Objective and Subjective Experiences and their Associations with Mental Health: a Genetically Informed Approach

by

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Declaration

I, Emma Ruby Francis, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Emma Ruby Francis

Abstract

Background. Subjective and objective measures are often used in psychological and epidemiological research to capture an individual's experience and understand how subjectively and objectively assessed risk factors subsequently associate with (mental) health outcomes. There is growing evidence however, that subjective and objective measures may not be highly correlated and may be differentially associated with mental health. Why this discrepancy between subjective and objective measures arises in the first place remains unclear. In particular, the role of underlying mental health vulnerabilities in altering individual perception of experiences and, thus, contributing to this discrepancy, remains to be elucidated. This thesis proposes three studies to address both the consequences and the origins of the discrepancy between subjective and objective measures of risk factors relevant to mental health.

Aims and Methods. The first study is a meta-analysis that aims to determine the agreement between subjective and objective measures of childhood adversities (bullying victimisation, childhood maltreatment, neighbourhood adversity) and examine whether these measures differentially predict psychopathology (**Chapter 2**). My second and third studies use data from the Avon Longitudinal Study of Parents and Children to address the origins of those discrepancies for several relevant risk factors relevant to mental health. Using structural equation models, I first test whether underlying mental health vulnerabilities, proxied by polygenic scores, predict the experience of bullying victimisation as captured by self-reports. To better capture the specificity of self versus other reports, I account

for reports from mothers and teachers (**Chapter 3**). In my final study, I turned to a putative risk factor for mental health, i.e., body-related dissatisfaction, for which I have objectively measured anthropometric counterparts (e.g. waist circumference versus waist dissatisfaction). I test whether the genetic predisposition to mental health can predict body-related dissatisfaction after accounting for the corresponding objective anthropometric measures (**Chapter 4**).

Results. My thesis revealed four key findings: (1) subjective and objective measures of adversities are not highly correlated, (2) the effects of childhood adversities on psychopathology are primarily driven by a person's subjective experience, (3) polygenic scores for certain mental health vulnerabilities predict self-reported bullying victimisation, over and above multi-informant reports, revealing both typical evocative gene-environment correlations but also suggesting that mental health vulnerabilities shape the perception of adverse experiences, and (4) polygenic scores for mental health vulnerabilities influence weight and waist dissatisfaction, beyond corresponding anthropometric measures, demonstrating how mental health vulnerabilities shape the perception of one's own body.

Conclusion. This thesis provides novel insights showing that (i) subjective measures of experiences are more strongly associated with mental health than corresponding objective measures, and (ii) mental health vulnerabilities can influence a person's perception of their experiences, beyond the objectively captured measure. Interventions that target the subjective appraisal of adversities and other risk factors may reduce the risk of subsequent psychopathology.

Impact statement

This PhD research has generated novel insights into the roles of (i) subjective and objective experiences of childhood adversity in psychopathology, and (ii) genetic predisposition for mental health vulnerabilities in subjective perceptions of experiences. As such, my findings have potential clinical and research implications.

Clinical implications

Prior to my thesis, it remained unclear whether subjective and objective measures differentially predict psychopathology. The meta-analytic findings in my second chapter suggest that the effects of childhood adversity on mental health are likely to be driven by a person's subjective appraisal of the event. As such, clinical interventions that target perception and memories of adversities may reduce the consolidation of adverse experiences into subsequent psychopathology. In my third and fourth chapter, I demonstrated that genetic predisposition to mental health vulnerabilities shape one's perception of mental health relevant risk factors. Therefore, findings highlight potential targets for intervention. For example, clinical interventions that target traits, such as neuroticism, may benefit children and adolescence who are susceptible to negative thoughts about their body.

Research implications

From a research perspective, my findings show the importance of jointly modelling subjective and objective measures when assessing the consequences of risk factors. In addition, they demonstrate the need to appropriately account

for (genetic) confounding when assessing the role of such risk factors in predicting subsequent mental health. My thesis findings show it is imperative that future research tests and addresses the underlying aetiological mechanisms and biases that may explain the stronger association found between subjective measures and psychopathology.

Open science practices

I am committed to open science practices. For example, I have shared all code used to produce the results from this thesis on GitHub, as well as the dataset used for my meta-analysis. I have also pre-registered my meta-analysis.

Dissemination

I have actively sought ways to disseminate my research to others in the field and beyond. First, I have presented at the Life History Research Society Meeting held at University of Oxford, UK (July, 2022), The Society for Research in Child Development held in Salt Lake City, Utah, USA (March, 2023), and at the Behavioural Genetics Association held in Murcia, Spain (June, 2023). Second, my PhD research was selected by the Faculty of Brain Sciences at University College London to be featured for mental health awareness week. Third, I was invited to discuss my meta-analysis on The Association for Child and Adolescent Mental Health podcast with listeners such as educators, clinicians and fellow researchers (2,243 listens across 59 different countries at the time of PhD submission). Finally, my meta-analysis (Chapter 3, published in the Journal of Child Psychology and Psychiatry [JCPP]) is one of the top 10 most downloaded JCPP articles in 2023, demonstrating the effectiveness of my ability to disseminate my research to fellow researchers.

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   Emma R. Francis, Jean-Baptiste Pingault, and Jessie R. Baldwin conceived and designed the meta-analysis; screening of eligible studies was carried out by Emma R. Francis, and Sarah E. Stock; extracting data was carried out by Emma R. Francis, Anna Tsaligopoulou and Jessie R. Baldwin; Emma R. Francis carried out the statistical analysis, with input from Jessie R. Baldwin; Emma R. Francis wrote and revised the manuscript; All authors critically reviewed the manuscript.

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   Chapter 2

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Francis, E.R.,* & Franklin, H.D.* (2023). UK PhD students' call to action amid the cost-of-living crisis. *Nature Human Behaviour*, 1-2.

Francis, E.R., Cadar, D., Steptoe, A., & Ajnakina, O. (2022). Interplay between polygenic propensity for ageing-related traits and the consumption of fruits and vegetables on future dementia diagnosis. *BMC psychiatry*, 22(1), 75.

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***** Denotes shared first authorship on the publications listed.

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Chapter 1 Introduction

1.1 Summary

Subjective and objective measures are often used to capture early life risk factors for mental health. The following chapter will introduce the methodological differences between these measures and the consequences of apparent discrepancies. In particular, I will discuss how it remains unclear whether subjective and objective measures show agreement and differentially predict psychopathology. Additionally, this chapter will explore why discrepancies between subjective and objective measures exist. Specifically, how genetic predisposition to mental health vulnerabilities may contribute to shaping one's perception of mental health relevant risk factors. The use of genetically informed approaches (i.e., using polygenic scores as genetic proxies for mental health vulnerabilities) to delineate the specific mechanisms that may contribute to subjective appraisal of experiences will be discussed.

Finally, this chapter will conclude by outlining the three studies carried out that sought to better understand (1) the relationship between subjective and objective measures of adverse experiences in mental health and (2) whether genetic predispositions to mental health vulnerabilities might affect child and adolescents' subjective experience of mental health risk factors.

1.2 Subjective and objective measures of experiences

Subjective and objective measures of experiences are used in psychological and epidemiological research, as well as in clinical practice.

Subjective measures. Subjective measures reflect a person's perception, appraisal, and memory of an experience or event. Capturing subjective experience of mental health relevant risk factors may, for example, involve asking an individual to self-report whether or not they were exposed to bullying. The subjective appraisal of an experience may also involve an individual sharing how they perceive their own body, for example by rating their level of body dissatisfaction. Various methods are used to capture subjective measures. One example may involve an adolescent being interviewed and asked to report their experiences (e.g., the modified Bullying and Friendship Interview Schedule to assess experience of bullying victimisation; Wolke et al., 2001). Another approach commonly employed is asking the child to self-report using a questionnaire (e.g., to ask about their level of satisfaction with their weight, waist or figure; Bornioli et al., 2019). It is worth noting that there is presently no agreed "gold standard" to measure subjective experiences. Some assessments administered may have demonstrated adequate validity whilst others may be simple unstandardised assessments that nevertheless can provide insight into individuals' perception.

Objective measures. In contrast to subjective measures, objective measures aim to capture the actual occurrence of an exposure or outcome in a manner that is free from bias arising from the subjective perception, appraisal, or memory of

that exposure. There are several types of objective measures that may be used, depending on the exposure or trait of interest. For example, objective measures of adverse childhood experiences include official records, such as crime records to assess violence exposure (Goldman-Mellor et al., 2016), child protection records to assess child maltreatment (Everson et al., 2008), or legal records demonstrating parental divorce or separation. For other adverse childhood experiences (e.g., bullying victimisation), official records do not exist, and so researchers may choose to capture reports from multiple informants (e.g., teacher-, parent- and peer-reports; Kochel et al., 2017), to identify consensus across informants, and minimise biases from any single reporter. For other traits (e.g., physical characteristics) objective assessments capture anthropometric measures where little subjectivity comes into play (e.g., the use of standardised scales to capture weight in kilograms (kg) and height in metres squared (m2) to calculate body mass index).

1.3 Methodological considerations

Subjective and objective measures have key methodological differences. This encapsulates distinct strengths supporting the use of these approaches to capture experiences, but also potential drawbacks which are important to be aware of.

***Limitations of subjective measures*.** First, the use of self-report to capture experiences can involve potential biases in reporting (Colman et al., 2016; Hardt & Rutter, 2004). Notably, recall bias due to current psychopathology may lead to greater self-reporting of adverse childhood experiences. Previous research examined the relationship between depression symptoms and self-reported

childhood maltreatment over time (Goltermann et al., 2023). Authors found that, within individuals, increases in depressive symptoms were associated with greater reporting of childhood trauma. This suggests that subjects with higher levels of depressive symptoms at the time of the self-report may have cognitive biases which lead to them being more prone to recalling experiences as negative. Second, personality traits of the individual may also influence subjective self-reports of experiences. Using the Dunedin cohort (n=1,037), prior research examined the agreement between childhood adversity prospectively measured throughout childhood (via largely objective measures, such as social service records as well as parent interviews) and retrospectively self-reported in adulthood, as well as the relative associations with midlife health outcomes (Reuben et al., 2016). Authors found that individuals who were high in neuroticism had retrospectively self-reported higher levels of adversity than were prospectively recorded, while participants with higher levels of agreeableness were less likely to self-report adversity than that was prospectively recorded. Taken together, findings suggest that an individuals' personality may influence the subjective reporting of experiences by biasing memory recall or self-appraisal of experiences.

***Limitations of objective measures*.** First, objective assessments relying on official records, such as medical, crime and court records, may not be sensitive enough to capture all experiences of adversities (Danese & Widom, 2021) and will likely identify only the most serious cases requiring intervention (Danese & Widom, 2020). This could lead to true cases of adversities being missed (i.e., resulting in a high rate of false negatives). Second, such objective measures may

not be readily obtained or integrated into cohort studies, for comparison with subjective self-report measures. This is in large part due to concerns around confidentiality and barriers to accessing relevant information, such as with court records (Danese & Widom, 2020). Third, it is important to consider that even measures considered to be 'objective' may still be partly influenced by an individual's perception of their experiences. For example, if children seek out support from official services for maltreatment, or confide in other informants (e.g., peers, teachers) about bullying. Similarly, more objective measures (in the sense of being more independent from the self) as obtained through other informants (for example, parents, teachers, and peers for measures of bullying) may still be biased by the target individual's perceptions (e.g. if the informant is influenced by reports from the target individual). On the other hand, there are measures (such as Body Mass Index) that do not need to rely on informants reporting their experiences. As such, the use of objective measures may capture accurate information not otherwise obtained through using subjective measures.

Despite these limitations, there are advantages of using subjective and objective measures to capture experiences that should be considered.

Advantages of subjective measures. Subjective self-report measures are a valuable way to capture the individuals' perception, thoughts and feelings about their experiences, which is essential in psychology and psychiatry when so much of the outcomes themselves are inherently subjective. Additionally, subjective measures are increasingly being used in epidemiological research as they are relatively easy and inexpensive to administer (Sassenberg & Ditrich, 2019). When compared to objective measures, such as court records, subjective

measures can be obtained through less in-depth phenotyping (e.g., self-reported bullying victimisation obtained using brief questionnaires; Wolke et al., 2001) or “minimal” phenotyping involving capturing self-report from single data points (e.g., self-reported weight dissatisfaction using a single question; Bornioli et al., 2019). Due to being quick to perform, larger sample sizes featuring subjective measures can be attained. This can be advantageous when aiming to increase statistical power.

***Advantages of objective measures*.** Objective measures allow researchers to more accurately identify true cases that are unlikely to be influenced by the perception of the individual. For example, official records are unlikely to wrongly classify an unexposed child as being exposed to adversity (i.e., high specificity). Due to the process of substantiation, these records will likely provide clear evidence that a case of adversity (e.g., childhood maltreatment) has occurred. Where official records are not available, assessing an experience using multiple informants, for example peers, parents and teachers, allows for a wider degree of information to be captured, that may otherwise not be identified or reported if researchers solely relied upon subjective self-report of experiences. This can minimise misclassification and relational bias that can occur when relying on single informants (Ladd & Kochenderfer-Ladd, 2002). Furthermore, to assess the relationship between childhood adversity and self-reported psychopathology, using more objective measures of adversity (e.g., child protection service records), ensures that any observed associations will not be explained by recall bias or shared method variance as a function of the same reporter.

1.4 Poor agreement between subjective and objective measures

In mental health research, there has historically been a lack of consideration of the methodological differences between subjective and objective measures of experiences, with researchers assuming equivalence between both measures. In other words, it is often assumed that both measures identify the same individuals exposed to negative experiences and as such, can be used interchangeably. For example, an assumption would be that official records for maltreatment identify the same subjects who self-report exposure to maltreatment. This has largely been due to the fact that many cohort studies do not include both types of measures, which has prevented researchers from systematically comparing subjective and objective measures. However, emerging meta-analytical evidence capitalising on studies that do include both types of measures suggests that they poorly overlap.

Specifically, a systematic review and meta-analysis featuring 16 studies and 25,471 participants examined the agreement between prospective and retrospective measures of child maltreatment (Baldwin et al., 2019). Prospective measures tended to include more objective assessments such as official records and research worker observations (as well as parent reports), while retrospective measures were based on self-reported questionnaires and interviews, thereby capturing the subjective experience. Retrospective self-reports of childhood maltreatment showed poor agreement with prospective measures (Cohen's kappa = 0.19). More than half of individuals (52%) with prospective measures of childhood maltreatment did not retrospectively report it, and similarly, over half

(56%) of individuals that retrospectively reported childhood maltreatment did not have a corresponding prospective measure.

Moderation analysis found that low agreement between prospective and retrospective measures did not differ by the type of prospective measures (e.g., official records, parents, interviews). Interestingly, authors found that the agreement between prospective and retrospective measures were higher when retrospective measures were based on more comprehensive methods such as interviews, compared to questionnaires (Baldwin et al., 2019). Previous research measuring life stress supports the notion that this finding may be explained due to the interview process allowing for a more detailed approach that allows for further exploration of the individual's perspective, when compared to a self-reported questionnaire (Monroe, 2008). Additionally, the authors reported that the characteristics of the sample, such as the sample size and sex, and study quality could not explain the variation between prospective and retrospective measures (Baldwin et al., 2019).

Overall, these findings suggest that prospective measures (which include, but are not restricted to objective assessments) and retrospective measures (based on subjective self-reports) of childhood adversity capture partially distinct groups of individuals. As such, the authors recommended these two measures should not be used interchangeably to study the associated health outcomes and risk mechanisms.

