities.
Alcohol use/harms	AH4*	Felt that I need more alcohol than I used to in order to get the same effect.
Alcohol use/harms	AH5	Noticed a change in my personality.
Alcohol use/harms	AH6	Tried to cut down or quit drinking.
Alcohol use/harms	AH7	Suddenly found myself in a place that I could not remember getting to.
Alcohol use/harms	AH8	Felt I was going crazy.
Conduct/inattention	SD2	I am restless. I cannot stay still for long.
Conduct/inattention	SD5	I get very angry and often lose my temper.
Conduct/inattention	SD10	I am constantly fidgeting or squirming.
Conduct/inattention	SD12	I fight a lot. I can make other people do what I want.
Conduct/inattention	SD15	I am easily distracted. I find it difficult to concentrate.
Conduct/inattention	SD18	I am often accused of lying or cheating.
Conduct/inattention	SD22	I take things that are not mine from home, school or elsewhere.
Distress	SD3	I get a lot of headaches, stomach-aches, or sickness.
Distress	SD8	I worry a lot.
Distress	SD13	I am often unhappy, down-hearted, or tearful.
Distress	K62R	… hopeless?
Distress	K64R	… so depressed that nothing could cheer you up?
Distress	K65R	… that everything was an effort?
Distress	K66R	… worthless?
Fear	K61R	…nervous?
Fear	K63R	… restless or fidgety?
Fear	SD16	I am nervous in new situations. I easily lose confidence.
Fear	SD24	I have many fears. I am easily scared.

Note. SD = items from Strengths and Difficulties Questionnaire; AH = Alcohol Harms, items from Rutgers Alcohol Problem Index (RAPI); K6 = Kessler 6 Plus scale (K6+); AUC = Alcohol use, AUDIT-C items. AH items prefaced with "*In the past 6 months how many times have you experienced the following as a consequence of drinking alcohol*". K6 items prefaced with "*In the last 4 weeks, about how often did you feel*". *AH4 was excluded from the final model due to convergence issues.*

Analytic Plan

Figure S1 below depicts the overarching analytic procedure, from measurement invariance assessment via moderated factor analysis (MNLFA) to the primary analyses using latent curve models with structured residuals (LCM-SR). Each step in the procedure is described in further detail below.

Figure S1. High level summary of data analytic approach
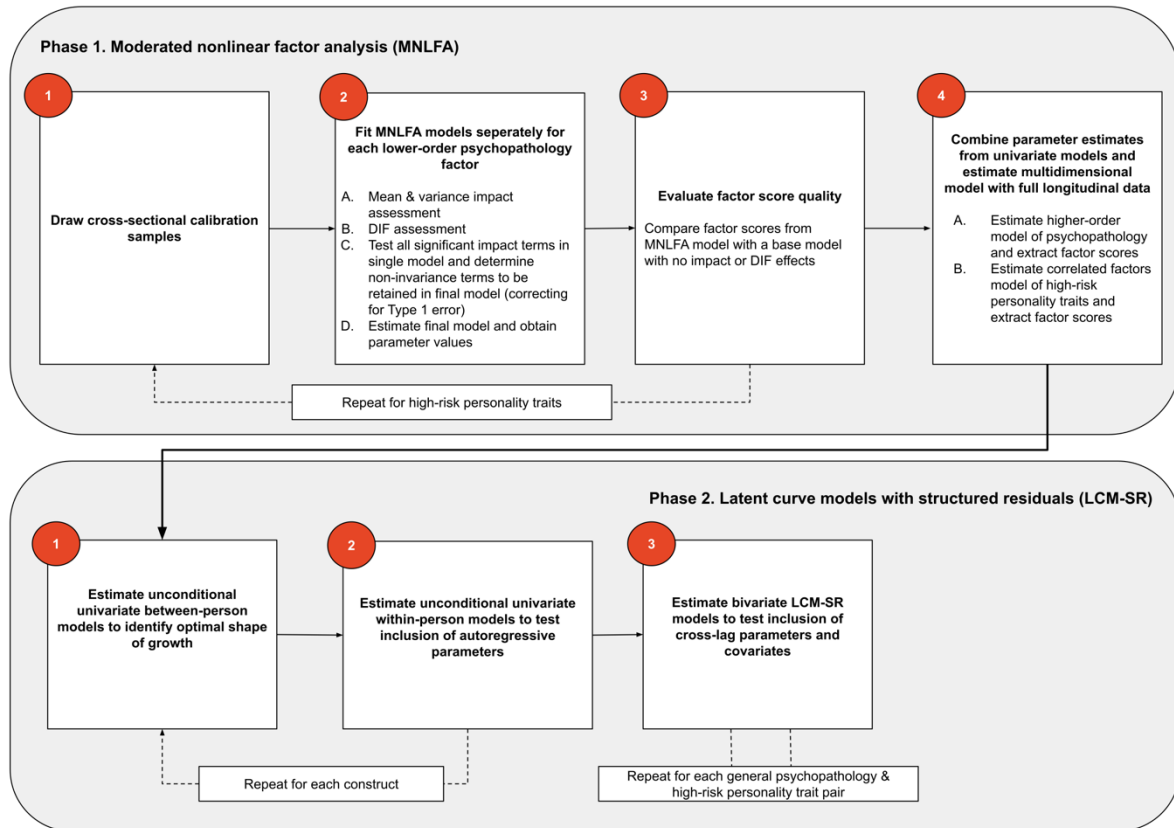
Measurement invariance

Moderated nonlinear factor analysis (MNLFA) was used to examine the measurement invariance of the psychopathology dimensions. MNLFA simultaneously assesses differential item functioning (DIF) and measurement invariance across multiple grouping variables (which can be either categorical or continuous), and ultimately aims to generate factor scores that have been corrected for measurement bias and can be used in subsequent analyses (Bauer, 2017; Curran, McGinley, et al., 2014). Building on the multiple groups and multiple-indicators-multiple-causes (MIMIC) approaches to measurement invariance, MNLFA evaluates DIF and mean and variance impact effects through moderation effects on model parameters in a sequential, iterative model building process. In the present study, the effects of age, sex, and cohort (i.e., CAP or CSC) were examined.

Drawing on the general procedures outlined by Bauer (2017) and Gottfredson et al. (2019), we conducted the analyses in four broad steps. Details of each step are described below.

Table M2 Moderated nonlinear factor analysis sequential model building process

Step	Description
Step 1. Draw cross-	We drew a cross-sectional calibration sample with one randomly

sectional calibration sample	selected observation per participant using the aMNLFA.sample function from the aMNLFA package. The use of a calibration sample strategy is necessary to preserve the assumption of independence, which is directly violated by longitudinal data (Curran, McGinley, et al., 2014). Different calibration samples were drawn for psychopathology and personality analyses.
Step 2. Fit MNLFA models separately for each lower-order psychopathology factor	MNLFA models were fit separately for each lower order factor (from the higher-order model of psychopathology; and each personality subscale of the SURPS), adopting the divide and conquer approach recommended by Bauer (2017). This step is comprised of the following sub-steps: - 2a. Estimated mean and variance impact models and examine impact effects (threshold to retain non-invariance effects is p < 0.1). - 2b. Estimated and examined DIF effects (threshold to retain non-invariance terms is p < .05) - 2c. Test all marginally significant terms in a single model and removed any remaining non-invariant terms, adjusting for Type 1 errors. For mean and variance impact terms, these were retained if p was less than .05, for DIF terms (loadings & intercepts) we applied a Benjamin-Hochberg correction. DIF terms where p values were lower than the BH correction were retained. - 2d. Estimated final model and obtain parameter values.
Step 3. Evaluate factor score quality	The quality of the adjusted factor scores derived from the MNLFA procedure were assessed by examining how closely they correlated with scores from a model with no non-invariance terms. A high correlation (e.g., r > .9) suggests that the model is invariant.
Step 4A. Combine parameter estimates from univariate models and estimate higher-order model of psychopathology with full longitudinal data	Using the parameter values (i.e., SVALUES) from the final univariate models for each lower-order factor, we estimated a higher-order model of psychopathology and extracted factor scores to be used in subsequent analyses
Repeat Steps 1 – 3 for each high-risk personality trait	As described above.
Step 4B. Combine parameter estimates from univariate models and estimate correlated factors model of high-risk personality traits with full longitudinal data	The parameter values from the final univariate models for each personality trait were combined and we estimated a correlated factors model and extracted adjusted factor scores to be used in subsequent analyses

Latent curve models with structured residuals

The co-development of general psychopathology and high-risk personality traits were examined using latent curve models with structured residuals (LCM-SR). Analyses were conducted in three broad steps, as depicted in Figure S1, based on the procedure described by Curran and colleagues (Curran, Howard, et al., 2014) and Wellman and colleagues (Wellman et al., 2020).

In the first step we examined three univariate between-person models for each construct to determine the optimal growth form (i.e., intercept only vs. intercept + linear slope vs. intercept + linear + quadratic slope). The intercept only model included mean and variance of the intercept factor and residual variances for each of the measurement points that were allowed to vary over time. This

model was then expanded to include linear and non-linear growth terms. The best fitting model was selected for subsequent analyses.