1.5 Differential associations between subjective and objective measures of experiences with mental health

Given that subjective and objective measures of experiences capture different constructs and possibly different groups of individuals, it is important to explore the potential different contributions that subjective and objective experiences may have to subsequent psychopathology. Initial evidence was obtained from a study including a cohort of 1,196 children examining whether psychopathology was primarily driven by objective court-documented records of childhood maltreatment, or subjective self-reported childhood maltreatment obtained in adulthood (Danese & Widom, 2020). Authors found subjective self-reported maltreatment predicted psychopathology in the absence of court-documented maltreatment. However, the risk of psychopathology linked to court-documented maltreatment was minimal in the absence of subjective self-reported maltreatment (Danese & Widom, 2020). These differential associations did not vary when factoring in participant characteristics such as gender and race. This study suggests subjective and objective measures may vary in how they predict psychopathology. Additionally, previous research using a birth cohort study of 2,232 twins examined the association between subjective self-report measures of neighbourhood disorder in adolescents, with adult psychotic experiences (Newbury et al., 2017). Findings demonstrated that adolescents who perceived higher levels of neighbourhood disorder and crime were more prone to report psychotic experiences at age 18, even after accounting for objectively measured records of crime.

Taken together, these two studies provide preliminary evidence to suggest that subjective appraisal of experiences may be related to an elevated risk of psychopathology. In other words, psychopathology may develop as a function of the subjective experience in addition to the objective experience. However, it remains unclear whether these results generalise to other samples and withstand across multiple adversities. This is a critical gap in the literature that prevents further understanding of how psychopathology develops in individuals who are exposed to adversity or other experiences (associated with psychopathology). Failing to factor in the differential impact of the objective versus subjective experience limits researchers and clinicians' knowledge of how negative experiences and perceptions can affect mental health.

If subjective measures of adverse experiences indeed show stronger associations with psychopathology than more objective measures, it would be critical to understand why subjective reports of experiences confer greater risk for psychopathology. From a clinical perspective, understanding the pathogenesis of psychopathology, in the context of experienced adversities and perceptions, may have important implications for designing effective treatments to help at-risk individuals.

1.6 Genetic predisposition to mental health vulnerabilities

One key factor that may partially explain the apparent stronger role of subjective experiences (versus objective experiences) in mental health could be underlying genetic influences that affect susceptibility to mental health problems, as well as influence perception of experiences. It is well established that there is a heritable component to psychiatric disorders, including internalising disorders such as

major depressive disorder (Howard et al., 2019), anxiety (Purves et al., 2020), and anorexia nervosa (Watson et al., 2019), as well as externalising disorders such as attention-deficit hyperactivity disorder (ADHD; Demontis et al., 2023). It is possible that individuals with a genetic predisposition to psychopathology may perceive environmental events and themselves in a more negative way, leading to an inflated association between subjective measures of experiences and psychopathology (i.e., genetic confounding).

Genetically informed approaches, such as polygenic scores, make it possible for researchers to identify potential traits and vulnerabilities (i.e., for mental health problems) and study these genetic proxies in relation to subjective reports of environmental events (e.g., childhood adversity) and psychological feelings (i.e., body dissatisfaction) (Pingault et al., 2022), as well as more objective measures. By utilising summary statistics from a discovery genome-wide association study (GWAS) for a given trait, a polygenic score aggregates the effects of many common genetic variants associated with a particular trait in a single individual-level score. A key advantage of the use of polygenic scores is that genetic risk to specific mental health vulnerabilities precedes any emergence or manifestation of mental health symptoms in childhood and adolescence. This makes it possible to test whether mental health vulnerabilities (proxied by polygenic scores) precede individual differences in perception and interpretation of experiences. In contrast, in studies examining the relationship between observed mental health vulnerabilities and subjective reports of experiences, any observed associations can be vulnerable to reverse causality (i.e., misinterpreting effects as causes). By harnessing genetically informed approaches therefore, I can disentangle the

relationship between genetic risk to mental health vulnerabilities, self-reported experiences, and objective experiences. In turn, this helps elucidate the underlying aetiology of subjective appraisal of experiences.

To date, however, there are relatively few studies that have incorporated polygenic scores of complex traits to understand relationships with both subjective and objective experiences.

First, evidence of the discrepancy in polygenic prediction of subjective versus objective measures comes from a recent study that used data from a cohort born in England and Wales (n=3,963). Authors tested whether the associations between polygenic scores (including for mental health vulnerabilities) and self-reported childhood trauma (i.e., emotional and physical abuse) remained after controlling for environmental adversity across development (Peel et al., 2022). Findings revealed that the polygenic scores for autism spectrum disorder and post-traumatic stress disorder were both associated with retrospective self-reported childhood trauma, independent from environmental adversity in childhood and adolescence. This suggests that the genetic predisposition to mental health vulnerabilities may influence the subjective experience or memory recall. In other words, they may be more prone to interpret experiences as traumatic. Second, a cohort study from the Netherlands (n=1,604) examined to what extent genetic predispositions to internalising (i.e., depression and anxiety) and externalising (i.e., ADHD) problems were associated with bullying victimisation. Findings showed polygenic scores for internalising and externalising problems were associated with bullying victimisation assessed through self-reports, but not through peer nominations. This suggests that

vulnerability to externalising and internalising traits affect more perception of bullying victimisation (as captured in self-reports) rather than a more subject-independent measure of risk (as captured by peer nominations). Third, capitalising on the availability of multi-informant reported experiences in a birth cohort study from Canada, Armitage et al (2022) explored the relationship between genetic predisposition to specific psychiatric, cognitive and physical traits, with self-report and other informant-reports (teacher and peer) of bullying victimisation (n=536). Findings demonstrated that genetic predispositions to mental health problems (such as depression) were more strongly associated with self-reported victimisation. In contrast, teacher and peer reported experiences were more closely related to cognitive and physical traits (Armitage et al., 2022). This provides evidence supporting differential association between genetic influence of specific traits and vulnerabilities, and self-report versus multiple informant (teacher and peer) reported experiences.

To comprehensively evaluate the influence of genetic predisposition to mental health vulnerabilities on self-reported experiences, it is important to account for the more objectively reported experiences (in the sense of being more independent from the target individual's own perception of the experience). Without accounting for other informants, it is difficult to determine the true association between genetic predisposition to mental health vulnerabilities and the subjective aspect of reporting.

1.7 Outline of thesis

The following three chapters present studies that aim to understand the relationship between subjective and objective experiences and their associations

with mental health, as well as whether genetic proxies for mental health vulnerabilities affect subjective experiences. **Chapter 2** investigates the agreement between subjective and objective measures of childhood adversity and identifies the independent contribution of these different measures to psychopathology. **Chapter 3** explores how genetic predisposition to mental health is associated with self-reported bullying victimisation, accounting for multi-informant reported bullying victimisation. Finally, **Chapter 4** tests whether findings from **Chapter 3** can be generalised to another subjective experience (body-related dissatisfaction) by exploring the relationship between genetic predisposition to mental health and subjective body-related dissatisfaction in adolescence, accounting for objectively measured anthropometric variables (such as body mass index). The thesis concludes with a discussion of research findings, potential mechanisms underlying the associations between subjective experiences and psychopathology, as well as implications for future research and clinical practice (**Chapter 5**).

Chapter 2 Subjective and Objective Experiences of Childhood Adversity: a Meta-analysis of their Agreement and Relationships with Psychopathology

2.1 Summary

Researchers use both subjective self-report and objective measures, such as official records, to investigate the impact of childhood adversity on psychopathology. However, it remained unclear whether subjective and objective measures of childhood adversity (a) show agreement, and (b) differentially predict psychopathology. To address this, I carried out a meta-analysis focusing on both subjective and objective measures of adverse childhood experiences (childhood maltreatment, bullying victimisation and neighbourhood adversity) and their relative associations with psychopathology. First, the agreement between subjective and objective measures were analysed using separate random-effects multi-level meta-analysis models for each type of adversity. Second, the meta-analytic association between (1) subjective measures and psychopathology, controlling for corresponding objective measures, and (2) objective measures and psychopathology, controlling for subjective measures, were calculated using random-effects multi-level meta-analysis models with three sources of variance. Finally, moderation analysis was carried out to determine whether the

independent associations between subjective and objective measures of childhood adversity were moderated by various predictors (such as informants).

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Supplementary material is located in Appendix A.

2.2 Introduction

Childhood adversities, such as maltreatment, bullying and neighbourhood deprivation, are well-established risk factors for psychopathology (Kessler et al., 1997). However, it is unclear if risk for psychopathology is driven by the subjective or objective experience of childhood adversity. Answering this question is critical to understand the pathways leading from childhood adversity to psychopathology, and, in turn, develop effective interventions.

Childhood adversity can be measured through a variety of different methods that index the subjective or objective experience. Most commonly, self-reports are used that assess an individual's subjective appraisal and memory of their experiences. Less often, more objective measures are used that do not rely on the target individual's perception of their experiences, but rather legal definitions (e.g. crime records to assess violence exposure) (Goldman-Mellor et al., 2016), safeguarding concerns (e.g. child protection records to assess maltreatment) (Everson et al., 2008) or consensus across multiple informants unrelated to the target individual (e.g. peer nominations to assess bullying) (Kochel et al., 2017). Though both subjective and objective measures are used to study the consequences of childhood adversity, such measures may not capture the same individuals. For example, a meta-analysis found that retrospective self-reports of childhood maltreatment showed poor agreement with prospective measures, mainly based on more objective assessments such as official records, research worker observations and parent reports (Cohen's kappa = .19) (Baldwin et al., 2019). This suggests that subjective and objective measures of childhood adversity might capture partially distinct groups of individuals.

If subjective and objective measures of childhood adversity do capture distinct groups of individuals, then both measures may be differentially associated with psychopathology. Indeed, initial evidence suggests that subjective measures of childhood adversity may show stronger associations with psychopathology than objective measures (Baldwin & Degli Esposti, 2021). For example, one study found that subjective self-reports of child maltreatment were associated with an increased risk of psychopathology in adulthood, independent of court-documented evidence (Danese & Widom, 2020). However, in the absence of self-reports, court records of maltreatment were not associated with psychopathology. This finding does not appear to be limited to studies examining child maltreatment, as similar findings have been found across other childhood adversities such as bullying victimisation (Bouman et al., 2012) and living in an area with neighbourhood disorder (Newbury et al., 2017). For example, one study observed that an increased risk of internalising problems was limited to subjective self-reports of bullying victimisation rather than peer nominations (i.e., reports from multiple children in a classroom) (Bouman et al., 2012). In addition, perceptions of neighbourhood disorder are associated with elevated risk of psychotic experiences, after accounting for objective levels of crime and disorder (Newbury et al., 2017). However, despite such evidence from individual studies, there has been no systematic evaluation of the relative contributions of subjective and objective measures of childhood adversity to psychopathology. Determining whether subjective experiences of childhood adversity drive an increased risk of psychopathology is critical to inform clinical practice, as such findings would indicate that therapeutic approaches that address perceptions of adversity could reduce related psychopathology.

To address these research gaps, I conducted a pre-registered meta-analysis of studies with subjective and objective measures of childhood adversity and assessment of psychopathology. My objectives were to examine (a) the agreement between subjective and objective measures of childhood adversity, (b) the independent contribution of subjective and objective measures of childhood adversity to psychopathology, and (c) moderators of these effects.

2.3 Method

2.3.1 Protocol and registration

This meta-analysis was pre-registered in the PROSPERO International prospective register of systematic reviews (CRD42021239454). In the pre-registered protocol, my primary review question regarded the association between subjective and objective measures of childhood adversity and psychopathology; however, I specified that I could also assess meta-analytic agreement between subjective and objective measures if sufficient data were available (which was the case). I conducted this meta-analysis in line with PRISMA guidelines (**Appendix A – Supplementary Table 1**).

2.3.2 Inclusion criteria

Studies were eligible if they (a) included subjective and objective measures of childhood adversity and (b) had data on the relative associations between subjective and objective measures of childhood adversity with psychopathology, and/or the agreement between subjective and objective measures of childhood adversity. Subjective measures were defined as an individual's perception of their own adverse childhood experiences, captured through self-reported interviews or

questionnaires. These measures assessed whether an event occurred (e.g. maltreatment) rather than its subjective impact. Objective measures were defined as assessments unlikely to be affected by the target individual's perception of their experience, such as (a) official records (e.g. child protection records, crime records or medical records) or (b) reports derived from multiple individuals who are not directly related to the individual (e.g. peer nominations for bullying). Note that for (b), reports were required from multiple informants, rather than a single individual, to maximise accuracy. Psychopathology was defined as diagnoses or symptoms of a psychiatric illness. I excluded studies that included non-human animals or human participants from a selected clinical sample or a clinical trial.

2.3.3 Literature search

I searched Embase, MEDLINE and PsycINFO using the Ovid platform for peer-reviewed articles written in English and published from database inception to March 2021. Search terms are shown in **Appendix A – Supplementary Method 1**. These include general search terms indexing child adversity and trauma, as well as specific terms indexing adversities known to have been previously assessed with both subjective and objective measures (e.g. maltreatment, bullying and neighbourhood adversities). Additional studies were identified via searching reference lists of included studies.

2.3.4 Study selection

Two authors (E.R.F. and S.E.S.) independently screened abstracts and titles before reviewing the full text of potentially eligible articles. Uncertainty of study inclusion was resolved through discussion with a third reviewer (J.R.B.).

2.3.5 Data extraction

Data on sample characteristics and effect sizes for the relative associations between subjective and objective measures of childhood adversity and psychopathology were systematically extracted from each article by two independent reviewers (E.R.F. and A.T.), blind to the other's data extraction (details in **Appendix A – Supplementary Method 2).** For data on the agreement between subjective and objective measures of adversity, one author (J.R.B.) extracted or calculated effect sizes from available data (correlations and/or Cohen's kappa), and this information was checked by another author (E.R.F.). Relevant missing information was requested from study authors.

I extracted information on study quality (risk of bias) for each article using an adapted version of the Newcastle-Ottawa Scale (Wells et al., 2000) shown in **Appendix A – Supplementary Table 2**. All articles were independently assessed by three reviewers (E.R.F., A.T. and J.R.B.). Results for each study are shown in **Appendix A – Supplementary Table 3**.

2.3.6 Effect size conversion

2.3.6.1 Effect size for the agreement between subjective and objective measures of childhood adversity

Studies with data on the agreement between subjective and objective measures of childhood adversity reported either (a) data to derive a contingency table comparing binary subjective measures of childhood adversity (yes/no) with binary objective measures of childhood adversity (yes/no) or (b) a Pearson's correlation coefficient for the association between continuous subjective and objective

measures of childhood adversity. To derive a common effect size metric (namely, a correlation coefficient), I used data in the contingency tables to calculate tetrachoric correlations, which are directly comparable to the Pearson's correlations reported by many of the studies.

2.3.6.2 Effect sizes for the associations between subjective and objective measures of childhood adversity and psychopathology

I converted effect sizes for the independent associations between subjective and objective measures of childhood adversity and psychopathology to partial correlation coefficients (*r*). Partial correlation coefficients represent the association between subjective measures of childhood adversity and psychopathology, controlling for objective measures of adversity, and vice versa. Formulae for converting effect sizes are shown in **Appendix A – Supplementary Table 4**. Where studies reported bivariate correlations between (a) subjective and objective measures with psychopathology and (b) subjective and objective measures, I calculated partial correlations using a procedure described in **Appendix A – Supplementary Method 3**.

2.3.7 Data analysis

Analyses were performed using the 'metafor' package (Viechtbauer, 2010) in R (version 4.1.2). First, I examined the agreement between subjective and objective measures of childhood adversity. To do so, I conducted separate random-effects multi-level meta-analysis models to pool the agreement (r) between subjective and objective measures of childhood adversity, with different models for different adversity types. To account for interdependencies between multiple effect sizes

from single studies and samples (Assink & Wibbelink, 2016), four different sources of variance were modelled: (1) sample variance of the effect sizes, (2) variance between effect sizes extracted from the same study, (3) variance between studies and (4) variance between samples (for instances where the same sample was used across multiple studies). To stabilise the variances, I transformed correlations to Fisher's z prior to meta-analysis (Borenstein et al., 2021) and back-transformed the meta-analytic results to r using Fisher's z-to-r transformation for interpretability (Borenstein et al., 2021). For the meta-analysis of agreement between subjective and objective measures of child maltreatment, Cohen's kappa effect sizes were available (as well as correlation coefficients), and so I also conducted a random-effects multi-level meta-analysis model for the agreement measured via Cohen's kappa. I then conducted a post-hoc analysis to examine whether the agreement between subjective and objective measures was moderated by the type of childhood adversity.

Second, for each form of childhood adversity, I tested the meta-analytic association (a) between subjective measures and psychopathology, controlling for corresponding objective measures, and (b) between objective measures and psychopathology, controlling for subjective measures. To do so, I used the same meta-analytic procedure as specified above (i.e., random-effects multi-level meta-analysis models with three sources of variance, using the Fisher's z transformation and z-to-r back-transformation).

Third, I examined whether the independent associations between subjective and objective measures of childhood adversity were moderated by various predictors. Where sufficient data were available, I used meta-regression to test whether

heterogeneity in effect sizes was predicted by the informant reporting on psychopathology (self vs. other), type of study (longitudinal vs. cross-sectional assessment of childhood adversity and psychopathology), type of psychopathology outcome (internalising or externalising problems), sex distribution of the sample and study quality.

2.3.8 Risk of bias across studies

I assessed the risk of bias across studies in two ways. First, I carried out a test for publication bias by performing an Egger's regression test for each multi-level random-effects meta-analysis (Egger et al., 1997). Second, I performed leave-one-out analysis for each meta-analysis, which assessed the undue effect of each individual study by testing changes in the meta-analytic effect estimates when each study was omitted in turn.

2.3.9 Data and code availability

The dataset and analysis code are available at: https://github.com/erfrancis/MetaAnalysis_ObjectiveSubjective.

2.4 Results

2.4.1 Search results

The study selection procedure is shown in **Appendix A – Supplementary Figure 1**. I identified 22 studies with data on the agreement between subjective and objective measures of childhood adversity (see **Table 2.1** for study details). These studies were based on 21 cohorts including 18,163 independent participants (51.3% female), with an average age of 14.8 years. As shown in **Table 2.1**, 9 studies focused on child maltreatment (41 effect sizes), 11 studies focused on bullying victimisation (20 effect sizes) and 2 studies focused on neighbourhood adversity (2 effect sizes). There were more effect sizes than studies as individual studies often reported multiple effect sizes. The average study quality score was 4 (range = 3–6), from a possible range of 0 (indicating very high bias) to 8 (indicating very low bias) using the adapted NOS **(**see **Appendix A – Supplementary Table 3**).

I identified 17 studies with data on the independent associations between both subjective and objective measures of childhood adversity and psychopathology (see **Table 2.1** for study details). These 17 studies were based on 15 cohorts comprising 14,789 independent participants (54.1% female) with an average age of 14.3 years. Among these studies, 6 focused on maltreatment (188 effect sizes), 9 focused on bullying victimisation (90 effect sizes) and 2 focused on neighbourhood adversity (4 effect sizes).

Table 2.1. Summary of study characteristics included in the meta-analysis for subjective and objective measures of childhood adversity

Author (Year)	Country	Total analytical sample size (% female)	Exposure type (objective)	Exposure type (subjective)	Type of objective measure	Type of subjective measure	Type of mental health outcome(s)	Average age of self-reported adversity (years)	Informant for psychopathology	Included in meta-analysis on agreement (Y/N)	Included in meta-analysis on psychopathology (Y/N)
Child maltreatment											
Cho & Jackson (2016)	U.S.A	285 (45.1)	Child maltreatment: Sexual abuse, physical abuse, emotional abuse	Child maltreatment: Sexual abuse, physical abuse, emotional abuse	Child Protection Service Records	Self-report interview	Internalising symptoms, Externalising symptoms	13.3	Parent	Y	Y
Danese & Widom (2020)	U.S.A.	1196 (48.7)	Child maltreatment	Child maltreatment	Crime records	Self-report interview	Any psychopathology diagnosis, Any internalising disorder diagnosis, Any externalising disorder diagnosis, Depression diagnosis, Dysthymia diagnosis, Generalized anxiety disorder diagnosis, PTSD diagnosis, Antisocial personality disorder diagnosis, Alcohol abuse and or dependence diagnosis, Drug abuse and/or dependence	28.7	Self-report	Y	Y
Everson et al (2008)	U.S.A	350 (51)	Child maltreatment: Physical abuse, sexual abuse, psychological abuse	Child maltreatment: Physical abuse, sexual abuse, psychological abuse	Child Protection Service Records	Self-report questionnaire	Psychological adjustment symptoms	12	Self-report	Y	Y
Havlicek & Courtney (2016)	U.S.A	474 (53 & 56)	Child maltreatment, Physical abuse, sexual abuse, neglect	Child maltreatment, Physical abuse, sexual abuse, neglect	Child Protection Service Records	Self-report interview	N/A	17.5 & 19	N/A	Y	N*

Author (Year)	Country	Total analytical sample size (% female)	Exposure type (objective)	Exposure type (subjective)	Type of objective measure	Type of subjective measure	Type of mental health outcome(s)	Average age of self-reported adversity (years)	Informant for psychopathology	Included in meta-analysis on agreement (Y/N)	Included in meta-analysis on psychopathology (Y/N)
McGee, Wolfe, Yuen, Wilson & Carnochan (1995)	Canada	160 (56.3)	Child maltreatment: physical violence, family violence, sexual abuse, emotional abuse, neglect	Child maltreatment: physical violence, family violence, sexual abuse, emotional abuse, neglect	Child Protection Service Records	Self-report interview	Internalising symptoms, Externalising symptoms	13.8	Self-report	Y	Y
Negriff, Schneiderman & Trickett (2017)	U.S.A	221 (50)	Child maltreatment: Sexual abuse, physical abuse, emotional abuse, neglect	Child maltreatment: Sexual abuse, physical abuse, emotional abuse, neglect	Child Protection Service Records	Self-report interview	Depression symptoms, PTSD symptoms, Anxiety symptoms, Marijuana Use, Alcohol use, Person offences externalising problems, Property offences externalising problems	18.49	Self-report	Y	Y
Sierau et al (2017)	Germany	944 (47.2)	Child maltreatment: Failure to provide, Lack of supervision, Physical abuse, Emotional maltreatment	Child maltreatment: Failure to provide, Lack of supervision, Physical abuse, Emotional maltreatment	Child Protection Service Records	Self-report interview	N/A	10.1	N/A	Y	N*
Smith, Ireland, Thornberry & Elwyn (2008)	U.S.A	1000 (50)	Child maltreatment	Child maltreatment	Child Protection Service Records	Self-report interview	N/A	23	N/A	Y	N*
White, English, Thompson & Roberts (2016)	U.S.A	770 (54.8)	Emotional maltreatment including violation of psychological safety and security; failure to support acceptance and self-esteem; failure to allow age-	Emotional maltreatment including violation of psychological safety and security; failure to support acceptance and self-esteem; failure to allow age-appropriate autonomy; and	Child Protection Service Records	Self-report interview	Anxiety symptoms, Depression symptoms, Suicidal symptoms	14	Self-report	Y	Y

Author (Year)	Country	Total analytical sample size (% female)	Exposure type (objective)	Exposure type (subjective)	Type of objective measure	Type of subjective measure	Type of mental health outcome(s)	Average age of self-reported adversity (years)	Informant for psychopathology	Included in meta-analysis on agreement (Y/N)	Included in meta-analysis on psychopathology (Y/N)
			appropriate autonomy; and restriction (e.g., confinement/isolation, binding)	restriction (e.g., confinement/isolation, binding)							
Bullying victimisation											
Bouman et al (2012)	Netherlands	1192 (49.8)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report interview	Depression symptoms, Anxiety symptoms	11.2	Self-report	Y	Y
De Los Reyes & Prinstein (2004)	U.S.A	203 (60)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	N/A	16.31	N/A	Y	N*
Flanagan, Erath & Bierman (2008)	U.S.A	383 (57)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	Social anxiety symptoms	12.8	Parent	Y	Y
Graham, Bellmore & Juvonen (2003)	U.S.A	785 (55.7)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	Anxiety symptoms, Depression symptoms, Internalising symptoms, Externalising symptoms	11.5	Self-report & teacher	Y	Y
Graham & Juvonen, (1998)	U.S.A	418 (50.7)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	Social anxiety symptoms	12.4	Self-report	Y	Y
Gromann, Goossens, Olthof, Pronk & Krabbenda (2013)	Netherlands	724 (48.3)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	Non clinical psychotic experiences symptoms	11.9	Self-report	Y	Y
Kochel, Bagwell, Ladd & Rudolph (2017)	U.S.A	5th, 6th grade: 483; 9th, 10th grade: 444 (49.69)	Peer victimisation	Peer victimisation	Peer nomination	Self-report questionnaire	Depressive symptoms	13.45	Self-report, teacher & parent	Y	Y
McClain, Younginer & Elledge (2020)	U.S.A	Male: 212 Female:270 (56)	Overt victimisation, relational victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	Depressive symptoms, Anxiety symptoms	9.16	Self-report	Y	Y

Author (Year)	Country	Total analytical sample size (% female)	Exposure type (objective)	Exposure type (subjective)	Type of objective measure	Type of subjective measure	Type of mental health outcome(s)	Average age of self-reported adversity (years)	Informant for psychopathology	Included in meta-analysis on agreement (Y/N)	Included in meta-analysis on psychopathology (Y/N)
Mulder, Hutteman & van Aken (2017)	Netherlands	Time 1: 1100 Time 2: 1139 (46)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	Social anxiety symptoms	12	Self-report	Y	Y
Rigby & Slee (1999)	Australia	450 & 395 (46.7)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	N/A	15	N/A	Y	N*
Zimmer-Gembeck & Pronk (2012)	Australia	335 (52.8)	Bullying victimisation	Bullying victimisation	Peer nomination	Self-report questionnaire	Depressive symptoms, Social anxiety symptoms	12.5	Self-report	Y	Y
Neighbourhood adversity											
Newbury et al (2017)	U.K.	2066 (51)	Neighbourhood crime	Neighbourhood disorder	Crime records	Self-report interview/ questionnaire	Psychotic Experiences Symptoms	18.4	Self-report	Y	Y
Goldman-Mellor, Margerison-Zilko, Allen & Cerda (2016)	U.S.A	4462 (49.2)	Neighbourhood violence	Neighbourhood safety	Crime records	Self-report questionnaire	Serious psychological distress symptoms	14.65	Self-report	Y	Y

* Five studies included in the meta-analysis of agreement between subjective and objective measures were not included in the meta-analysis on the independent associations between these measures and psychopathology (De Los Reyes & Prinstein, 2004; Havlicek & Courtney, 2016; Rigby & Slee, 1999; Sierau et al., 2017; Smith et al., 2008). This was due to these studies not containing effect sizes that could be extracted or calculated from the data available, or no contact from study author.

2.4.2 What is the agreement between subjective and objective measures of childhood adversity?

2.4.2.1 Child maltreatment

I first examined the meta-analytic agreement between subjective self-reports of childhood maltreatment and objective measures (comprising child protection records or court records). The correlation between subjective and objective measures of maltreatment was only medium in magnitude (r = .32, 95% CI, 0.23–0.41; p < .0001; 41 effect sizes) (**Figure 2.1**). Furthermore, the agreement between subjective and objective measures of maltreatment as assessed through Cohen's kappa was poor (k = .16, 95% CI, 0.10–0.22; p < .0001), indicating that agreement was only 16% greater than that expected due to chance. I did not find evidence of publication bias, and leave-one-out analysis suggested that the meta-analytic estimates were not unduly influenced by any individual study (see **Appendix A – Supplementary Table 5**).

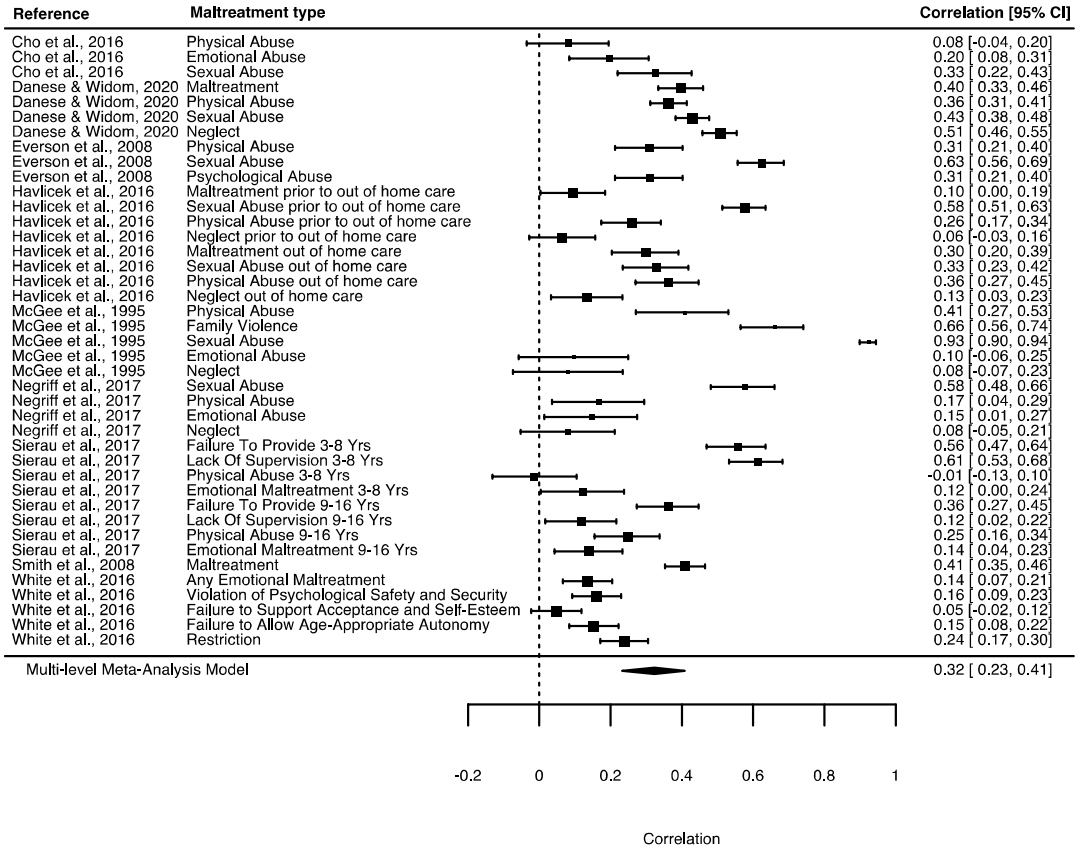


Figure 2.1. Forest plot for studies examining the correlation between subjective and objective measures of childhood maltreatment.