In the second step, we examined univariate within-person models by expanding the best-fitting model from step 1 to include autoregression parameters among residuals and tested the inclusion of equality constraints of the autoregressions (i.e., autoregression parameters constrained to equality vs. freely estimated). This approach helps determine how best to represent the autoregressive parameters and provides an indication of whether the effect is consistent overtime. If the autoregressive parameters constrained to equality are found to improve overall fit, this would suggest that the effect is consistent over time. In contrast, if estimating autoregressive parameters freely improves overall fit, this can indicate that the size and significance of an effect may fluctuate overtime. Within the context of LCM-SR, autoregressive parameters reflect time-point specific deviations from individual-specific mean levels and growth curve (Curran, Howard, et al., 2014; Mund et al., 2021). For example, within-person deviations in psychopathology at time point T might predict within-person deviations from the person-specific trajectory of psychopathology at the subsequent time point T+1, such that an adolescent experiencing heightened levels in psychopathology at T might continue to experience heightened levels of psychopathology at T+1. Statistically significant autoregressive effects indicate that deviations from the person-specific curve are enduring, whereas non-significant autoregressive effects indicate that individuals tend to fall back to their typical person-specific trajectory in between assessments (Falkenström et al., 2022).

In the third step, cross-lags were introduced sequentially in a series of bivariate models to examine cross-construct relations at the latent factor and time-specific residual levels and test equality constraints on the cross-lagged regressions. First a base bivariate model that combines the best fitting univariate models for general psychopathology and a personality trait of interest from the previous step was estimated. In this model the intercept and slope for each construct were allowed to covary within and across constructs. Time-specific residuals were allowed to covary between constructs, and these covariances were constrained to be equal across time for time two, three and four. The autoregressive components among the structured residuals for each construct were retained (i.e., best fitting structure from Step 2 was incorporated into the model). We then introduced regressions of the residuals and evaluated each side of the reciprocal effects separately. Specifically, we first introduced the regression of the structured residual of general psychopathology onto the relevant personality trait (while holding the regression of the structured residual of the personality trait onto the structured residual of general psychopathology to zero). We compared a model with the regression estimates freely estimated with another constraining these estimates to equality over time. We then removed these regressions and introduced the regression of structured residual of the personality trait onto the structured residual of general psychopathology.

The optimal parameter constraints for each direction of influence were then combined, and an unconditional bivariate model was estimated. This model was then expanded to include sex and age at baseline as time invariant covariates by regressing the slope and intercept factors onto the covariates. This allowed us to control for the influence of sex and age at baseline in the interpretation of our final models. As with the autoregressive parameters, the cross-lag effects in an LCM-SR reflect the degree to which deviations from an individual's typical level of general psychopathology can be predicted from the individuals prior deviation from their expected score on personality (Curran, Howard, et al., 2014). Recently published guidelines for interpreting cross-lagged effects recommend .03 (small effect), .07 (medium effect) and .13 (large effect) can be used as benchmark values for CLMP and RI-CLPM models (Orth et al., 2022). Given the interpretation of the within-person parameters of the RI-CLPM are similar to the LCM-SR (Mund et al., 2021), we have applied the same guidelines when interpreting the cross-lagged effects in the present study (these are likely conservative thresholds due to the additional variance captured in the between-person components of the LCM-SR).

As described in the main text, goodness-of-fit for all models was assessed using root mean square error of approximation (RMSEA), comparative fit index (CFI) and Tucker-Lewis index (TLI)t, where RMSEA values < 0.06, and CFI and TLI values > .95 indicate acceptable fit (Brown, 2014). Models

were also compared using the information criteria, including the Akaike information criterion (AIC), Bayesian information criterion (BIC), and the sample-size adjusted BIC (aBIC), where lower values indicate superior fit (Raftery, 1995). Changes in model fit between nested models were also formally evaluated with the likelihood ratio test using a scaled difference chi-square. If there was no statistically significant improvement in model fit, the best fitting model was determined based on overall fit, parsimony and theoretical basis for components.

Table M3. Summary of iterative model building process for latent curve models with structured residuals (LCM-SR)

Step/Model	Description
Step 1. Unconditional univariate between-person models to identify optimal shape of growth	
Random intercept only	– Mean and variance of the intercept factor – Residual variances for each repeated measure (freely estimated over time)
Random intercept + linear slope	– Mean and variance of the intercept and linear slope factors – Residual variances for each repeated measure (freely estimated over time) – Intercept & slope covariance
Random intercept + linear slope + quadratic slope	– Mean and variance of the intercept and linear and quadratic slope factors – Residual variances for each repeated measure (freely estimated over time) – Intercept & slope covariances
Model evaluation – Assess overall fit – Test linear vs. quadratic growth with nested chi-square difference test – Retain growth parameters that result in significant improvement in model fit	
Step 2. Unconditional univariate within-person models to test inclusion of autoregressive paths	
Autoregressive parameters (equal)	Best fitting model from Step 1 + - Add autoregressive path among the time-specific residuals - Constrain AR paths to be **held equal across time**
Autoregressive parameters (free)	Best fitting model from Step 1 + - Add autoregressive path among the time-specific residuals - Allow AR paths to **be freely estimated across time**
Model evaluation – Test inclusion of free vs. constrained AR paths with nested chi-square difference test – Retain autoregressive path that results in significant improvement in model fit – If there is no statistically significant improvement in model fit, the best fitting model is determined based on overall fit, parsimony and theoretical basis for components	
Repeat Steps 1 and 2 for each construct	
Step 3. Estimate bivariate LCM-SR models to test inclusion of cross-lag parameters and covariates	
Bivariate LCM-SR (no cross-lags)	– Combine two univariate LCMs into single bivariate LCM (e.g., P and NT) – Allow the latent factors from each univariate model to covary with each other – Allow the time-specific residuals to covary between the two constructs, and constrain to equality from T2 to T4 – Include AR paths among the structured residuals identified in step 2, but did not include any prospective paths between two constructs (i.e., no cross-lag effects were estimated)

Bivariate LCM-SR (P on SURPS cross-lags, equal)	– Bivariate LCM-SR + – Cross-lag paths from P to SURPS trait – Constrain cross-lag paths to be equal across time – Assess improvement in model fit with chi-square differences test (compare with bivariate LCM-SR without cross-lags)
Bivariate LCM-SR (P on SURPS cross-lags, free)	– Bivariate LCM-SR + – Cross-lag paths from P to SURPS trait – Allow cross-lag paths to be freely estimated across time – Assess improvement in model fit with chi-square differences test (compare with bivariate LCM-SR without cross-lags; and bivariate LCM-SR with P on SURPS cross-lags held equal)
Bivariate LCM-SR (SURPS on P cross-lags, equal)	– Bivariate LCM-SR + – Remove P on SURPS cross-lags – Cross-lag paths from SURPS trait to P – Constrain cross-lag paths to be equal across time – Assess improvement in model fit with chi-square differences test (compare with bivariate LCM-SR without cross-lags)
Bivariate LCM-SR (SURPS on P cross-lags, free)	– Bivariate LCM-SR + – Cross-lag paths from P to SURPS trait – Allow cross-lag paths to be freely estimated across time – Assess improvement in model fit with chi-square differences test (compare with bivariate LCM-SR without cross-lags; and bivariate LCM-SR with SURPS on P cross-lags held equal)

Model evaluation
- Retain cross-lag paths that results in significant improvement in model fit.
- If there is no statistically significant improvement in model fit, the best fitting model is determined based on overall fit, parsimony and theoretical basis for components

Full unconditional LCM-SR	– Bivariate LCM-SR + best-fitting P on SURPS and SURPS on P cross-lag structures – Examine model results and overall fit
Final conditional LCM-SR	– Bivariate LCM-SR + best-fitting P on SURPS and SURPS on P cross-lag structures – Regress latent curve and intercept factors on baseline age and sex – Examine model results and overall fit

Repeat Step 3 for each P and SURPS pairing (i.e., P and NT, P and AS, P and IMP, P and SS).
- Answer research questions using the results from this model, assessing the significance of the autoregressive and reciprocal paths between constructs as well as the variation sin the magnitude of the reciprocal relation over time

Note. P = general psychopathology, NT = negative thinking, AS = anxiety sensitivity, IMP = impulsivity, SS = sensation seeking, SURPS = Substance Use Risk Profile Scale

Supplementary Results

Table S1 Intraclass Correlation Coefficients (ICC)

Variable	ICC
IMP_T3	0.016
SS_T1	0.019
SS_T0	0.020
P_T0	0.021
P_T3	0.024
AS_T3	0.027
IMP_T2	0.027
IMP_T0	0.028
IMP_T1	0.028
SS_T2	0.029
AS_T2	0.034
P_T1	0.034
P_T2	0.034
AS_T1	0.035
NT_T0	0.037
SS_T3	0.038
AS_T0	0.043
NT_T1	0.049
NT_T2	0.064
NT_T3	0.080

Table S2 Logistic regressions comparing baseline characteristic analyses between participants who were absent for all follow-ups vs participants present at any follow-ups

		Any follow-ups	No follow-ups	OR (95% CI)
General Psychopathology	Mean (SD)	0.0 (0.8)	0.3 (0.9)	1.19 (0.90-1.58, p=0.225)
Negative Thinking	Mean (SD)	-0.2 (0.8)	0.1 (0.9)	**1.37 (1.01-1.85, p=0.044)**
Anxiety Sensitivity	Mean (SD)	-0.1 (0.6)	0.0 (0.6)	0.99 (0.69-1.43, p=0.973)
Impulsivity	Mean (SD)	0.3 (0.9)	0.5 (0.9)	1.14 (0.88-1.49, p=0.323)
Sensation Seeking	Mean (SD)	-0.0 (0.6)	-0.0 (0.6)	0.97 (0.68-1.37, p=0.863)
Sex	Female	1167 (92.3)	97 (7.7)	-
	Male	567 (92.8)	44 (7.2)	0.90 (0.59-1.36, p=0.621)
Cohort	CSC	1427 (91.7)	129 (8.3)	-
	CAP	496 (94.1)	31 (5.9)	0.73 (0.47-1.12, p=0.161)

Table S3 Logistic regressions comparing Cohort x baseline variable interactions between participants who were absent for all follow-ups vs participants present at any follow-ups, and participants who present for all follow-ups vs participants absent at any follow-ups

Cohort x Baseline variable	OR (95% CI), Any follow-ups (vs. 0 follow-ups)
General Psychopathology, CAP	0.92 (0.55-1.56, p=0.767)
Negative Thinking, CAP	1.23 (0.65-2.32, p=0.525)
Anxiety Sensitivity, CAP	0.89 (0.31-2.55, p=0.835)
Impulsivity, CAP	1.38 (0.77-2.42, p=0.271)
Sensation Seeking, CAP	0.91 (0.38-2.14, p=0.825)
Male, CAP	0.96 (0.37-2.34, p=0.936)

Table S4 Logistic regressions comparing Sex x baseline variable interactions between participants who were absent for all follow-ups vs participants present at any follow-ups, and participants who present for all follow-ups vs participants absent at any follow-ups

Sex x Baseline variable	OR (95% CI), Any follow-ups (vs. 0 follow-ups)
General Psychopathology, Male	0.84 (0.54-1.32, p=0.449)
Negative Thinking, Male	1.17 (0.73-1.87, p=0.519)
Anxiety Sensitivity, Male	0.76 (0.39-1.51, p=0.430)
Impulsivity, Male	0.82 (0.53-1.28, p=0.384)
Sensation Seeking, Male	0.70 (0.37-1.33, p=0.267)

Table S5 Correlation between MNLFA adjusted factor scores and unadjusted factor scores

Construct	r
Fear	0.99***
Distress	1.00***
Alcohol	0.94***
Conduct	0.99***
AS	1.00***
NT	1.00***
IMP	1.00***
SS	1.00***

*** p <.001.

Table S6 Summary of model fit and comparison of nested models from latent curve models with structured residuals

Model		Model fit indices								χ² Difference Test for Nested Models Based on Loglikelihood	
	N	χ² (df)	BIC	AIC	aBIC	CFI	TLI	RMESEA (90% CI)		χ²Δ	Models Compared
Step 1: Unconditional univariate between-person models											
General psychopathology											
1 Intercept only	2078	203.937 (8)***	16480.28	16446.45	16461.22	0.848	0.886	0.109 (0.096-0.122)			
2 Intercept + linear slope	**2078**	**52.189 (5)***	**16331.9**	**16281.15**	**16303.31**	**0.963**	**0.956**	**0.067 (0.052-0.085)**		**148.3228***	**2 vs 1**
3 Intercept + linear + quadratic slope	2078	20.208 (2)***	16318.65	16250.98	16280.52	0.986	0.958	0.066 (0.042-0.094)			
Negative Thinking											
4 Intercept only	2051	247.031 (8)***	15180.97	15147.21	15161.91	0.712	0.784	0.121 (0.108-0.134)			
5 Intercept + linear slope	**2051**	**10.241 (5)**	**14872.25**	**14821.61**	**14843.65**	**0.994**	**0.992**	**0.023 (0.000-0.042)**		**239.1303***	**5 vs 4**
6 Intercept + linear + quadratic slope	2051	4.083 (2)	14886.36	14818.85	14848.24	0.997	0.992	0.023 (0.000-0.054)			
Anxiety Sensitivity											
7 Intercept only	2051	38.502 (8)***	11949.67	11915.91	11930.61	0.921	0.941	0.043 (0.030-0.057)			
8 Intercept + linear slope	**2051**	**3.296 (5)**	**11917.34**	**11866.71**	**11888.75**	**1**	**1**	**0.000 (0.000-0.025)**		**32.3201***	**8 vs 7**
9 Intercept + linear + quadratic slope	2051	2.931 (2)	11939.7	11872.18	11901.57	0.998	0.993	0.015 (0.000-0.049)			
Impulsivity											
10 Intercept only	2051	44.569 (8)***	16809.38	16775.63	16790.32	0.935	0.951	0.047 (0.034-0.061)			
11 Intercept + linear slope	**2051**	**8.112 (5)**	**16779.32**	**16728.68**	**16750.72**	**0.994**	**0.993**	**0.017 (0.000-0.038)**		**33.3178***	**11 vs 10**
12 Intercept + linear + quadratic slope	2051	4.051 (2)	16796.66	16729.15	16758.53	0.996	0.989	0.022 (0.000-0.054)			
Sensation Seeking											
13 Intercept only	2051	69.259 (8)***	12696.16	12662.41	12677.1	0.884	0.913	0.061 (0.048-0.075)			
14 Intercept + linear slope	**2051**	**3.608 (5)**	**12605.55**	**12554.91**	**12576.95**	**1**	**1**	**0.000 (0.000-0.026)**		**60.7874***	**14 vs 13**
15 Intercept + linear + quadratic slope	2051	0.959 (2)	12624.17	12556.66	12586.05	1	1	0.000 (0.000-0.035)			
Step 2: Unconditional univariate within-person models											
General Psychopathology											
16 Model 2 + autoregressive parameters (equal)	2078	23.844 (4)***	16306.02	16249.63	16274.25	0.985	0.977	0.049 (0.031-0.069)		45.3223***	16 vs 2
17 Model 2 + autoregressive parameters (free)	**2078**	**4.336 (2)**	**16301.6**	**16233.93**	**16263.47**	**0.998**	**0.995**	**0.024 (0.000-0.055)**		**19.3232***	**17 vs 16**
18 Model 2 + autoregressive parameters (free, modified)	2078	4.257 (3)	16294.06	16232.03	16259.12	0.999	0.998	0.014 (0.000-0.042)			
Negative Thinking											
19 Model 5 + autoregressive parameters (equal)	**2051**	**4.791 (4)**	**14871.6**	**14815.34**	**14839.83**	**0.999**	**0.999**	**0.010 (0.000-0.036)**		**4.3396***	**19 vs 5**
20 Model 5 + autoregressive parameters (free)	2051	0.559 (2)	14881.25	14813.74	14843.13	1	1	0.000 (0.000-0.030)		3.5666	20 vs 19
Anxiety Sensitivity											
21 Model 8 + autoregressive parameters (equal)	**2051**	**2.046 (4)**	**11922.82**	**11866.56**	**11891.05**	**1**	**1**	**0.000 (0.000-0.024)**		**1.0352**	**21 vs 8**
22 Model 8 + autoregressive parameters (free)	2051	2.076 (2)	11937.41	11869.9	11899.29	1	0.999	0.004 (0.000-0.044)		0.3982	22 vs 21
Impulsivity											
23 Model 11 + autoregressive parameters (equal)	**2051**	**6.593 (4)**	**16784.02**	**16727.76**	**16752.25**	**0.995**	**0.993**	**0.018 (0.000-0.041)**		**1.5559**	**23 vs 11**
24 Model 11 + autoregressive parameters (free)	2051	2.350 (2)	16793.67	16726.16	16755.55	0.999	0.998	0.009 (0.000-0.046)		3.9576	22 vs 23
Sensation Seeking											
25 Model 14 + autoregressive parameters (equal)	**2051**	**4.281 (4)**	**12613.08**	**12556.82**	**12581.31**	**0.999**	**0.999**	**0.006 (0.000-0.034)**		**0.0359**	**25 vs 14**
26 Model 14 + autoregressive parameters (free)	2051	1.000 (2)	12623.5	12555.99	12585.38	1	1	0.000 (0.000-0.036)		2.7923	26 vs 25
Step 3. Bivariate models											