2.4.2.2 Bullying victimisation

I next examined the agreement between subjective self-reports of bullying victimisation and objective measures (comprising peer nominations from multiple children in a classroom). The correlation between subjective and objective measures of bullying victimisation was medium in magnitude (r = .35, 95% CI, 0.27–0.42; p < .0001, 20 effect sizes) (**Figure 2.2**). The Egger's test was statistically significant (Q_moderation = 7.8016; p = .0052) but visual inspection of the effect sizes showed that smaller studies reported smaller, rather than larger effect sizes which would be indicative of publication bias (see Appendix A – **Supplementary Figure 2**). Leave-one-out analysis suggested that the meta-analytic estimate was not unduly influenced by any individual study (see Appendix A – **Supplementary Table 6**).

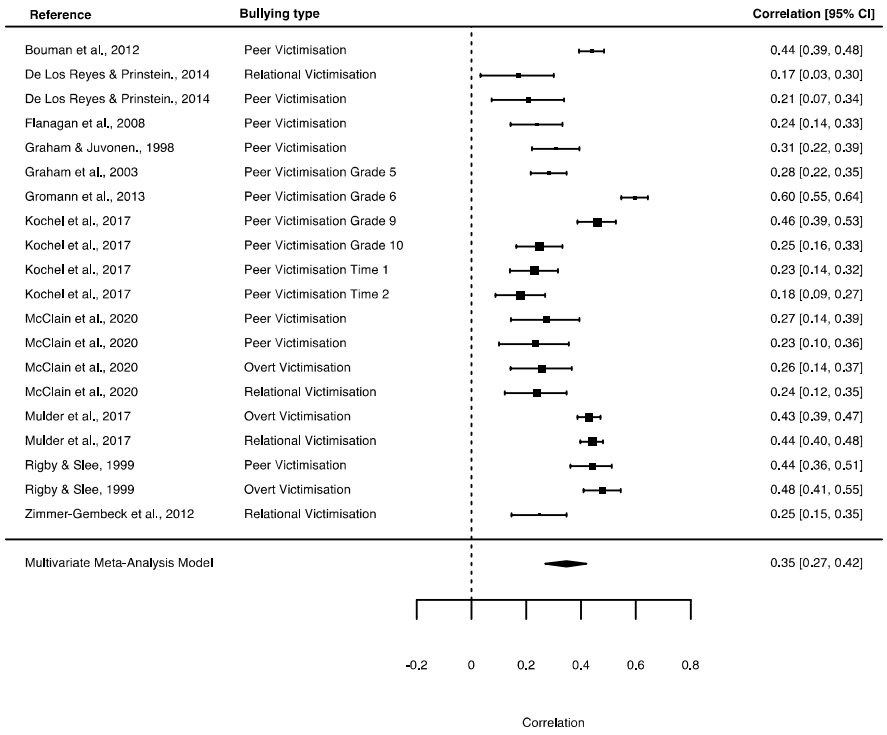


Figure 2.2. Forest plot for studies examining the correlation between subjective and objective measures of bullying victimisation.

2.4.2.3 Neighbourhood adversity

I then examined the agreement between subjective self-reports of neighbourhood violence/disorder and corresponding objective measures (crime records). Notably, only two studies contained available data, so these findings should be interpreted as preliminary. The correlation between the subjective and objective measures of neighbourhood adversity was small to medium in magnitude (r = .25, 95% CI, 0.11–0.39; p = .0007, 2 effect sizes) (see Appendix A – Supplementary **Figure 3**). I did not conduct an Egger's test or leave-one-out analysis due to the limited number of studies.

2.4.3 Is the agreement between subjective and objective measures moderated by the type of childhood adversity?

I next conducted a post-hoc (i.e., non-pre-registered) analysis to examine whether heterogeneity in the agreement between subjective and objective measures was influenced by the type of childhood adversity. I found that agreement between subjective and objective measures differed according to the type of childhood adversity (Q_moderation = 25.28, p = .0003), with stronger agreement for sexual abuse (r = .60, CI, 0.48–0.69; k [number of studies] = 6, ES [number of effect sizes] = 7) than for other forms of adversity, including physical abuse (r = .25, CI, 0.11–0.38; k = 7, ES = 9), emotional abuse (r = .21, CI, 0.07–0.33; k = 6, ES = 12), neglect (r = .30, CI, 0.16–0.43; k = 5, ES = 9), broad measures of maltreatment (r = .33, CI, 0.13–0.50; k = 3, ES = 4), bullying victimisation (r = .33, CI, 0.24–0.42; k = 11, ES = 20) and neighbourhood adversity (r = .25, CI, −0.03–0.50; k = 2, ES = 2).

2.4.4 Do subjective and objective measures of childhood adversity independently predict psychopathology?

2.4.4.1 Child maltreatment

Next, I examined the relative associations between subjective and objective measures of childhood maltreatment and psychopathology. Subjective self-reports of maltreatment were significantly associated with psychopathology, independent of objective measures ($r = .16$, 95% CI, 0.09–0.22; $p < .0001$; 90 effect sizes; **Figure 2.3**). In contrast, objective measures of maltreatment were not associated with psychopathology, independent of subjective measures ($r = .06$, 95% CI, −0.02–0.13; $p = .14$; 90 effect sizes; **Figure 2.3**). I did not find evidence of publication bias for either meta-analysis, and findings were not unduly influenced by any individual study (**Appendix A – Supplementary Table 6**).

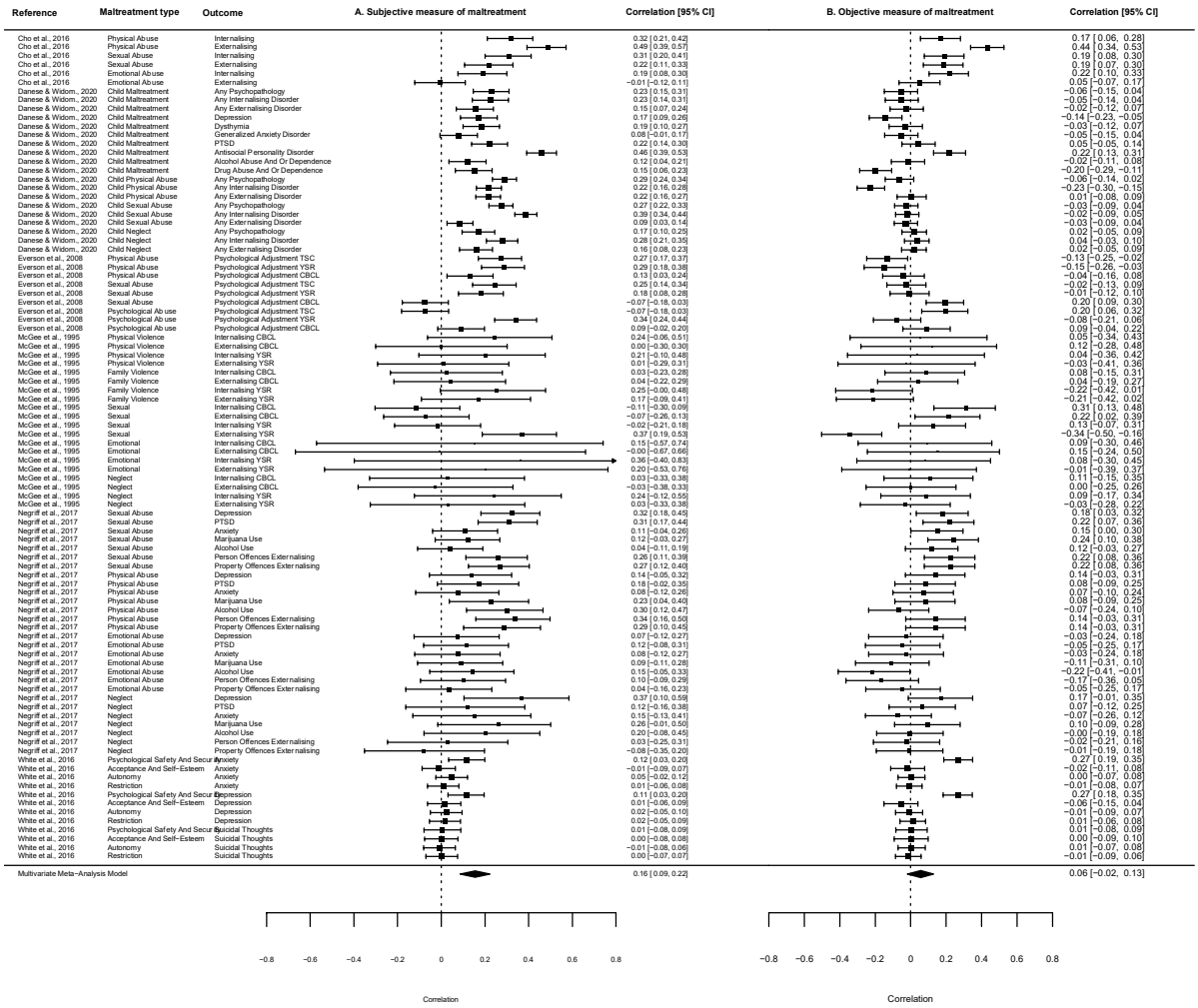


Figure 2.3. Meta-analytic associations between subjective measures of child maltreatment and psychopathology, independent of objective measures (Panel A), and objective measures of child maltreatment and psychopathology, independent of subjective measures (Panel B).

2.4.4.2 Bullying victimisation

Similar to the findings on child maltreatment, subjective self-reports of bullying victimisation were significantly associated with psychopathology, independent of objective measures ($r = .12$, 95% CI, 0.08–0.17; $p < .0001$; 45 effect sizes; **Figure 2.4**. However, objective measures of bullying victimisation were not significantly associated with psychopathology, independent of subjective measures ($r = .03$, 95% CI, −0.01–0.08; $p = .13$; 45 effect sizes; **Figure 2.4**). I did not find evidence of publication bias for either meta-analysis, although smaller studies were more likely to report smaller independent effects of objective measures on psychopathology (**Appendix A – Supplementary Figure 4**). Findings for both meta-analyses were not unduly influenced by any individual study (see **Appendix A – Supplementary Table 6**).

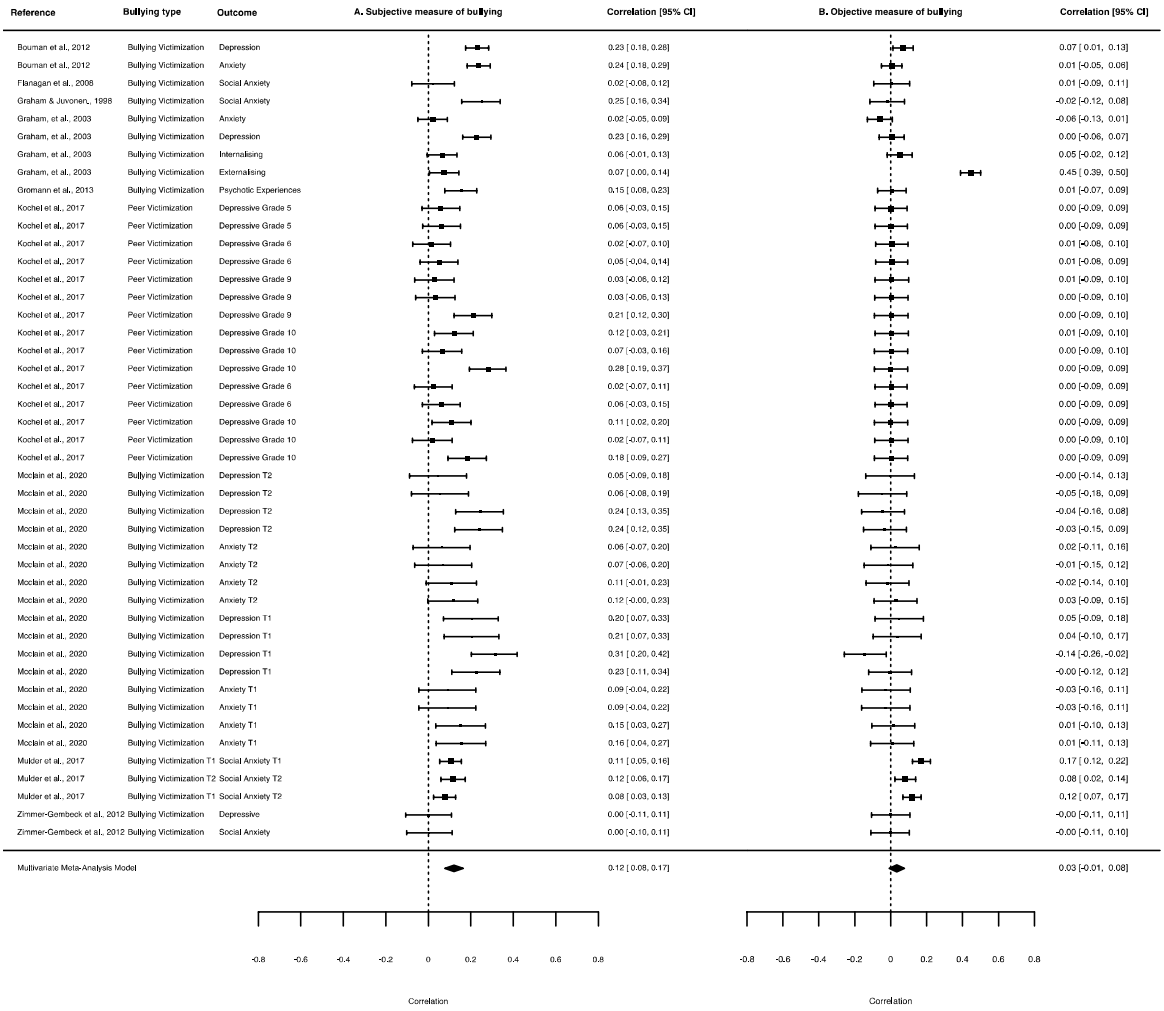


Figure 2.4. Meta-analytic associations between subjective measures of bullying victimisation and psychopathology, independent of objective measures (Panel A), and objective measures of bullying victimisation and psychopathology, independent of subjective measures.

2.4.4.3 Neighbourhood adversity

Among the two available studies, subjective self-reports of neighbourhood adversity were significantly associated with psychopathology, independent of objective measures ($r = .26$, 95% CI, 0.22–0.29; $p < .001$; 2 effect sizes; **Appendix A – Supplementary Figure 2.5).** Objective measures of neighbourhood adversity also showed a small association with psychopathology, independent of subjective measures ($r = .04$, 95% CI, 0.02–0.07; $p = .0003$; 2 effect sizes; **Appendix A – Supplementary Figure 5**), although this effect size was significantly smaller than the association between subjective measures and psychopathology ($p < .001$). Given the small number of studies with data for neighbourhood adversity, I did not conduct further analyses assessing publication bias, undue influence of individual studies and moderation of these effects.

2.4.5 What moderates the independent associations between subjective and objective measures of childhood adversity and psychopathology?

Lastly, I examined predictors of heterogeneity in the relative associations between subjective and objective measures of childhood adversity with psychopathology. As the meta-analytic findings were very similar for maltreatment and bullying, I combined effect sizes for both exposures in the moderation analyses to benefit from greater statistical power (**Table 2.2**). However, I present results for maltreatment and bullying separately in **Appendix A – Supplementary Table 7** for transparency.

Table 2.2. Moderators of the Association Between Subjective and Objective Measures of Bullying Victimisation and Childhood Maltreatment, and Psychopathology.