Model			Model fit indices							χ² Difference Test for Nested Models Based on Loglikelihood	
	N	χ² (df)	BIC	AIC	aBIC	CFI	TLI	RMESEA (90% CI)		χ² Δ	Models Compared
Negative Thinking x General Psychopathology											
27 Bivariate LCM-SR (no cross-lags)	2078	42.851 (16)***	30016.2	29858.3	29927.24	0.991	0.984	0.028 (0.018-0.039)			
28 Bivariate LCM-SR (P on NT lags, equal)	**2078**	**42.029 (15)***	**30022.63**	**29859.1**	**29930.5**	**0.991**	**0.983**	**0.029 (0.019-0.040)**			
29 Bivariate LCM-SR (P on NT lags, free)	2078	41.428 (13)***	30035.6	29860.79	29937.12	0.99	0.979	0.032 (0.022-0.044)		1.5247	29 vs 28
30 Bivariate LCM-SR (NT on P lags, equal)	**2078**	**39.443 (15)***	**30020.1**	**29856.56**	**29927.96**	**0.992**	**0.985**	**0.028 (0.018-0.039)**			
31 Bivariate LCM-SR (NT on P lags, free)	2078	40.721 (13)***	30023.89	29849.08	29925.4	0.991	0.98	0.032 (0.021-0.043)		3.3945	31 vs 30
32 Full unconditional LCM-SR	2078	35.117 (14)**	30021.43	29852.25	29926.12	0.993	0.986	0.027 (0.016-0.038)			
33 Final conditional LCM-SR	**2067**	**63.153 (26)***	**29835.75**	**29599.13**	**29702.31**	**0.99**	**0.98**	**0.026 (0.018-0.035)**			
Anxiety Sensitivity x General Psychopathology											
34 Bivariate LCM-SR (no cross-lags)	2078	33.640 (16)**	27728.29	27570.4	27639.34	0.992	0.985	0.023 (0.012-0.034)			
35 Bivariate LCM-SR (P on AS lags, equal)	**2078**	**32.344 (15)**	**27734.08**	**27570.55**	**27641.95**	**0.992**	**0.985**	**0.024 (0.012-0.035)**			
36 Bivariate LCM-SR (P on AS lags, free)	2078	28.668 (13)**	27743.97	27569.15	27645.48	0.993	0.984	0.024 (0.012-0.036)		3.7518	35 vs 36
37 Bivariate LCM-SR (AS on P lags, equal)	**2078**	**33.099 (15)**	**27734.78**	**27571.24**	**27642.64**	**0.991**	**0.984**	**0.024 (0.013-0.035)**			
38 Bivariate LCM-SR (AS on P lags, free)	2078	31.169 (13)**	27745.13	27570.31	27646.64	0.991	0.982	0.026 (0.014-0.038)		2.7511	38 vs 37
39 Full unconditional LCM-SR	2078	28.910 (14)*	27736.76	27567.59	27641.45	0.993	0.986	0.023 (0.011-0.034)			
40 Full conditional LCM-SR	2067	41.054 (22)**	27626.81	27412.72	27506.08	0.992	0.985	0.020 (0.010-0.030)			
41 Final unconditional LCM-SR (no AS slope)	2078	52.318 (19)***	27730.35	27589.37	27650.92	0.984	0.977	0.029 (0.020-0.039)			
42 Final conditional LCM-SR (no AS slope)	**2067**	**73.899 (34)***	**27551.84**	**27360.29**	**27443.82**	**0.985**	**0.977**	**0.024 (0.016-0.031)**			
Impulsivity x General Psychopathology											
43 Bivariate LCM-SR (no cross-lags)	2078	38.839 (16)**	32561.39	32403.49	32472.43	0.991	0.984	0.026 (0.016-0.037)			
44 Bivariate LCM-SR (P on IMP lags, equal)	**2078**	**37.894 (15)***	**32567.1**	**32403.56**	**32474.97**	**0.991**	**0.982**	**0.027 (0.016-0.038)**			
45 Bivariate LCM-SR (P on IMP lags, free)	2078	37.245 (13)***	32580.93	32406.11	32482.44	0.99	0.979	0.030 (0.019-0.041)		1.0964	44 vs 45
46 Bivariate LCM-SR (IMP on P lags, equal)	**2078**	**37.570 (15)**	**32567.01**	**32403.47**	**32474.87**	**0.991**	**0.983**	**0.027 (0.016-0.038)**			
47 Bivariate LCM-SR (IMP on P lags, free)	2078	35.537 (13)***	32577.58	32402.76	32479.09	0.991	0.98	0.029 (0.018-0.040)		2.897	47 vs 46
48 Full unconditional LCM-SR	2078	32.892 (14)**	32568.36	32399.18	32473.05	0.992	0.985	0.025 (0.014-0.037)			
49 Final conditional LCM-SR	**2067**	**58.952 (26)***	**32411.48**	**32174.86**	**32278.05**	**0.989**	**0.978**	**0.025 (0.016-0.033)**			
Sensation Seeking x General Psychopathology											
50 Bivariate LCM-SR (no cross-lags)	2078	18.402 (16)	28946.47	28788.57	28857.51	0.999	0.998	0.008 (0.000-0.023)			
51 Bivariate LCM-SR (P on SS lags, equal)	**2078**	**18.421 (15)**	**28954.11**	**28790.57**	**28861.97**	**0.998**	**0.997**	**0.010 (0.000-0.024)**			
52 Bivariate LCM-SR (P on SS lags, free)	2078	18.081 (13)	28968.49	28793.67	28870	0.997	0.995	0.014 (0.000-0.028)		0.6057	52 vs 51
53 Bivariate LCM-SR (SS on P lags, equal)	**2078**	**18.148 (15)**	**28953.43**	**28789.89**	**28861.29**	**0.998**	**0.997**	**0.010 (0.000-0.024)**			
54 Bivariate LCM-SR (SS on P lags, free)	2078	13.401 (13)	28961.81	28786.99	28863.32	1	1	0.004 (0.000-0.022)		4.2075	54 vs 53
55 Final unconditional LCM-SR	2078	18.150 (14)	28960.83	28791.65	28865.51	0.998	0.996	0.012 (0.000-0.026)			
56 Final conditional LCM-SR	**2067**	**44.655 (26)***	**28858.23**	**28621.6**	**28724.79**	**0.993**	**0.985**	**0.019 (0.009-0.028)**			

Notes. NT = Negative Thinking; AS = Anxiety Sensitivity; IMP = Impulsivity; SS = Sensation Seeking; P = General Psychopathology

*p<.05, **P<.01, ***p<.001

Table S7 Results of conditional LCM-SR with general psychopathology and negative thinking

	Unstandardised	Standardised		
Between-person	*b* (SE)	β	SE	*p*
Mean				
P Intercept	0.027 (0.017)			
P Slope	**0.023 (0.008) ****			
NT Intercept	**-0.195 (0.018) *****			
NT Slope	**0.097 (0.008) *****			
Variance				
P Intercept	**0.290 (0.083) *****			
P Slope	**0.032 (0.015) ***			
NT Intercept	**0.351 (0.050) *****			
NT Slope	**0.034 (0.011) ****			
Covariances				
P Intercept with P Slope	0.002 (0.029)	0.024	0.320	0.941
P Intercept with NT Intercept	**0.205 (0.046)*****	**0.658**	**0.077**	**<.001**
P Intercept with NT Slope	-0.012 (0.015)	-0.125	0.135	0.353
NT Intercept with Slope NT	**-0.031 (0.017)**	**-0.288**	**0.102**	**0.005**
NT Intercept with Slope P	-0.003 (0.016)	-0.025	0.148	0.864
P Slope with NT Slope	0.011 (0.008)	0.342	0.177	0.053
Within-person	*b* (SE)	β	SE	*p*
Autoregressive coefficients				
P T1 -> P T2	0.185 (0.098)	0.169	0.100	0.091
P T2 -> P T3	**0.220 (0.055)*****	**0.218**	**0.052**	**<.001**
P T3 -> P T4	0.070 (0.121)	0.084	0.139	0.544
NT T1 -> NT T2	0.131 (0.069)	0.116	0.064	0.070
NT T2 -> NT T3	0.131 (0.069)	0.122	0.065	0.061
NT T3 -> NT T4	0.131 (0.069)	**0.159**	**0.078**	**0.042**
Cross-lag coefficients				
NT T1 -> P T2	0.097 (0.051)	0.077	0.043	0.070
NT T2 -> P T3	0.097 (0.051)	0.087	0.046	0.059
NT T3 -> P T4	0.097 (0.051)	0.112	0.059	0.058
P T1 -> NT T2	**0.105 (0.04)****	**0.107**	**0.044**	**0.015**
P T2 -> NT T3	**0.105 (0.04)****	**0.109**	**0.043**	**0.011**
P T3 -> NT T4	**0.105 (0.04)****	**0.134**	**0.054**	**0.013**
Concurrent coefficients				
NT T1 -> P T1	**0.133 (0.046)****	**0.399**	**0.089**	**<.001**
NT T2 -> P T2	**0.128 (0.02)*****	**0.324**	**0.042**	**<.001**
NT T3 -> P T3	**0.128 (0.02)*****	**0.305**	**0.038**	**<.001**
NT T4 -> P T4	**0.128 (0.02)*****	**0.442**	**0.056**	**<.001**

Notes. P = general psychopathology; NT = negative thinking. Study cohort, sex, and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

Table S8 Results of conditional LCM-SR between general psychopathology and anxiety sensitivity

	Unstandardised	Standardised		
Between-person	*b* (SE)	β	SE	*p*
Mean				
P Intercept	0.035 (0.017) *			
P Slope	0.016 (0.008) *			
AS Intercept	-0.046 (0.011) ***			
AS Slope	-			
Variance				
P Intercept	0.286 (0.067) ***			
P Slope	0.047 (0.024) ***			
AS Intercept	0.126 (0.013) ***			
AS Slope	-			
Covariances				
P Intercept with P Slope	0.002 (0.024)			
P Intercept with AS Intercept	0.070 (0.012)***			
P Intercept with AS Slope	-			
AS Intercept with Slope AS	-			
AS Intercept with Slope P	0.006 (0.005)			
P Slope with AS Slope	-			
Within-person	*b* (SE)	β	SE	*p*
Autoregressive coefficients				
P T1 -> P T2	0.231 (0.083)**	0.203	0.083	0.015
P T2 -> P T3	0.204 (0.044)***	0.228	0.046	<.001
P T3 -> P T4	-0.131 (0.153)	-0.192	0.257	0.454
AS T1 -> AS T2	0.123 (0.046)**	0.113	0.041	0.007
AS T2 -> AS T3	0.123 (0.046)**	0.114	0.044	0.009
AS T3 -> AS T4	0.123 (0.046)**	0.128	0.048	0.008
Cross-lag coefficients				
AS T1 -> P T2	0.080 (0.037)*	0.055	0.026	0.032
AS T2 -> P T3	0.080 (0.037)*	0.067	0.031	0.031
AS T3 -> P T4	0.080 (0.037)*	0.105	0.054	0.052
P T1 -> AS T2	0.035 (0.027)	0.042	0.031	0.180
P T2 -> AS T3	0.035 (0.027)	0.044	0.033	0.186
P T3 -> AS T4	0.035 (0.027)	0.041	0.031	0.193
Concurrent coefficients				
AS T1 -> P T1	0.095 (0.013)***	0.319	0.04	<.001
AS T2 -> P T2	0.078 (0.011)***	0.219	0.029	<.001
AS T3 -> P T3	0.078 (0.011)***	0.230	0.03	<.001
AS T4 -> P T4	0.078 (0.011)***	0.347	0.09	<.001

Notes. P = general psychopathology; AS = anxiety sensitivity. Study cohort, sex, and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

Table S9 Results for conditional LCM-SR between general psychopathology and impulsivity

	Unstandardised	Standardised		
Between-person	*b* (SE)	β	SE	*p*
Mean				
P Intercept	0.028 (0.017)			
P Slope	**0.021 (0.008) ****			
IMP Intercept	**0.270 (0.019) *****			
IMP Slope	-0.013 (0.009)			
Variance				
P Intercept	**0.270 (0.089) ****			
P Slope	**0.045 (0.016) ****			
IMP Intercept	**0.317 (0.075) *****			
IMP Slope	0.013 (0.017)			
Covariances				
P Intercept with P Slope	0.008 (0.032)	0.074	0.323	0.818
P Intercept with IMP Intercept	**0.124 (0.051)***	0.445	0.112	**<.001**
P Intercept with IMP Slope	0.008 (0.017)	0.149	0.365	0.683
IMP Intercept with Slope IMP	0.002 (0.026)	0.025	0.448	0.956
IMP Intercept with Slope P	0.017 (0.018)	0.149	0.18	0.408
P Slope with IMP Slope	-0.008 (0.008)	-0.361	0.535	0.499
Within-person	*b* (SE)	β	SE	*p*
Autoregressive coefficients				
P T1 -> P T2	**0.233 (0.092)***	0.208	0.096	0.031
P T2 -> P T3	**0.202 (0.049)*****	**0.228**	**0.05**	**<.001**
P T3 -> P T4	-0.136 (0.169)	-0.200	0.287	0.485
IMP T1 -> IMP T2	0.109 (0.074)	0.103	0.073	0.161
IMP T2 -> IMP T3	0.109 (0.074)	0.108	0.073	0.143
IMP T3 -> IMP T4	0.109 (0.074)	0.113	0.073	0.121
Cross-lag coefficients				
IMP T1 -> P T2	**0.072 (0.033)***	**0.071**	**0.035**	**0.040**
IMP T2 -> P T3	**0.072 (0.033)***	**0.085**	**0.040**	**0.032**
IMP T3 -> P T4	**0.072 (0.033)***	**0.127**	**0.065**	**0.050**
P T1 -> IMP T2	0.094 (0.048)	0.081	0.044	0.069
P T2 -> IMP T3	0.094 (0.048)	0.089	0.046	0.054
P T3 -> IMP T4	0.094 (0.048)	0.083	0.045	0.067
Concurrent coefficients				
IMP T1 -> P T1	**0.155 (0.052)****	**0.354**	**0.079**	**<.001**
IMP T2 -> P T2	**0.121 (0.021)*****	**0.243**	**0.036**	**<.001**
IMP T3 -> P T3	**0.121 (0.021)*****	**0.272**	**0.038**	**<.001**
IMP T4 -> P T4	**0.121 (0.021)*****	**0.413**	**0.104**	**<.001**

Notes. P = general psychopathology; IMP = impulsivity. Study cohort, sex, and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

Table S10 Results of conditional LCM-SR between general psychopathology and sensation seeking

	Unstandardised	Standardised		
Between-person	*b* (SE)	β	SE	*p*
Mean				
P Intercept	0.028 (0.017)			
P Slope	**0.031 (0.008) ****			
SS Intercept	-0.007 (0.014)			
SS Slope	0.003 (0.007)			
Variance				
P Intercept	**0.337 (0.089) *****			
P Slope	**0.067 (0.017) *****			
SS Intercept	**0.245 (0.022) *****			
SS Slope	**0.032 (0.0007) *****			
Covariances				
P Intercept with P Slope	-0.018 (0.033)	-0.123	0.196	0.531
P Intercept with SS Intercept	-0.003 (0.021)	-0.012	0.074	0.869
P Intercept with SS Slope	0.002 (0.009)	0.016	0.086	0.85
SS Intercept with Slope SS	**-0.023 (0.009)***	**-0.264**	**0.071**	**<.001**
SS Intercept with Slope P	0.000 (0.009)	-0.002	0.069	0.977
P Slope with SS Slope	-0.007 (0.004)	-0.158	0.093	0.089
Within-person	*b* (SE)	β	SE	*p*
Autoregressive coefficients				
P T1 -> P T2	0.200 (0.127)	0.166	0.120	0.168
P T2 -> P T3	**0.183 (0.039)***	**0.209**	**0.041**	**<.001**
P T3 -> P T4	-0.306 (0.231)	-0.800	1.315	0.543
SS T1 -> SS T2	0.020 (0.072)	0.015	0.052	0.777
SS T2 -> SS T3	0.020 (0.072)	0.020	0.069	0.775
SS T3 -> SS T4	0.020 (0.072)	0.025	0.086	0.772
Cross-lag coefficients				
SS T1 -> P T2	-0.013 (0.043)	-0.007	0.023	0.765
SS T2 -> P T3	-0.013 (0.043)	-0.011	0.037	0.763
SS T3 -> P T4	-0.013 (0.043)	-0.030	0.096	0.750
P T1 -> SS T2	-0.028 (0.031)	-0.031	0.034	0.367
P T2 -> SS T3	-0.028 (0.031)	-0.035	0.039	0.366
P T3 -> SS T4	-0.028 (0.031)	-0.038	0.042	0.368
Concurrent coefficients				
SS T1 -> P T1	-0.005 (0.02)	-0.023	0.096	0.813
SS T2 -> P T2	0.003 (0.01)	0.009	0.029	0.759
SS T3 -> P T3	0.003 (0.01)	0.010	0.032	0.760
SS T4 -> P T4	0.003 (0.01)	0.051	0.280	0.855

Notes. P = general psychopathology; SS = sensation seeking. Study cohort, sex, and age at T1 included as covariates. *p<.05, **p<.01, ***p<.001

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Appendix H

Supplementary materials for Chapter 5

Supplementary Methods

Indicators of psychopathology

Table A1 below provides the item wording and coding of responses, and the corresponding factor of psychopathology.