Moderators by adversity type	No. of studies	No. of effect sizes	Effect Size Estimate, r (95% CI)	Q Moderation	*P* value
Subjective measure of child adversity					
Informant for psychopathology				4.87	**0.027**
Self-report	13	118	0.15 (0.11-0.20)		
Other informant	4	21	0.07 (0.00-0.15)		
Study type				4.11	**0.043**
Cross-sectional	14	113	0.15 (0.11-0.19)		
Longitudinal	4	26	0.09 (0.03-0.15)		
Type of psychopathology				0.04	0.84
Internalising problems	13	88	0.14 (0.09-0.18)		
Externalising problems	5	37	0.13 (0.07-0.19)		
Sex (percentage female)	15	139	-0.00 (-0.00-0.00)	0.12	0.73
Study quality	15	139	-0.00 (-0.04-0.04)	0.00	0.99
Objective measure of child adversity					
Informant for psychopathology				6.40	**0.011**
Self-report	13	118	0.02 (-0.02-0.06)		
Other informant	4	21	0.11 (0.05-0.18)		
Study type				0.06	0.81
Cross-sectional	14	113	0.04 (0.00-0.08)		
Longitudinal	4	26	0.03 (-0.03-0.10)		
Type of psychopathology				1.29	0.26
Internalising problems	13	88	0.04 (0.00-0.08)		
Externalising problems	5	37	0.07 (0.01-0.13)		
Sex (percentage female)	15	139	-0.00 (-0.00-0.00)	1.34	0.25
Study quality	15	139	-0.02 (-0.06-0.02)	0.74	0.39

First, I found that the independent association between subjective measures of childhood adversity and psychopathology was stronger when psychopathology was self-reported ($r = .15$, 95% CI = 0.11–0.20) versus reported by another informant (i.e., a parent or teacher, $r = .07$, 95% CI = 0.00–0.15, Q_moderation = 4.87, $p = .027$). In contrast, objective measures of childhood adversity showed a stronger independent association with psychopathology reported by another informant ($r = .11$, 95% CI = 0.05–0.18) versus self-reports ($r = .02$, 95% CI = −0.02–0.06, Q_moderation = 6.40, $p = .011$).

Second, the independent association between subjective measures of childhood adversity and psychopathology was stronger when psychopathology was assessed concurrently to self-reports of adversity ($r = .15$, 95% CI = 0.11–0.19) versus longitudinally ($r = .09$, 95% CI = 0.03–0.15, Q_moderation = 4.11, $p = .043$). No such moderation effect was found for objective measures of childhood adversity (**Table 2.2**).

Finally, the independent associations between subjective and objective measures of childhood adversity with psychopathology were not moderated by the type of psychopathology, sex distribution of the sample or study quality (**Table 2.2**). The findings were broadly similar when maltreatment and bullying were examined separately (see **Appendix A –Supplementary Table 7**), although there was no statistically significant moderation by informant for analyses on maltreatment, or study type for analyses on bullying (though the direction of effects was consistent).

2.5 Discussion

This meta-analysis examined whether subjective and objective measures of childhood adversity overlap, and are independently associated with psychopathology. First, I found only modest associations between subjective and objective measures of childhood adversity. Second, I found that subjective measures of childhood adversity were associated with psychopathology, independent of corresponding objective measures. In contrast, objective measures of childhood adversity had null or very small associations with psychopathology, independent of subjective measures. These findings were consistent across multiple types of childhood adversity, including childhood maltreatment, bullying victimisation and neighbourhood violence, relying on different types of objective measures (e.g. child protection records, peer nominations and crime records).

The modest associations between subjective and objective measures of childhood adversity suggest that individual perceptions and memories of adverse experiences do not closely match what is recorded more objectively (such as through child protection or crime records, or reports across multiple informants). These findings mirror low agreement observed between retrospective self-reports of child maltreatment with prospective measures (assessed through parent/informant reports as well as official records) (Baldwin et al., 2019), as well as between self-reports and objective records of other experiences, such as media use (Parry et al., 2021).

There are several plausible explanations for moderate agreement between subjective and objective measures of childhood adversity. On the one hand,

objective measures might identify only the most severe or visible cases of childhood adversity (such as from official records or peer nominations from multiple informants), and self-report measures may detect more true cases (Mulder et al., 2017). On the other hand, subjective measures might be less accurate in detecting childhood adversity because of biases due to individual motivations and memory (Baldwin et al., 2019). For example, some may underreport or minimise adversity experienced due to social desirability bias (Fisher et al., 2011), self-protective mechanisms, personality traits (e.g. high agreeableness; Reuben et al., 2016) or fear of perpetrator repercussions. Various memory fallibilities can also limit accuracy of self-reports, such as not remembering adversity in early childhood due to infantile amnesia (Lebois et al., 2021), or over-recalling adversity due to a negative bias in autobiographical memory involved in psychopathology (Colman et al., 2016). Notably though, the majority of studies included in my meta-analysis involved self-reports obtained prospectively in childhood (**Table 2.1**) which reduces the likelihood that the results I found are due to inaccuracies in retrospective memory. Finally, it is possible that low agreement was due to differences in the assessment of childhood adversity (e.g. in the definition used, or observational period assessed) between subjective and objective measures (Baldwin et al., 2019). However, only a few studies reported different definitions of adversity (Goldman-Mellor et al., 2016; McClain et al., 2020; Newbury et al., 2017) or different observation periods (Gromann et al., 2013; Newbury et al., 2017; Smith et al., 2008) between subjective and objective measures, and so low overall agreement cannot solely be due to these differences.

Notably, in post-hoc analyses, I found that agreement between subjective and objective measures differed according to the type of childhood adversity. Specifically, there was higher agreement between subjective and objective measures of sexual abuse compared to physical and emotional abuse, neglect, and broader measures of maltreatment, bullying and neighbourhood adversity. This may be because sexual abuse is a more clear-cut form of adversity compared to other experiences (e.g. emotional abuse or neglect, or bullying), which can involve a more subjective interpretation. Indeed, previous research showed higher agreement between prospective and retrospective measures of other clear-cut forms of adversity (e.g. parental loss; Reuben et al., 2016), or childhood experiences (e.g. residence changes; Henry et al., 1994) compared to more ambiguous psychosocial experiences.

My finding that subjective self-reports of childhood adversity are more strongly associated with psychopathology than objective measures might be due to aetiological mechanisms or bias. With regard to aetiological mechanisms, perception and memories of adverse childhood experiences might mediate the relationship between objective experiences and mental ill health (Elwyn & Smith, 2013). That is, memories and recollections of traumatic experiences may drive the risk of psychopathology in those exposed to adversity, for example by evoking negative views about the self and others. In contrast, individuals exposed to childhood adversity who do not remember it, or do not perceive it to be adversity, may not develop psychopathology. This mediation interpretation is supported by the evidence that objective measures of childhood adversity are associated with psychopathology when subjective measures are not controlled for (Bouman et al., 2012; Cutajar et al., 2010; Kochel et al., 2017; Mills et al., 2016; Smith et al.,

2008; Widom et al., 2007), including in studies applying stringent causal inference methods (Capusan et al., 2021; Kugler et al., 2019).

With regard to bias, three potential explanations exist. First, the stronger association between subjective measures of childhood adversity and psychopathology relative to objective measures might partly be explained by reverse causation or recall bias. For example, individuals with mental ill health might be more likely to perceive current experiences as harmful due to cognitive biases (e.g. negative attentional bias) (Beck, 2008), or recall past experiences more negatively due to mood-congruent memory (Brewin et al., 1993). Indeed, longitudinal research has suggested that increases in depression symptoms over time predicted small increases in retrospective reports of child maltreatment (Goltermann et al., 2023). I found some evidence to suggest the existence of such recall bias, as self-reports of childhood adversity were more strongly associated with psychopathology in cross-sectional studies than in longitudinal studies, suggesting that perceived childhood adversity is more closely related to concurrent than later mental ill health. However, it is also possible that such effect size differences might be due to effects of perceived childhood adversity on psychopathology decreasing over time.

Second, subjective measures of childhood adversities might be more strongly associated with psychopathology than objective measures due to shared method variance as self-reports were used to assess subjective experiences and, in most instances, psychopathology (Widom & Shepard, 1996). In contrast, objective measures did not rely on self-reports and showed minimal (or no) independent association with self-reported psychopathology. This explanation is supported by my finding showing that self-reports of childhood adversity were associated with

psychopathology that was self-reported, but not reported by another informant (though this appeared to be driven by studies on bullying). Similarly, previous studies found that retrospective self-report measures of childhood adversity were associated with poor self-reported outcomes relating to mental and physical health, but not objectively recorded outcomes (Gehred et al., 2021; Osborn & Widom, 2020; Reuben et al., 2016).

Third, the stronger relationship between subjective compared to objective measures of childhood adversity and psychopathology may partly be explained by a confounding variable that results in an individual perceiving experiences as more negative and also developing psychopathology. For example, previous research showed that personality traits such as neuroticism and low agreeableness are associated with recalling more childhood adversity than was recorded prospectively (Reuben et al., 2016), and these traits also predispose to psychopathology (Hengartner et al., 2016). Furthermore, previous research found that genetic predisposition to psychopathology (e.g. depression and low well-being) is associated with self-reports of bullying victimisation, but not more objective measures (teacher or peer reports) (Armitage et al., 2022), implying potential for genetic confounding.

These findings should be interpreted in the context of some limitations. First, only two studies (Goldman-Mellor et al., 2016; Newbury et al., 2017) focused on neighbourhood adversities, which limits my ability to draw conclusions for this form of childhood adversity. Nevertheless, I observed broadly similar findings to those observed for maltreatment and bullying victimisation. Second, the comparatively small number of studies included in each level of the moderator analyses prevents us from drawing strong conclusions about these results. For

example, only four studies were longitudinal (Kochel et al., 2017; McClain et al., 2020; Mulder et al., 2017; White et al., 2016), and only four studies assessed psychopathology through reports from other informants (rather than self-reports) (Cho & Jackson, 2016; Flanagan et al., 2008; Graham et al., 2003; Kochel et al., 2017). Third, because data were unavailable, I could not examine whether the findings were moderated by key factors, such as the time interval between childhood adversity exposure and psychopathology, and race or ethnicity. Finally, it is possible that measures of childhood adversity defined as 'objective' (e.g. official records and peer nominations) could still be partly influenced by the target individual's perceptions of their experiences (e.g. if children seek out support from official services or confide in their peers). Nevertheless, because official records and peer nominations rely on evidence from a large number of sources, they are likely to capture much more information than only the individual's subjective experience.

My findings have implications for future research. To understand why subjective measures of childhood adversity are more strongly associated with psychopathology than objective measures, future studies should aim to test whether the finding is due to sources of bias or an aetiological mechanism. To understand the direction of the relationship (and test recall bias/reverse causation), longitudinal analyses are needed on datasets with repeated measures of self-reported childhood adversity and psychopathology. To test shared method variance, studies could further examine whether subjective measures of childhood adversity are associated with psychopathology outcomes reported by multiple informants or through objective records. To test confounding, studies should examine the extent to which factors predisposing individuals to

negative perceptions and psychopathology (e.g. personality traits, genetic vulnerabilities) account for the relationship between the subjective experience of adversity and psychopathology (Pingault et al., 2022).

If subjective appraisal of childhood adversity directly contributes to psychopathology, then therapeutic approaches which target perceptions and memories could help to reduce and prevent psychopathology (Danese & Widom, 2021). Such interventions might involve techniques that help to modify cognitive appraisal of the experience, the affective response and associated views about the self and others (Creamer et al., 2005). Of note, this finding would not undermine the importance of preventing objective experiences of childhood adversity, which is a moral priority for parents and society. Rather, it would provide new avenues for transdiagnostic cognitive interventions to protect survivors of childhood adversity from mental illness.

2.6 Conclusion

My findings show there is only moderate agreement between subjective and objective measures of childhood adversities. Additionally, results indicate that the effects of childhood adversity on psychopathology are primarily driven by a person's subjective experience. This suggests that clinical interventions targeting perception, appraisal and memories of childhood adversity may reduce the risk of subsequent psychopathology in exposed individuals.

Chapter 3 Identifying Genetic Predictors of Self-reported Bullying Victimisation: a Multi-Informant, Multi-Polygenic Score Approach

3.1 Summary

This chapter expands on results from chapter 2 by aiming to understand whether mental health vulnerabilities influence subjective self-report measures of adverse childhood experiences, independent of objective measures. Notably, evidence suggests that self-reports of bullying victimisation may be more strongly associated with mental health problems, compared to reports from other-informants (i.e., teachers, parents). In order to identify potential contributing factors to explain this, researchers have begun using polygenic scores (as proxies for mental health vulnerabilities) to capture whether the genetic predisposition to mental health vulnerabilities predict multi-informant reports of victimisation. These studies provide preliminary evidence showing that genetic predisposition to mental health vulnerabilities may be differentially associated with self-reports of perceptions of bullying victimisation versus reports from other informants (i.e., parents, teachers). However, no study has examined this relationship after accounting for reports of bullying from external informants. This has important implications as by jointly modelling reports of victimisation I am able to identify what in self-reports could be due to the subjective process (i.e.,

without objective influence). To address this research gap, I investigated whether genetic predisposition to mental health vulnerabilities, cognitive traits and anthropometric measures predict self-reported victimisation, after adjusting for reports from other informants (parents and teachers). I used data from a population-based cohort of adolescents, the Avon Longitudinal Study of Children and Adolescents. I used the most recent Genome Wide Association Studies to derive polygenic scores using the LD-pred2 software for depression, schizophrenia, anxiety disorder, neuroticism and attention deficit/hyperactivity disorder (ADHD), as well as body mass index (BMI) and educational attainment. Using the structural equation modelling package 'Lavaan,' I tested my hypothesis of the genetic predisposition to mental health vulnerabilities (i.e., depression, schizophrenia, anxiety disorder, neuroticism and ADHD) will be associated with self-reported victimisation, when adjusted for other-informant (parent and teacher) reports.

Supplementary material is located in **Appendix B.**

3.2 Introduction

Bullying is defined as the repeated occurrence of hurtful actions between peers, where a power imbalance exists between perpetrators and their victims (Olweus, 2013). In adolescence, 1 in 5 individuals are exposed to bullying, which comprises different types of experiences such as cyberbullying, relational victimisation and physical aggression (Modecki et al., 2014). Several epidemiological studies have demonstrated that bullying victimisation is associated with a range of later adverse health and socioeconomic outcomes (Arseneault, 2017; Copeland et al., 2013; Wolke et al., 2001). For example, evidence from a prospective, population-study found that child and adolescent victims of bullying have elevated rates of psychiatric disorders in early adulthood, even after accounting for any occurrence of psychiatric disorder prior to being bullied (Copeland et al., 2013). Furthermore, quasi-experimental studies show that there is a small, causal contribution of being bullied to mental health outcomes, independent of genetic and environmental confounding (Schoeler et al., 2018; Singham et al., 2017).