Table M1 Psychopathology indicators and corresponding factor organised by source measure

Factor	Item ID	Item / description	Values	Value Labels
Conduct/inattention	SD2	I am restless. I cannot stay still for long.	0	Not true
	SD2		1	Somewhat true or Certainly true
Distress	SD3	I get a lot of headaches, stomach-aches, or sickness.	0	Not true
	SD3		1	Somewhat true or Certainly true
Conduct/inattention	SD5	I get very angry and often lose my temper.	0	Not true
	SD5		1	Somewhat true or Certainly true
Distress	SD8	I worry a lot.	0	Not true
	SD8		1	Somewhat true or Certainly true
Conduct/inattention	SD10	I am constantly fidgeting or squirming.	0	Not true
	SD10		1	Somewhat true or Certainly true
Conduct/inattention	SD12	I fight a lot. I can make other people do what I want.	0	Not true
	SD12		1	Somewhat true or Certainly true
Distress	SD13	I am often unhappy, down-hearted, or tearful.	0	Not true
	SD13		1	Somewhat true or Certainly true
Conduct/inattention	SD15	I am easily distracted. I find it difficult to concentrate.	0	Not true
	SD15		1	Somewhat true or Certainly true
Fear	SD16	I am nervous in new situations. I easily lose confidence.	0	Not true
	SD16		1	Somewhat true or Certainly true
Conduct/inattention	SD18	I am often accused of lying or cheating.	0	Not true
	SD18		1	Somewhat true or Certainly true
Fear	SD24	I have many fears. I am easily scared.	0	Not true
	SD24		1	Somewhat true or Certainly true
Conduct/inattention	SD22	I take things that are not mine from home, school or elsewhere.	0	Not true
	SD22		1	Somewhat true or Certainly true

Factor	Item ID	Item / description	Values	Value Labels
Alcohol use/harms	AUC2	How often do you have 5+ std drinks in the past 6 mths?	0	Never
	AUC2		1	Less than monthly, Once a month, 2-3 times a month, Weekly, Daily or almost daily
Alcohol use/harms	AUC3	In the past 6 mths, how many std drinks on a typical day?	0	None
	AUC3		1	1-2, 3-4, 5-6,7-9, 10+
		In the past 6 months how many times have you experienced the following as a consequence of drinking alcohol		
Alcohol use/harms	AH2	Caused shame or embarrassment to someone.	0	Never
	AH2		1	1-2 times, 3-4 times, 5+6 times, More than 6 times
Alcohol use/harms	AH3	Neglected my responsibilities.	0	Never
	AH3		1	1-2 times, 3-4 times, 5+6 times, More than 6 times
Alcohol use/harms	AH5	Noticed a change in my personality.	0	Never
	AH5		1	1-2 times, 3-4 times, 5+6 times, More than 6 times
Alcohol use/harms	AH6	Tried to cut down or quit drinking.	0	Never
	AH6		1	1-2 times, 3-4 times, 5+6 times, More than 6 times
Alcohol use/harms	AH7	Suddenly found myself in a place that I could not remember getting to.	0	Never
	AH7		1	1-2 times, 3-4 times, 5+6 times, More than 6 times
Alcohol use/harms	AH8	Felt I was going crazy.	0	Never
	AH8		1	1-2 times, 3-4 times, 5+6 times, More than 6 times
		In the last 4 weeks, about how often did you feel		
Fear	K61R	…nervous?	0	None of the time
	K61R		1	A little of the time, some of the time, most of the time, all of the time
Distress	K62R	… hopeless?	0	None of the time
	K62R		1	A little of the time, some of the time, most of the time, all of the time
Fear	K63R	… restless or fidgety?	0	None of the time
	K63R		1	A little of the time, some of the time, most of the time, all of the time
Distress	K64R	… so depressed that nothing could cheer you up?	0	None of the time
	K64R		1	A little of the time, some of the time, most of the time, all of the time
Distress	K65R	… that everything was an effort?	0	None of the time

Factor	Item ID	Item / description	Values	Value Labels
	K65 R		1	A little of the time, some of the time, most of the time, all of the time
Distress	K66 R	… worthless?	0	None of the time
	K66 R		1	A little of the time, some of the time, most of the time, all of the time

Note. SD = Strengths and Difficulties Questionnaire, AUC = patterns of alcohol use; AH = Rutgers's Alcohol Problem Index, K6 = Kessler Psychological Distress Scale (R indicates reverse scored item).

Measurement invariance

Moderated nonlinear factor analysis (MNLFA) was used to examine the measurement invariance of the psychopathology dimensions. MNLFA simultaneously assesses differential item functioning (DIF) and measurement invariance across multiple grouping variables (which can be either categorical or continuous), and ultimately aims to generate factor scores that have been corrected for measurement bias and can be used in subsequent analyses (Bauer, 2017; Curran et al., 2014). Building on the multiple groups and multiple-indicators-multiple-causes (MIMIC) approaches to measurement invariance, MNLFA evaluates DIF and mean and variance impact effects through moderation effects on model parameters in a sequential, iterative model building process. In the present study, the effects of age, sex, personality risk group (i.e., anxiety sensitivity, negative thinking, impulsivity, and sensation seeking) and intervention (i.e., *Preventure* or no *Preventure*) were assessed.

Analyses were conducted in Mplus version 8.4 for Mac (Muthén & Muthén, 2017), in combination with R packages aMNLFA (Gottfredson et al., 2019) and Mplus Automation (Hallquist & Wiley, 2018). All coding and output files are available online at https://osf.io/9haem/?view_only=28292fe33ad842599f5d66efd42027be. Drawing on the general procedures outlined by Bauer (2017) and Gottfredson et al. (2019), we conducted the analyses in three broad steps. Details of each step are described below and depicted in Figure S1.

Figure S1. Process for longitudinal multigroup measurement invariance with moderated nonlinear factor analyses (MNLFA) for a multidimensional model.
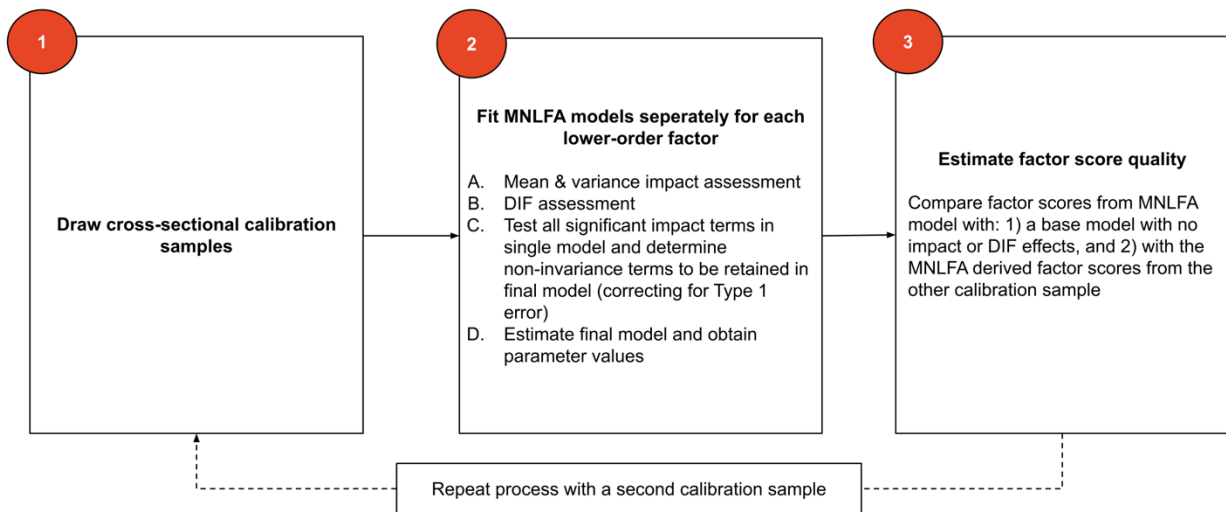
Step 1 involved drawing a cross-sectional calibration sample with one randomly selected observation per participant using the aMNLFA.sample function from the aMNLFA package. The use of a calibration sample strategy is necessary to preserve the assumption of independence, which is directly violated by longitudinal data (Curran et al., 2014). The MNLFA procedure described below was applied to two calibration samples, with the factor scores derived these samples compared in the final step.

In *Step 2,* MNLFA models were fit separately for each lower order factor, adopting the divide and conquer approach recommended by Bauer (2017). This step can be broken down into the following sub-steps:

2a. Estimated mean and variance impact models and examine impact effects (threshold to retain non-invariance effects is $p < 0.1$).

2b. Estimated and examined DIF effects (threshold to retain non-invariance terms is $p < .05$)

2c. Test all marginally significant terms in a single model and removed any remaining non-invariant terms, adjusting for Type 1 errors. For mean and variance impact terms, these were retained if p was less than .05, for DIF terms (loadings & intercepts) we applied a Benjamin-Hochberg correction. DIF terms where p values were lower than the BH correction were retained.

2d. Estimated final model and obtain parameter values.

Finally, *Step 3* was to evaluate the quality of the factor scores derived from the MNLFA models. First, we cross-validated the factor scores by examining the correlation

between factors scores obtained from the two calibration samples (Curran et al., 2014). A high correlation (e.g., r > .9) demonstrates the stability of estimated scores across samples. Second, we compared the factor scores estimates from the MNLFA models with scores from a CFA model with no DIF or impact effects to assess the influence of the non-invariance terms on the factor score estimates. A high correlation (e.g., r > .9) suggests that the model is invariant.

Supplementary Results

Structure of psychopathology and measurement invariance

Results from MNLFA models are provided in the supplementary materials. Longitudinal- and group-invariant factor scores generated from MNLFA models were highly correlated with a base model without non-invariance terms ($r = 0.93$ to 0.99, $P<.001$, supplementary tables S5.1 and S5.2). These high correlations suggest that the factor scores generated by our model are robust against non-invariance across age, intervention group and personality group. In addition, Mplus does not currently allow model constraints (i.e., non-invariance terms) to be specified when generating BPVs. As such, the base model without any non-invariance terms was used for intervention effect analyses.