Bullying victimisation can be assessed in different ways, through interviews and/or questionnaires with various informants, including children (i.e., self-reports) or other-informants (e.g., parents, teachers). Different informants capture different sources of information about bullying and potential reporting biases. Self-report measures capture a child's personal perception of bullying experiences, including their memories of the occurrence and frequency of the events (Wolke et al., 2001). Additionally, self-report measures capture individual differences in how a child understands and interprets the event(s) (e.g., the same

event may be interpreted as bullying or not bullying by different children). This subjectivity however may lead to self-reports of exposure to bullying being influenced by the child's traits, such as internalising problems (Bouman et al., 2012), which might lead to over-reporting of bullying due to a greater tendency to interpret events as being traumatic. In contrast, reports of bullying from other informants (e.g., teachers and parents) reflect an external observer's assessment of whether a child is exposed to bullying, rather than the child's own perception. Teacher reports are likely to capture observed instances of bullying at school, while parent reports may capture bullying witnessed at home, or reports of instances from the parent's child. It is important however, to consider that both teacher and parent reports will also capture the subjective perspective of that particular informant (e.g., on what experiences constitute bullying).

Notably, studies have found limited agreement in reports of bullying victimisation from multiple informants (Chow et al., 2023; Shakoor et al., 2011), likely reflecting the varying sources of information that different informants have access to, and individual biases. Specifically, low to modest agreement has been found between child- and teacher-reports at age 11 (r=0.15) (Chow et al., 2023), and between child- and parent-reports of victimisation in both primary school (kappa coefficient=0.20) and secondary school (kappa coefficient=0.29) (Shakoor et al., 2011). This aligns with my meta-analytic finding (**Chapter 2**) showing that self-reports of bullying only show moderate correlations with reports from other informants (peer nominations; r=0.35, 95% CI=0.27-0.42; p<0.001). Importantly, evidence suggests that self-reports of bullying victimisation may show stronger associations with mental health problems than reports from other informants

(**Chapter 2**; Løhre et al., 2011). Therefore, it is important to understand what factors influence a child's perception of bullying victimisation, over and above reports from other external informants. Identifying these potential factors could help us understand why children's perceptions of bullying show stronger relationships with mental health problems, in comparison to reports from other informants.

Genetic vulnerabilities may be associated with a child's experience and perception of bullying victimisation. Twin studies have shown that bullying victimisation is heritable, with genetic factors accounting for 34-35% of variability in children's self-reports of bullying (Fisher et al., 2015; Shakoor et al., 2015) and 61-65% in parent and teacher-reported experiences of bullying (Ball et al., 2008; Veldkamp et al., 2019). These findings reflect gene-environment correlation (Plomin et al., 1977), whereby a child's genetic propensities correlate with the environment they experience.

More recently, studies have used polygenic scores to identify specific genetic predispositions associated with bullying victimisation. Polygenic scores are commonly used in developmental research to capture an individual's susceptibility by deriving genetic proxies for selected traits and vulnerabilities (Allegrini et al., 2022; Pingault et al., 2022). In particular, one study used polygenic scores to examine the role of genetic predisposition to psychiatric, behavioural, educational and anthropometric traits to self-reported bullying victimisation in a sample of 5,028 children (Schoeler et al., 2019). When accounting for the effects of other polygenic scores, authors found small but significant associations between polygenic scores for depression, attention-

deficit hyperactivity disorder (ADHD), and body mass index (BMI) with children's self-reports of bullying victimisation (standardised betas ranged between 0.04 to 0.06). This may be because children who exhibit early mental health vulnerabilities or higher BMI are more likely to be bullied by others. For example, children with a higher genetic predisposition to ADHD are likely to act more impulsively and evoke harsher reactions from their peers, which illustrates the concept of evocative gene-environment correlation (evocative r_{GE}). However, it is also possible that children with pre-existing vulnerabilities to mental health problems (e.g., higher genetic risk for depression) are prone to perceiving and thereby self-reporting exposure to bullying. This could be due to the underlying genetic variants for depression increasing the risk of cognitive biases (associated with depression) which shape how an individual perceives experiences. Indeed, longitudinal within-person studies have shown that individuals self-report higher levels of childhood adversity when they are depressed, compared to when they are not experiencing depression (Colman et al., 2016).

To understand the influence of genetic predisposition to mental health problems on children's perceptions versus experiences of bullying victimisation, it is important to incorporate reports from external informants (i.e., teachers), who may provide more objective information, in the sense that it is more independent from the child's perception and self-report. Two studies have examined whether genetic factors differentially predict bullying victimisation as assessed by different informants. First, Vrijen et al (2023) found that polygenic scores for internalising and externalising problems were associated with bullying victimisation assessed through self-reports, but not through peer nominations, in a cohort from the

Netherlands (n=1,604). Second, Armitage et al (2022) examined the relationship between polygenic scores for psychiatric, cognitive and physical traits, and multiple informant reports of victimisation (self, teacher, and peer) using the Quebec Newborn Twin Study (n=536) (Armitage et al., 2022). Findings indicated that the polygenic scores for mental health problems (e.g., depression, poor wellbeing) were more strongly associated with self-reported bullying victimisation, whereas polygenic scores for cognitive and physical traits (e.g., low educational attainment, high BMI) were more strongly related to teacher and peer-reports. These studies provide preliminary evidence indicating that genetic predispositions to mental health vulnerabilities may be differentially associated with self-reported perceptions of bullying victimisation versus reports from other informants.

However, to my knowledge, no study has examined the relationship between genetic predisposition to mental health vulnerabilities and self-reported bullying victimisation, after accounting for reports of bullying from external informants. In other words, the previous studies did not jointly model informants and, hence, did not explicitly aim at identifying what, in self-reports, may be specifically due to subjective processes.

To address this research gap, I investigated whether polygenic scores for mental health vulnerabilities, cognitive traits, and anthropometric characteristics predicted self-reported victimisation, after accounting for reports from other informants. To do so, I used data from a large, prospective birth cohort - the Avon Longitudinal Study of Children and Adolescents– with measures of self-, teacher- and parent-reported bullying victimisation at multiple time points in childhood and

adolescence. I hypothesised that the polygenic scores for mental health problems and related traits (depression, anxiety, schizophrenia, ADHD, neuroticism) would be associated with self-reported victimisation, when adjusted for other-informant (parent and teacher) reports.

3.3 Methods

3.3.1 Participants

Phenotype and genetic data from The Avon Longitudinal Study of Parents and Children (ALSPAC) study were used. This is an ongoing population-based birth cohort study (Boyd et al., 2013; Fraser et al., 2013) that recruited pregnant women resident in Avon, UK with expected delivery dates between 1st April 1991 and 31st December 1992. The total sample available after the age of 7 years is 15, 447 pregnancies (alive at the age of 1 year=14,901). Throughout participation, the study child participants, parents (caregivers) and teachers were assessed with questionnaires, and clinical interviews, health records and physical examinations were obtained from the study child. The study website contains information on study design and variables including a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data/).

Following quality control, I retained 8,966 participants (see **Appendix B - Supplementary Methods 1**). Participants included in the present study were those who had at least genetic data (to compute polygenic scores), and at least one of either self-report bullying victimisation (study child age 8 and 10), parent-report (mother) bullying victimisation (study child age 9 and 10) or teacher-reported bullying victimisation (study child age 7 and 10) (total analytical sample=8,319; see **Figure 3.1, Appendix B - Supplementary Table 1** for sample overlap and **Supplementary Table 2** for sample overlap of those not included).

Ethical approval was obtained from the ALSPAC Law and Ethics Committee and South West– Central Bristol National Health Service Research Ethics Committee, and written informed consent was provided by participants (including mother and teachers). Caregivers provided consent for child participation prior to the age of 16 years. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004).

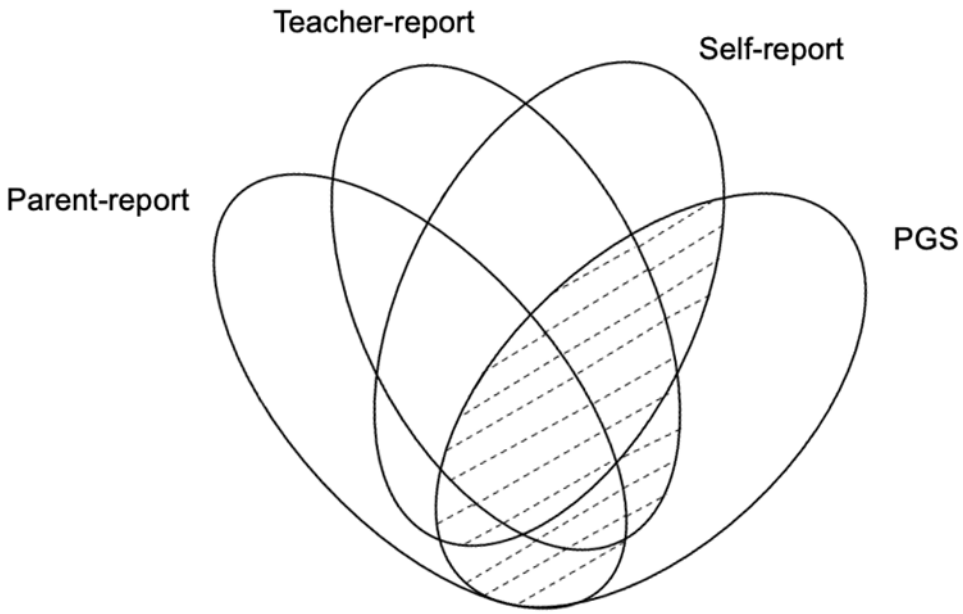


Figure 3.1. Sample overlap for the phenotypes self-report bullying victimisation, teacher-reported bullying victimisation, parent-reported bullying victimisation and polygenic scores (PGS).

Note. Total meeting inclusion criteria indicated by shaded region (n=8,319).

3.3.2 Measures

3.3.2.1 Self-reported measure of bullying victimisation

Self-reported bullying victimisation was captured from a modified version of the Bullying and Friendship Interview Schedule (BFIS) administered at age 8 and 10 years (see **Appendix B - Supplementary Table 3** for item details) (Wolke et al., 2001). This scale assesses 9 bullying experiences in the past 6 months (including both overt and relational types of bullying). Overt victimisation was assessed with 5 items (hitting or beating; threatening or blackmailing; taking personal belongings; tricking in a nasty way; calling bad/nasty names), and relational victimisation was assessed via 4 items (telling lies or nasty things about them; spoiling games; excluding to upset them; pressuring them to do things they don't want to). Each BFIS item score ranges from 0 to 3 (0= none, 1=seldom [1-3 times], 2=frequently [>4 times but <1/week], and 3=very frequently [at least once per week]). Using reported bullying across age 8 and/or 10, an overall self-report bullying victimisation sum score was computed. This approach to creating a BFIS composite score has been applied elsewhere (Schoeler et al., 2019).

3.3.2.2 Parent-reported measure of bullying victimisation

Parent-reported bullying victimisation was obtained from the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 2001) that was administered to the mother when the study child was age 9 and 11 years. For the present study, one item from this scale was used: 'child picked on or bullied by other children' (with responses: 1= doesn't apply, 2= somewhat applies, 3= certainly applies). Using the reported bullying available at age 9 and/or 11, an overall composite sum score

was computed ranging from minimum 2 (doesn't apply across both ages) to 6 (certainly applies across both ages).

3.3.2.3 Teacher-reported measure of bullying victimisation

Teacher-reported bullying victimisation was obtained from the SDQ (Goodman, 2001) that was administered to the teacher when the study child was approximately age 7 and 10 years. Similar to the parent-reported measure, the item 'child picked on or bullied by other children' was used (responses: 1= doesn't apply, 2= somewhat applies, 3= certainly applies). Using reports obtained across both ages an overall composite sum score of teacher-reported victimisation was computed ranging from minimum 2 (doesn't apply across both ages) to 6 (certainly applies across both ages).

3.3.2.4 Covariates

To improve precision in the effect estimates, age, sex, and 10 principal components were included as covariates. Age was obtained at both study focus clinic 8 (at age 8 years) and focus clinic 10 (at age 10 years) coinciding with the administration of the self-reported measure of bullying victimisation. Both ages were included as covariates. Sex of the child was obtained from either the recording in the delivery room, obstetric records or birth notifications. To account for population stratification, principal components analysis was conducted using the genetic data. The top 10 principal components were obtained (Price et al., 2006) and included as covariates in all regression models.

3.3.2.5 Polygenic score analysis

Seven polygenic scores (PGSs) (for psychiatric, behavioural, physical and educational traits) were computed including ADHD (Demontis et al., 2023), lifetime anxiety disorder (Purves et al., 2020), major depressive disorder, neuroticism (Nagel et al., 2018), schizophrenia (Trubetskoy et al., 2022), body mass index (Yengo et al., 2018) and educational attainment (Okbay et al., 2022). Summary statistics were obtained from publicly available Genome Wide Association Studies derived from discovery cohorts of European ancestry that did not include ALSPAC participants (see **Table 3.1** for details). These summary statistics were selected based on the study aim to examine the effect of genetic predisposition of mental health vulnerabilities on self, teacher and parent-reported bullying victimisation. The polygenic scores for body mass index and educational attainment were included based on prior research indicating they predict multi-informant victimisation (Armitage et al., 2022; Schoeler et al., 2019).

Table 3.1. GWAS Summary Statistics of the 7 Included Samples.

Trait	Total sample size	Number of cases (affected)	Number of controls (unaffected)	Year of publication	Link to summary statistics file	Publication DOI/URL	Reference
ADHD	225534	38691	186843	2023	https://pgc.unc.edu/for-researchers/download-results/	10.1038/s41588-022-01285-8	Demontis, D., Walters, G. B., Athanasiadis, G., Walters, R., Therrien, K., Nielsen, T. T., ... & Børglum, A. D. (2023). Genome-wide analyses of ADHD identify 27 risk loci, refine the genetic architecture and implicate several cognitive domains. Nature genetics, 55(2), 198-208.
Lifetime Anxiety Disorder (UKB)	83566	25453	58113	2020	https://drive.google.com/drive/folders/1fguHvz7l2G45sbMl9h_veQun4aXNTy1v	10.1038/s41380-019-0559-1	Purves, K. L., Coleman, J. R., Meier, S. M., Rayner, C., Davis, K. A., Cheesman, R., ... & Eley, T. C. (2020). A major role for common genetic variation in anxiety disorders. Molecular psychiatry, 25(12), 3292-3303.
BMI	681275	NA	NA	2018	https://www.pgscatalog.org/score/PGS000027/	10.1093/hmg/ddy271	Yengo, L., Sidorenko, J., Kemper, K. E., Zheng, Z., Wood, A. R., Weedon, M. N., ... & Giant Consortium. (2018). Meta-analysis of genome-wide association studies for height and body mass index in~ 700000 individuals of European ancestry. Human molecular genetics, 27(20), 3641-3649.
Education Attainment (UKB)	441121	NA	NA	2022	http://www.thessgac.org/data	10.1038/s41588-022-01016-z	Okbay, A., Wu, Y., Wang, N., Jayashankar, H., Bennett, M., Nehzati, S. M., & Esko, T. (2022). Polygenic prediction of educational attainment within and between families from genome-wide association analyses in 3 million individuals. Nature genetics, 54(4), 437-449.
Major Depressive Disorder	38695	15726	22969	2019	https://datashare.ed.ac.uk/handle/10283/3203	10.1038/s41593-018-0326-7	Howard, D. M., Adams, M. J., Clarke, T. K., Hafferty, J. D., Gibson, J., Shirali, M., ... & McIntosh, A. M. (2019). Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. Nature neuroscience, 22(3), 343-352.
Neuroticism	449484	NA	NA	2018	https://ctg.cncr.nl/software/summary_statistics/	10.1038/s41588-018-0151-7	Nagel, M., Jansen, P. R., Stringer, S., Watanabe, K., De Leeuw, C. A., Bryois, J., ... & Posthuma, D. (2018). Meta-analysis of genome-wide association studies for neuroticism in 449,484 individuals identifies novel genetic loci and pathways. Nature genetics, 50(7), 920-927.
Schizophrenia	175799	74776	101023	2022	https://pgc.unc.edu/for-researchers/download-results/	10.1038/s41586-022-04434-	Trubetskoy, V., Pardiñas, A. F., Qi, T., Panagiotaropoulou, G., Awasthi, S., Bigdeli, T. B., ... & Lazzeroni, L. C. (2022). Mapping genomic loci implicates genes and synaptic biology in schizophrenia. Nature, 604(7906), 502-508.