Table S5.1 Correlations between lower-order factor scores produced by MNLFA and factor scores from base CFA model with no non-invariance terms with calibration sample 1

	Fear	Distress	Alcohol use/ harms	Conduct/ inattention
Fear (MNLFA)	0.98*			
Distress (MNLFA)		0.99*		
Alcohol use/ harms (MNLFA)			0.93*	
Conduct/ inattention (MNLFA)				0.99*

Note. * indicates *p*<.001. MNLFA models incorporate non-invariance terms to adjust for effects of age, sex, personality risk group and intervention (*Preventure* or *No Preventure*).

Table S5.2 Correlations between lower-order factor scores produced by MNLFA and factor scores from base CFA model with no non-invariance terms with calibration sample 2

	Fear	Distress	Alcohol use/ harms	Conduct/ inattention
Fear (MNLFA)	0.98*			
Distress (MNLFA)		0.99*		
Alcohol use/ harms (MNLFA)			0.95*	
Conduct/ inattention (MNLFA)				1.00*

Note. * indicates $P<.001$. MNLFA models incorporate non-invariance terms to adjust for effects of age, sex, personality risk group and intervention (*Preventure* or *No Preventure*).

Attrition analyses

Among high-risk students, only 38 (1.7%) were present at baseline only. There were no differences between participants who were present at baseline only compared to participants who completed any follow ups (Table S5.3). However, attrition was more likely to occur in the *Preventure* group compared to control (OR 2.32, 95% CI 1.07 to 5.81, p=0.048, Table S5.3). Students who missed any follow ups were more likely to have greater levels of conduct/inattention at baseline (OR 1.20. 95% CI 1.05 to 1.36, p=0.006, Table S5.4), compared to students who participated in all follow ups. There was no evidence of differential attrition in group x baseline psychopathology interaction analyses (Table S5.5).

Table S5.3 Logistic regressions comparing baseline characteristic analyses between participants who were absent for all follow-ups vs participants present at any follow-ups

		Any follow-ups	0 follow-ups	OR (95% CI)
General Psychopathology	Mean (SD)	0.1 (0.9)	0.4 (0.9)	1.37 (0.93-2.03, p=0.111)
Fear	Mean (SD)	0.4 (2.9)	1.1 (3.0)	1.09 (0.97-1.23, p=0.138)
Distress	Mean (SD)	0.5 (2.9)	1.3 (3.1)	1.09 (0.98-1.23, p=0.129)
Alcohol use/harms	Mean (SD)	0.0 (1.0)	0.1 (1.0)	1.09 (0.78-1.53, p=0.620)
Conduct/inattention	Mean (SD)	0.1 (1.2)	0.4 (1.2)	1.19 (0.90-1.58, p=0.227)
Sex	Male	426 (64.3)	27 (73.0)	-
	Female	237 (35.7)	10 (27.0)	0.67 (0.30-1.36, p=0.283)
Group	Control	228 (34.4)	7 (18.4)	-
	Preventure	435 (65.6)	31 (81.6)	**2.32 (1.07-5.81, p=0.048)**

Table S5.4 Logistic regressions comparing baseline characteristic analyses between participants who were present for all follow-ups vs participants absent at any follow-ups

		All follow-ups	Missed 1+	OR (95% CI)
General Psychopathology	Mean (SD)	0.1 (0.8)	0.2 (0.9)	1.12 (0.94-1.34, p=0.197)
Fear	Mean (SD)	0.4 (2.8)	0.5 (2.9)	1.02 (0.96-1.07, p=0.551)
Distress	Mean (SD)	0.4 (2.8)	0.7 (3.0)	1.04 (0.99-1.10, p=0.133)
Alcohol use/harms	Mean (SD)	0.0 (1.0)	0.1 (1.0)	1.08 (0.93-1.26, p=0.314)
Conduct/inattention	Mean (SD)	0.0 (1.1)	0.3 (1.2)	**1.20 (1.05-1.36, p=0.006)**
Sex	Male	204 (45.0)	249 (55.0)	-
	Female	128 (51.8)	119 (48.2)	0.76 (0.56-1.04, p=0.086)
Group	Control	136 (57.9)	99 (42.1)	-
	Preventure	196 (42.1)	270 (57.9)	**1.89 (1.38-2.60, p<0.001)**

Table S5.5 Logistic regressions comparing Group x baseline variable interactions between participants who were absent for all follow-ups vs participants present at any follow-ups, and participants who present for all follow-ups vs participants absent at any follow-ups

Group x Baseline variable	OR (95% CI), Any follow-ups (vs. 0 follow-ups)	OR (95% CI), All follow-ups (vs. Missed 1+)
General Psychopathology, Preventure	1.30 (0.47-3.56, p=0.611)	1.00 (0.68-1.46, p=0.999)
Fear, Preventure	1.03 (0.76-1.39, p=0.838)	0.98 (0.87-1.10, p=0.724)
Distress, Preventure	1.06 (0.79-1.42, p=0.689)	0.99 (0.88-1.10, p=0.805)
Alcohol use/harms, Preventure	1.41 (0.59-3.37, p=0.440)	1.04 (0.75-1.45, p=0.800)
Conduct/inattention, Preventure	1.52 (0.71-3.30, p=0.283)	1.06 (0.80-1.42, p=0.673)
Sex, Preventure	2.03 (0.30-13.47, p=0.452)	0.98 (0.48-1.98, p=0.946)

Exploratory analyses

Table S5.6 Fixed-effects coefficients from the mixed-effects models for general psychopathology and distress in the negative thinking subgroup (n=146, observations = 566)

General Psychopathology	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	0.17 (0.15)	.243	-0.12 to 0.46			
Main effects						
Preventure	0.26 (0.16)	.096	-0.05 to 0.57			
Time (years)	0.02 (0.06)	.745	-0.09 to 0.13			
Female	**0.58 (0.14)**	**<.001**	**0.31 to 0.85**			
Intervention effects						
Preventure x Time	-0.12 (0.07)	.107	-0.26 to 0.03			
Distress	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	0.67 (0.49)	.174	-0.30 to 1.63	0.12 (0.16)	.458	-0.19 to 0.42
Main effects						
Preventure	0.93 (0.53)	.081	-0.11 to 1.97	0.11 (0.18)	.527	-0.24 to 0.47
Time (years)	0.04 (0.19)	.810	-0.32 to 0.41	-0.01 (0.08)	.926	-0.17 to 0.15
Female	**2.05 (0.46)**	**<.001**	**1.15 to 2.95**	0.24 (0.14)	.090	-0.04 to 0.53
General psychopathology				**3.13 (0.07)**	**<.001**	**3.00 to 3.27**
Intervention effects						
Preventure x Time	-0.42 (0.24)	.078	-0.89 to 0.05	-0.06 (0.11)	.562	-0.28 to 0.15

Note. Time coded as baseline = 0, 6m= 0.5, 12m = 1, 24m = 2, 36m = 3. Results in the last three columns show mixed effects model for distress controlling for general psychopathology

Table S5.7 Fixed-effects coefficients from the mixed-effects models for general psychopathology and distress in the anxiety sensitivity subgroup (n=207, observations = 818)

General Psychopathology	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	0.01 (0.17)	.937	-0.32 to 0.34			
Main effects						
Preventure	0.01 (0.17)	.951	-0.32 to 0.35			
Time (years)	0.03 (0.05)	.543	-0.07 to 0.13			
Female	0.12 (0.14)	.406	-0.16 to 0.40			
Intervention effects						
Preventure x Time	0.01 (0.06)	.861	-0.11 to 0.13			
Fear	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	0.07 (0.56)	.906	-1.02 to 1.15	0.01 (0.16)	.925	-0.30 to 0.33
Main effects						
Preventure	0.06 (0.57)	.911	-1.05 to 1.17	0.04 (0.16)	.801	-0.28 to 0.36
Time (years)	0.11 (0.18)	.542	-0.25 to 0.47	0.01 (0.08)	.931	-0.15 to 0.17
Female	0.38 (0.48)	.433	-0.56 to 1.31	0.01 (0.12)	.931	-0.22 to 0.25
General psychopathology				**3.15 (0.05)**	**<.001**	**3.05 to 3.26**
Intervention effects						
Preventure x Time	-0.003 (0.22)	.991	-0.43 to 0.42	-0.03 (0.10)	.766	-0.22 to 0.16
Distress	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	0.07 (0.56)	.906	-1.02 to 1.15	0.06 (0.16)	.729	-0.26 to 0.37
Main effects						
Preventure	0.06 (0.57)	.911	-1.05 to 1.17	-0.06 (0.17)	.711	-0.40 to 0.27
Time (years)	0.11 (0.18)	.542	-0.25 to 0.47	-0.03 (0.08)	.744	-0.18 to 0.13
Female	0.38 (0.48)	.433	-0.56 to 1.31	0.03 (0.12)	.782	-0.21 to 0.28
General psychopathology				**3.19 (0.05)**	**.000**	**3.08 to 3.30**
Intervention effects						
Preventure x Time	0.09 (0.20)	.647	-0.30 to 0.49	0.05 (0.09)	.623	-0.14 to 0.23