Abbreviations: GWAS, Genome-Wide Association Study; UKB, UK Biobank; ADHD, Attention Deficit Hyperactivity Disorder; BMI, Body Mass Index.

Polygenic scores were generated using the LDPred2-auto approach, which is an extension from LDPred with improved predictive performance (Privé et al., 2020; Vilhjálmsson et al., 2015). This approach accounts for the linkage disequilibrium between variants (non-random association between alleles at different loci). Additionally all models are run over the 1.1 million HapMap3 variants at once (genome-wide) hence no p-value threshold is applied. Providing quality control is carried out on the discovery summary statistics, this approach automatically estimates the proportion of causal variants (p) and the SNP heritability (h2); therefore there is no requirement for a validation dataset to tune hyper-parameters (Privé et al., 2020). All polygenic scores were standardised (mean=0, SD=1).

Polygenic scores leverage summary statistics produced from genome-wide association studies of large, discovery samples to compute an individual-level score in the target sample by aggregating the identified common single nucleotide polymorphisms that are associated with complex traits (Allegrini et al., 2022). The principal use of the polygenic approach is routed in the knowledge that complex traits and behaviours (i.e., depression) are not produced by a single gene or even polymorphisms located in the same chromosome, but rather multiple single nucleotide polymorphisms across the genome that contribute to an increased risk. Given this, a polygenic score for depression can be computed (proxy for depression) to analyse how the genetic predisposition to this trait is associated with bullying victimisation.

Often, single polygenic score models are computed to assess the genetic predisposition to a specific trait. This involves analysing the effect of an individual

polygenic score (i.e., for depression) on a phenotype. Additionally, a multi-polygenic score model can be run which involves using a multivariate approach to assess the unique effect of each polygenic score, while controlling for others.

3.3.3 Statistical Analysis

All statistical analyses were carried out in R version 4.2.0 (Team, R.D.C., 2022). These are presented in **Figure 3.2**. The analysis code is available at https://github.com/erfrancis/genetic_predictors_bullying_multi-informant. I set out to determine whether the genetic predisposition to mental health and behavioural related traits predicts self-reported bullying victimisation, over and above that of the multi-informant (parent and teacher) reported bullying victimisation.

First, to examine the associations between each polygenic score and bullying victimisation as reported by each informant (self, parent, and teacher), separate regression models were computed using the 'Lavaan' package version 0.6-16 (Rosseel, 2012). Here, the models were only adjusted for covariates (self-reported age, sex and 10 principle components) but not for other informants and other polygenic scores (see **Figure 3.2: Panel A**). The common missing data method full information maximum likelihood (FIML) was applied. The 'ggplot2' package (Wickham, 2016) was used to plot these results.

Second, to estimate the effect of each polygenic score on children's reports of bullying victimisation, the association between each polygenic score and self-reported bullying victimisation, adjusting for both parent and teacher-reports was examined (model referred to as "Single-PGS", see **Figure 3.2: Panel B**). As a

sensitivity analysis, parent and teacher-reports were analysed separately to determine whether polygenic scores would predict self-report adjusting only for one informant's report of bullying.

Third, to examine the unique effect of each polygenic score on reports of bullying victimisation, I used structural equation modelling to examine whether the individual polygenic scores (e.g., for depression) influenced self-reported bullying victimisation, when accounting for both parent and teacher-report, as well as the effects of other polygenic scores (model referred to as "Multi-PGS", see **Figure 3.2: Panel C**). Additional analyses were run to analyse parent and teacher-reports separately to determine if there were any differences in findings when only accounting for one informant. FIML was applied to all regression models to account for missing data.

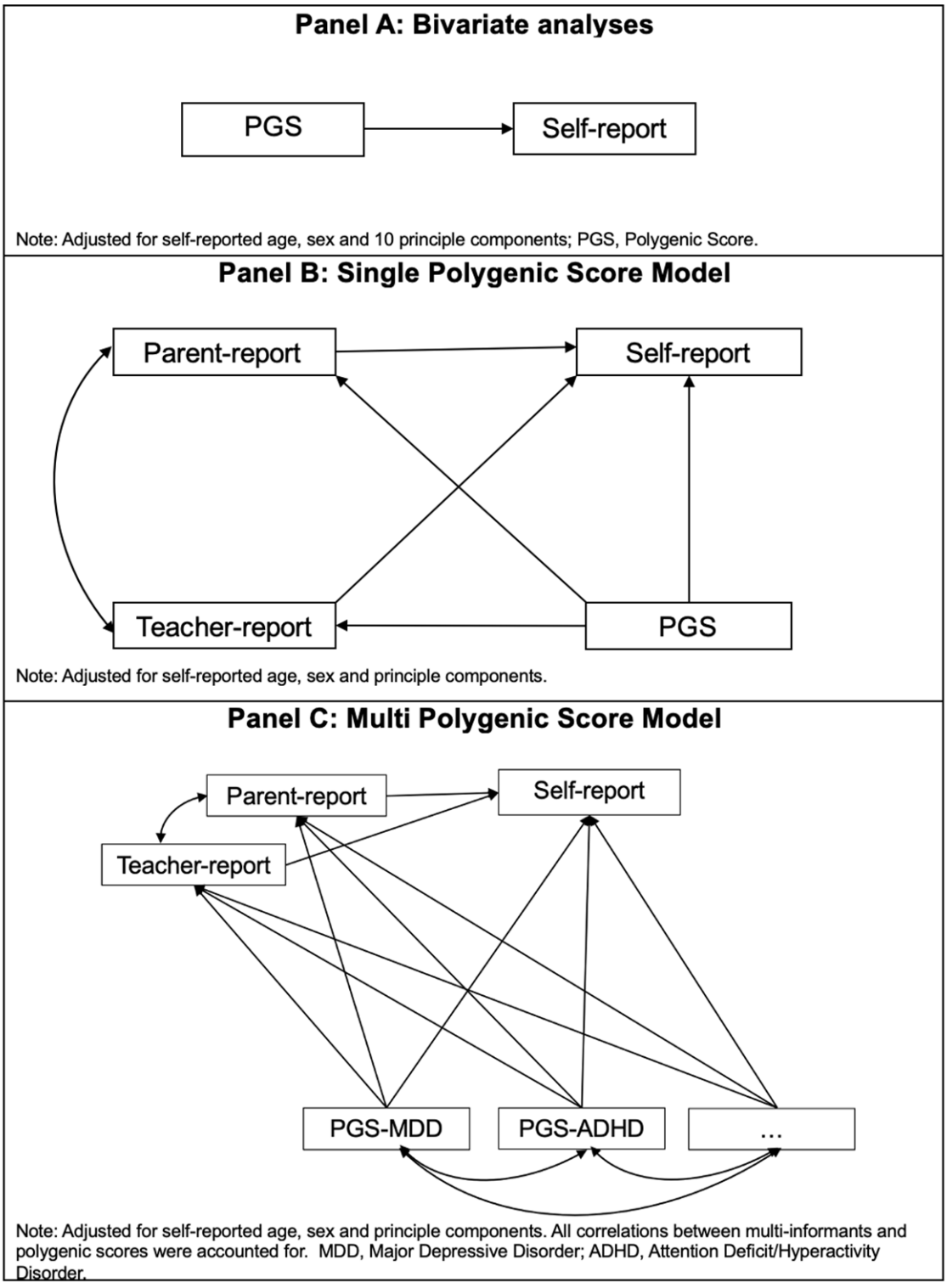


Figure 3.2. Statistical analyses used in Chapter 3.

3.4 Results

3.4.1 Descriptive statistics

A total of 8,319 participants met the inclusion criteria (49.2% female). Study children included in the analytical sample differed from those not included in terms of maternal age and social class (with included children having older mothers and a higher maternal occupation social class, see **Table 3.2**)

The correlations between the 7 polygenic scores and the reports of bullying victimisation across multiple informants are shown visually in **Figure 3.3** (see correlation values in **Appendix B - Supplementary Table 4**). The self-reported bullying victimisation sum score showed a small correlation with teacher-reported victimisation (r=0.19; 95% Confidence Interval [CI]= 0.16-0.22; p<0.001), and a moderate correlation with parent-reported victimisation (r=0.28; 95% CI= 0.26-0.31; p<0.001).

Table 3.2. Descriptive data and mean victimisation scores across ages (informants included versus not included).

	Participants included (n=8319)			Participants not included (n=7450)			Test of differences		
	N (%)	**Mean (SD)**	**Range (Min-Max)**	**N (%)**	**Mean (SD)**	**Range (Min-Max)**	***p* value***	**X2 / t**	**N (total)**
Age of mother at study child birth (years)[a] ($N_{included}$=7281, $Not_{included}$=4613)									
	n/a	28.86 (4.58)	15-45	n/a	27.56 (5.08)	15-45	**<0.001**	627.15	11894
Female									
	4082 (49.2)			3316 (48.4)			0.3235	0.97466	7398
Maternal occupational social class[b] ($N_{included}$=6403, $N_{not\ included}$=3809)									
Professional	408 (6.37)	n/a	n/a	191 (2.56)	n/a	n/a	**<0.001**	81.151	10212
Managerial and technical occupations	2132 (33.30)	n/a	n/a	1080 (14.50)	n/a	n/a			
Skilled occupations non-manual	2726 (42.57)	n/a	n/a	1638 (21.99)	n/a	n/a			
Skilled occupations manual	453 (7.07)	n/a	n/a	349 (4.68)	n/a	n/a			
Partly-skilled occupations	581 (9.07)	n/a	n/a	426 (5.72)	n/a	n/a			
Unskilled occupation	102 (1.59)	n/a	n/a	122 (1.64)	n/a	n/a			
Maternal education[c] ($N_{included}$=7547, $N_{not\ included}$=5117)									
University degree	1128 (14.95)	n/a	n/a	498 (9.73)	n/a	n/a	**<0.001**	73.272	12664
A-Level	2301 (30.49)	n/a	n/a	1061(20.73)	n/a	n/a	**<0.001**	147.52	12664
O-Level	5508 (72.98)	n/a	n/a	2975 (58.14)	n/a	n/a	**<0.001**	303.17	12664
CSE	4478 (59.33)	n/a	n/a	2931 (57.28)	n/a	n/a	**<0.001**	5.2634	12664
No qualification	285 (3.78)	n/a	n/a	334 (6.53)	n/a	n/a	**<0.001**	49.231	12664
Mean victimisation sum scores across informants[d]									
Self-reported sum score	6258	-0.01(0.98)	-0.9-6.99	1703	0.05 (1.05)	-0.91-6.64	**0.0246**	2.249	7961
Parent-model	6668	2.51 (0.90)	2-6	2140	2.53 (0.95)	2-6	0.3668	0.90269	8808
Teacher-model	6258	2.29 (0.74)	2-6	3741	2.34 (0.81)	2-6	**0.001201**	3.24	9999

[a]Completed by mother (age: 8 weeks). [b]Completed by mother (age: 32 weeks). Categories based on the Standard Occupation Classification: SOC90 (https://www.hesa.ac.uk/support/documentation/occupational/soc90). [c]Completed by mother (age: 32 weeks). Data from maternal education is not mutually exclusive i.e., mothers can indicate more than one education qualification. Percentage female refers to the proportion of females that reported having the qualification. [d]Self-report sum score created from report at age 8 and 10; Teacher-report sum score created from reports at study child age 7 and 10; Parent-report sum score created from reports at study child age 9 and 11. For teacher-report ages 7 and 10 answers range from 1-3. As 1= doesn't apply, the mean for the bullying victimisation score is based on reports that do indicate bullying victimisation. For parent-report ages 9 and 11 answers range from 1-3. As 1= doesn't apply, the mean for the bullying victimisation score is based on reports that do indicate bullying victimisation. *p-value estimates calculated from Welch Two Sample t-test (continuous) or Pearson's Chi-squared test with Yates' continuity correction (binary/ordinary) assuming unequal variances.

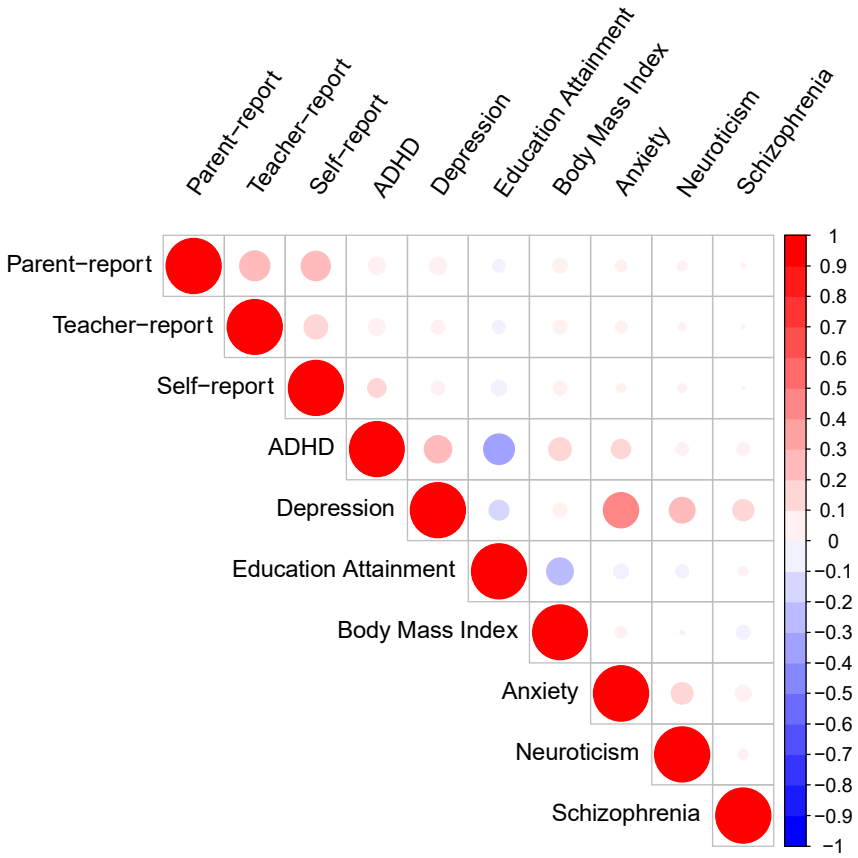


Figure 3.3. Heatmap of correlations between bullying victimisation phenotypes and polygenic scores.

Abbreviations: Self-report, Self-reported bullying victimisation sum score; Parent-report Parent-reported bullying victimisation sum score; Teacher-report, Teacher-reported bullying victimisation sum score; ADHD, Attention Deficit/Hyperactivity Disorder; Depression, Major Depressive Disorder.

Polygenic scores were computed for all variables other than the three phenotypes: self, parent and teacher-reported bullying victimisation. See **Appendix B - Supplementary Table 4** for significance.

3.4.2 Associations between polygenic scores and reports of bullying victimisation across informants

I next examined the associations between polygenic scores and reports of bullying victimisation across the three informants, adjusting for covariates (self-reported age, sex and 10 principal components). As shown in **Figure 3.4**, polygenic scores for neuroticism, depression, anxiety, ADHD, education attainment and BMI predicted self-reported bullying victimisation.