Note. Time coded as baseline = 0, 6m= 0.5, 12m = 1, 24m = 2, 36m = 3. Results in the last three columns show mixed effects models for fear and distress controlling for general psychopathology

Table S5.8 Fixed-effects coefficients from the mixed-effects models for general psychopathology and conduct/inattention in the impulsivity subgroup (n=163, observations = 620)

General Psychopathology	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	0.06 (0.14)	.669	-0.22 to 0.35			
Main effects						
Preventure	0.07 (0.16)	.676	-0.24 to 0.37			
Time (years)	0.07 (0.05)	.163	-0.03 to 0.18			
Female	0.26 (0.14)	.060	-0.01 to 0.54			
Intervention effects						
Preventure x Time	**-0.16 (0.07)**	**.024**	**-0.29 to -0.02**			
Conduct/inattention	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	0.34 (0.22)	.114	-0.08 to 0.66	0.32 (0.17)	.065	-0.02 to 0.66
Main effects						
Preventure	0.15 (0.23)	.509	-0.30 to 0.00	0.09 (0.19)	.641	-0.28 to 0.45
Time (years)	0.04 (0.07)	.578	-0.10 to 0.45	-0.01 (0.06)	.833	-0.14 to 0.11
Female	0.04 (0.21)	.837	-0.37 to 0.11	-0.19 (0.16)	.243	-0.51 to 0.13
General psychopathology				**0.76 (0.06)**	**<.001**	**0.64 to 0.87**
Intervention effects						
Preventure x Time	-0.19 (0.10)	.058	-0.38 to 0.13	-0.07 (0.09)	.435	-0.24 to 0.10

Note. Time coded as baseline = 0, 6m= 0.5, 12m = 1, 24m = 2, 36m = 3. Results in the last three columns show mixed effects model for conduct/inattention controlling for general psychopathology

Table S5.9 Fixed-effects coefficients from the mixed-effects models for general psychopathology and alcohol use/harms in the sensation seeking subgroup (n=185, observations = 742)

General Psychopathology	b(se)	p	95% CI	b(se)	p	95% CI
Intercept	**-0.39 (0.16)**	**.014**	**-0.70 to -0.08**			
Main effects						
Preventure	0.09 (0.17)	.599	-0.24 to 0.42			
Time (years)	**0.13 (0.05)**	**.008**	**0.03 to 0.22**			
Female	**0.48 (0.14)**	**.001**	**0.20 to 0.76**			
Intervention effects						
Preventure x Time	-0.07 (0.06)	.247	-0.19 to 0.05			
Alcohol use/harms	*b(se)*	*p*	*95% CI*	*b(se)*	*p*	*95% CI*
Intercept	-0.16 (0.17)	.352	-0.49 to 0.17	-0.04 (0.16)	.784	-0.36 to 0.28
Main effects						
Preventure	0.13 (0.18)	.477	-0.23 to 0.49	0.11 (0.18)	.543	-0.24 to 0.46
Time (years)	**0.25 (0.06)**	**<.001**	**0.13 to 0.37**	**0.21 (0.06)**	**.001**	**0.09 to 0.33**
Female	0.04 (0.15)	.787	-0.26 to 0.34	-0.09 (0.15)	.535	-0.38 to 0.20
General psychopathology				**0.31 (0.05)**	**<.001**	**0.21 to 0.41**
Intervention effects						
Preventure x Time	-0.01 (0.08)	.931	-0.17 to 0.15	0.01 (0.08)	.858	-0.14 to 0.17

Note. Time coded as baseline = 0, 6m= 0.5, 12m = 1, 24m = 2, 36m = 3. Results in the last three columns show mixed effects model for alcohol use/harms controlling for general psychopathology

Table S5.10 Fixed-effects coefficients from the mixed-effects models for general psychopathology, fear, distress, alcohol use/harms and conduct/inattention in the high risk + low risk sample (n=1,605, observations = 6,471)

	Model 1			Model 2 (controlling for general psychopathology)		
General Psychopathology	*b(se)*	*p*	*95% CI*	*b(se)*	*p*	*95% CI*
Intercept	**-0.26 (0.07)**	**.001**	**-0.40 to -0.11**			
Main effects						
Preventure	0.11 (0.08)	.178	-0.05 to 0.26			
Time (years)	**0.07 (0.02)**	**<.001**	**0.04 to 0.10**			
Female	**0.30 (0.06)**	**<.001**	**0.18 to 0.43**			
Intervention effects						
Preventure x Time	**-0.04 (0.02)**	**.034**	**-0.09 to -0.0003**			
Fear	*b(se)*	*p*	*95% CI*	*b(se)*	*p*	*95% CI*
Intercept	**-0.78 (0.24)**	**.001**	**-1.26 to -0.31**	0.02 (0.05)	.729	-0.09 to 0.13
Main effects						
Preventure	0.28 (0.26)	.275	-0.22 to 0.79	-0.05 (0.06)	.428	-0.17 to 0.07
Time (years)	**0.20 (0.06)**	**.001**	**0.09 to 0.32**	-0.01 (0.03)	.581	-0.07 to 0.04
Female	**0.98 (0.21)**	**<.001**	**0.57 to 1.39**	0.02 (0.04)	.640	-0.07 to 0.11
General psychopathology				**3.15 (0.02)**	**<.001**	**3.12 to 3.19**
Intervention effects						
Preventure x Time	-0.13 (0.07)	.076	-0.28 to 0.01	0.01 (0.03)	.728	-0.05 to 0.08
Distress	*b(se)*	*p*	*95% CI*	*b(se)*	*p*	*95% CI*
Intercept	**-0.89 (0.25)**	**.000**	**-1.39 to -0.40**	-0.08 (0.06)	.167	-0.19 to 0.03
Main effects						
Preventure	0.40 (0.27)	.140	-0.13 to 0.92	0.05 (0.06)	.382	-0.07 to 0.17
Time (years)	**0.23 (0.06)**	**<.001**	**0.12 to 0.34**	0.01 (0.03)	.624	-0.04 to 0.06
Female	**1.09 (0.22)**	**<.001**	**0.66 to 1.51**	**0.10 (0.05)**	**.024**	**0.01 to 0.19**
General psychopathology				**3.19 (0.02)**	**<.001**	**3.15 to 3.23**
Intervention effects						
Preventure x Time	**-0.16 (0.07)**	**.023**	**-0.30 to -0.02**	-0.02 (0.03)	.570	-0.09 to 0.05
Alcohol use/harms	*b(se)*	*p*	*95% CI*	*b(se)*	*p*	*95% CI*
Intercept	**-0.35 (0.08)**	**<.001**	**-0.49 to -0.20**	-0.28 (0.07)	**<.001**	-0.42 to -0.13
Main effects						
Preventure	**0.18 (0.08)**	**.026**	**0.02 to 0.34**	0.15 (0.08)	.053	0.00 to 0.31
Time (years)	**0.24 (0.02)**	**<.001**	**0.19 to 0.28**	0.22 (0.02)	**<.001**	0.17 to 0.26
Female	0.10 (0.06)	.094	-0.02 to 0.23	0.02 (0.06)	.715	-0.10 to 0.14
General psychopathology				0.28 (0.02)	**<.001**	0.25 to 0.31
Intervention effects						
Preventure x Time	**-0.08 (0.03)**	**.007**	**-0.14 to -0.02**	**-0.07 (0.03)**	**.021**	**-0.12 to -0.01**
Conduct/inattention	*b(se)*	*p*	*95% CI*	*b(se)*	*p*	*95% CI*
Intercept	**-0.23 (0.09)**	**.010**	**-0.40 to -0.05**	0.00 (0.05)	.937	-0.11 to 0.10

Main effects

Preventure	0.12 (0.09)	.217	-0.07 to 0.30	0.02 (0.06)	.749	-0.09 to 0.13
Time (years)	**0.07 (0.03)**	**.006**	**0.02 to 0.12**	0.01 (0.02)	.519	-0.03 to 0.06
Female	**0.17 (0.08)**	**.033**	**0.01 to 0.33**	**-0.10 (0.04)**	**.031**	**-0.18 to -0.01**
General psychopathology				**0.84 (0.02)**	**<.001**	**0.81 to 0.87**

Intervention effects

Preventure x Time	-0.04 (0.03)	.263	-0.10 to 0.03	0.0002 (0.03)	.992	-0.05 to 0.05

Note. Time coded as baseline = 0, 6m= 0.5, 12m = 1, 24m = 2, 36m = 3. Results in the last three columns show mixed effects models for fear, distress, alcohol use/harms and conduct/inattention controlling for general psychopathology

Supplementary References

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Appendix I

Analysis code

The analysis code, including R Scripts and Mplus output files, for each empirical chapter are available at the below links:

Chapter 3	https://osf.io/cq2rz
Chapter 4	https://osf.io/xdftb
Chapter 5	https://osf.io/9haem