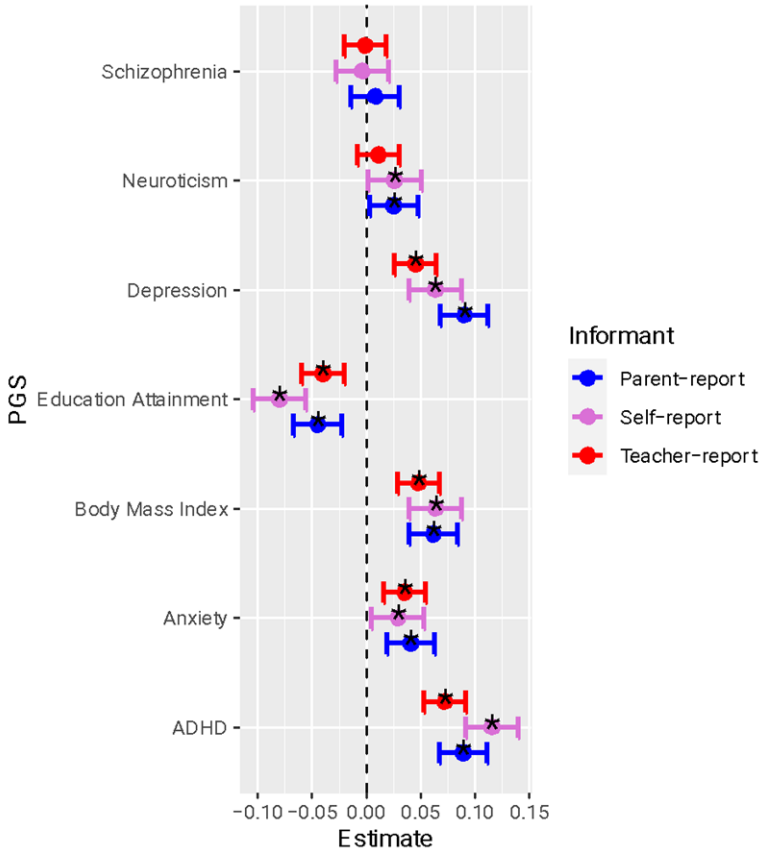


Figure 3.4. Associations between polygenic scores and reports of bullying victimisation across multiple informants.

Note. Associations adjusted for covariates sex, self-reported age and 10 principle components. Abbreviations: PGS, Polygenic Score; ADHD, Attention Deficit Hyperactive Disorder. All correlations significant (<0.05) denoted by asterisk (*).

From the bivariate analyses (**Table 3.3**), the effect size appeared larger for the associations between self-reported victimisation and the polygenic scores for ADHD and Educational Attainment. The polygenic score for neuroticism appeared to predict both self and parent-reported but not teacher reported bullying victimisation.

3.4.3 Polygenic predictors of self-reported bullying victimisation

In the Single-PGS model (**Figure 3.2: Panel B**), when adjusting for multi-informant reported victimisation, 4 polygenic scores remained significantly associated with self-reported victimisation: depression (β=0.030; *p*=0.010), ADHD (β=0.078; 95%, *p*<0.001), education attainment (β=-0.061, *p*<0.001) and body mass index (β=0.037; *p*=0.002) (**Table 3.3**). Interestingly, whilst the polygenic score for anxiety and the polygenic score for neuroticism were initially significantly correlated with self-reported victimisation (see **Bivariate Analysis, Table 3.3**) they were not after adjusting for multi-informant reported victimisation. When additionally adjusting for the effects of other polygenic scores in the Multi-PGS model (**Figure 3.2: Panel C**), only 2 polygenic scores had a small but significant association with self-reported bullying victimisation: ADHD (β=0.063; *p*<0.001) and education attainment (β=-0.036; *p*=0.004) (see **Table 3.3**)

Table 3.3. Bivariate Analysis, Single-PGS Model and Multi-PGS Model findings with Multi-informant Reported Victimisation.

Regression	Bivariate analysis				Single-PGS Model					Multi-PGS Model				
	Estimate	Lower 95% CI	Upper 95% CI	*p*	*b*	Lower 95% CI	Upper 95% CI	*p*	β	*b*	Lower 95% CI	Upper 95% CI	*p*	β
Parent-Report → Self-Report	NA				NA	-	-	-		0.271	0.242	0.300	**<0.001**	0.247
Teacher-Report → Self-Report	NA				NA	-	-	-		0.149	0.110	0.188	**<0.001**	0.112
Self-Reported Victimisation[a]														
PGS-Major Depressive Disorder	0.064	0.04	0.088	**<0.001**	0.030	0.007	0.052	**0.010**	0.030	0.012	-0.014	0.038	0.361	0.012
PGS-Schizophrenia	-0.004	-0.028	0.020	0.758	-0.005	-0.027	0.018	0.684	-0.005	-0.007	-0.029	0.016	0.573	-0.007
PGS-ADHD	0.116	0.092	0.140	**<0.001**	0.077	0.054	0.100	**<0.001**	0.078	0.062	0.038	0.087	**<0.001**	0.063
PGS-Anxiety	0.029	0.005	0.053	**0.018**	0.010	-0.013	0.032	0.394	0.010	-0.005	-0.030	0.019	0.683	-0.005
PGS-Neuroticism	0.026	0.002	0.050	**0.037**	0.016	-0.007	0.039	0.171	0.016	0.011	-0.013	0.034	0.373	0.011
PGS-Educational Attainment	-0.080	-0.104	-0.055	**<0.001**	-0.060	-0.082	-0.037	**<0.001**	-0.061	-0.036	-0.060	-0.012	**0.004**	-0.036
PGS-Body Mass Index	0.064	0.040	0.088	**<0.001**	0.036	0.013	0.059	**0.002**	0.037	0.017	-0.006	0.041	0.142	0.018
Parent-Reported Victimisation														
PGS-Major Depressive Disorder	0.090	0.068	0.112	**<0.001**	0.086	0.065	0.107	**<0.001**	0.096	0.068	0.044	0.092	**<0.001**	0.076
PGS-Schizophrenia	0.008	-0.014	0.030	0.466	0.008	-0.014	0.030	0.466	0.009	0.000	-0.022	0.021	0.964	-0.001
PGS-ADHD	0.089	0.067	0.111	**<0.001**	0.086	0.064	0.107	**<0.001**	0.095	0.059	0.036	0.082	**<0.001**	0.066
PGS-Anxiety	0.041	0.019	0.063	**<0.001**	0.040	0.018	0.061	**<0.001**	0.044	-0.001	-0.024	0.022	0.938	-0.001
PGS-Neuroticism	0.025	0.003	0.048	**0.026**	0.022	0.001	0.044	**0.044**	0.025	0.004	-0.018	0.026	0.710	0.005
PGS-Educational Attainment	-0.045	-0.067	-0.023	**<0.001**	-0.044	-0.065	-0.022	**<0.001**	-0.048	-0.008	-0.031	0.015	0.477	-0.009
PGS-Body Mass Index	0.062	0.040	0.084	**<0.001**	0.060	0.039	0.082	**<0.001**	0.067	0.046	0.024	0.067	**<0.001**	0.050
Teacher-Reported Victimisation														
PGS-Major Depressive Disorder	0.045	0.026	0.065	**<0.001**	0.043	0.025	0.061	**<0.001**	0.058	0.021	0.001	0.042	**0.043**	0.029
PGS-Schizophrenia	-0.001	-0.020	0.018	0.924	0.000	-0.019	0.018	0.974	0.000	-0.006	-0.025	0.012	0.490	-0.009
PGS-ADHD	0.072	0.053	0.091	**<0.001**	0.068	0.050	0.086	**<0.001**	0.092	0.055	0.035	0.075	**<0.001**	0.074
PGS-Anxiety	0.035	0.016	0.054	**<0.001**	0.033	0.015	0.051	**<0.001**	0.045	0.015	-0.004	0.035	0.125	0.021
PGS-Neuroticism	0.011	-0.008	0.031	0.255	0.013	-0.006	0.031	0.175	0.017	0.000	-0.018	0.019	0.994	0.000
PGS-Educational Attainment	-0.040	-0.059	-0.020	**<0.001**	-0.036	-0.054	-0.017	**<0.001**	-0.048	-0.005	-0.024	0.015	0.649	-0.006
PGS-Body Mass Index	0.048	0.029	0.067	**<0.001**	0.045	0.026	0.063	**<0.001**	0.060	0.033	0.014	0.052	**0.001**	0.044

[a]Adjusted for multiple informants (parent and teacher-reported bullying victimisation). Abbreviations: b, unstandardised coefficient betas; β, standardised coefficient betas; PGS, Polygenic Score; CI, 95% Confidence Interval; ADHD, Attention Deficit Hyperactivity Disorder. Single-PGS and Multi-PGS models adjusted for age, sex and 10 principal components (genetic ancestry). Bold *p* value represents significant ($p<0.05$).

3.4.4 Polygenic predictors of parent-reported bullying victimisation

When examining the relationships between polygenic scores and parent-reported bullying victimisation in the Single-PGS model (**Figure 3.2: Panel B**), 6 polygenic scores showed significant associations: depression (β=0.096; *p*<0.001), ADHD (β=0.095; *p*<0.001), lifetime anxiety disorder (β=0.044; *p*<0.001), neuroticism (β=0.025; *p*=0.044), education attainment (β=-0.048; *p*<0.001) and body mass index (β=0.067; *p*<0.001). The only polygenic score not associated with parent reported-victimisation was schizophrenia (see **Table 3.3**). This is in line with findings from the bivariate analyses indicating no significant association between the polygenic score for schizophrenia and parent-reported victimisation (**Table 3.3**). When accounting for the effect of other polygenic scores in the multi-PGS model (**Figure 3.2: Panel C**), only the polygenic scores for depression (β=0.076; *p*<0.001), ADHD (β=0.066, *p*<0.001) and body mass index (β=0.050; *p*<0.001) were significantly associated with parent-reported bullying victimisation (see **Table 3.3**).

3.4.5 Polygenic predictors of teacher-reported bullying victimisation

In bivariate analyses, all of the polygenic scores apart from schizophrenia and neuroticism were associated with teacher-reported victimisation (see **Table 3.3**). In the Single-PGS Model (**Figure 3.2: Panel B**), I observed no change in the direction of these findings. The polygenic scores for depression (β=0.058; *p*<0.001), ADHD (β=0.092; *p*<0.001), lifetime anxiety disorder (β=0.045; *p*<0.001), education attainment (β=-0.048; *p*<0.001) and body mass index (β=0.060; *p*<0.001) were all significantly associated with teacher-reported

victimisation. The polygenic scores for schizophrenia and neuroticism were not associated with teacher-reported victimisation (see **Table 3.3**). In the Multi-PGS model, only the polygenic scores for depression (β=0.029; *p*=0.043), ADHD (β=0.074; *p*<0.001) and body mass index (β=0.044; *p*=0.001) had a very small but significant association with teacher-reported bullying victimisation (see **Table 3.3**).

When examining the relationship between polygenic scores and self-reported victimisation adjusting for one informant only (either parent or teacher-report) findings were not fundamentally different (see **Appendix B – Supplementary Methods 2, Supplementary Figures 1 and 2, Supplementary Tables 5 and 6**).

3.5 Discussion

Using data from a large, prospective longitudinal birth cohort, I tested the hypothesis that genetic predisposition to mental health vulnerabilities would be associated with self-reported bullying victimisation after accounting for reports from external informants (parents and teachers). The present study findings indicate partial support for this hypothesis. The following discussion will outline (1) how the present study findings extend previous research findings examining the effect of polygenic scores for mental health vulnerabilities on self-reported victimisation, (2) insights into the aetiology of self-versus other-informant reports of bullying victimisation, and (3) directions for future research.

In bivariate analyses, I found that polygenic scores for a range of mental health vulnerabilities (depression, anxiety, neuroticism, and ADHD) were associated with self-reported bullying victimisation, as well as parent and teacher reports. This suggests that children with genetic predispositions to mental health vulnerabilities (internalising problems and ADHD) have an elevated risk of experiencing bullying (as reported by children, parents, and teachers). However, among psychiatric polygenic scores, only the polygenic scores for depression and ADHD remained associated with self-reported victimisation, after adjusting for parent and teacher reports. This suggests that the genetic predisposition to depression and ADHD may also influence a child's unique perception of bullying victimisation (indexed by self-reports of bullying that are not captured by parent and/or teacher reports). Notably though, this appeared to be largely driven by ADHD polygenic risk, as when additionally adjusting for the effects of other polygenic scores, the polygenic score for depression was no longer associated

with self-reported victimisation. Overall, my hypothesis was only partially supported, as polygenic scores for other mental health vulnerabilities (i.e., schizophrenia, anxiety, neuroticism) were not uniquely associated with self-reported victimisation, independent of other informant reports.

The polygenic score for ADHD was uniquely associated with self-reports (beyond other-informant reports), but also associated with teacher and maternal reports which are more independent of the child's perception. This suggests two pathways by which genetic predisposition to ADHD can influence self-reported victimisation. First, the underlying genetic variants associated with ADHD may influence the child's cognitive functioning (i.e., negative attentional biases), which in turn may make them more prone to perceive events more negatively and thereby self-report exposure to bullying (Fogleman et al., 2019). Second, genetic variants associated with ADHD may manifest in children's symptoms (i.e., impulsivity-hyperactivity) leading to behaviours (e.g. impulsive or aggressive behaviours) that result in bullies targeting them. This is an example of evocative r_{GE} (Pingault et al., 2022).

The inclusion of polygenic scores for educational attainment and BMI led to additional insights. First, the polygenic score for educational attainment was negatively associated with parent, teacher, and self-reported victimisation, in bivariate analyses. After adjusting for multi-informants reports and the effect of other polygenic scores, the polygenic score for educational attainment remained associated with children's self-reports of victimisation. This suggests that children with genetic predisposition to low educational achievement are more likely to (i) experience bullying (due to consistent reports across informants), and (ii)

perceive bullying victimisation that is not captured by teacher or parent reports. Further research is warranted to tease apart the underlying constructs that may explain how the polygenic score for (low) educational attainment influences children's perceptions of victimisation; for example, by exploring the role of cognitive (i.e., intelligence; Verlinden et al., 2014) and non-cognitive skills (i.e., personality traits; Demange et al., 2021; Morris et al., 2021). Alternatively, the polygenic score for education is associated with family socioeconomic status and children may be particularly sensitive to their socioeconomic status when rating occurrences of bullying victimisation.

Second, the polygenic score for BMI was associated with self-reported victimisation, via parent- and teacher-report only, when accounting for the effect of other polygenic scores. This suggests that children with genetic predisposition to higher BMI have an elevated risk of experiencing bullying victimisation (captured in reports from parents and teachers), but that this is unlikely to affect their perception of victimisation over and above levels of victimisation reported by other informants.

In the context of previous evidence, my study extends prior findings by showing that children with genetic predisposition to ADHD are not only more likely to experience bullying victimisation, but also to perceive victimisation beyond that reported by parents and teachers. These findings contradict earlier results from Armitage et al (2022), which did not identify an association between the polygenic score for ADHD with self-report or other informant-reports of victimisation. However, there are two plausible explanations for this discrepancy. First, this could be due to the larger sample size in the present study (n=8,132, versus

n=536), which would have improved statistical power to detect a true effect. Notably, previous research focusing only on self-reported bullying victimisation found a significant association with the ADHD polygenic score (Schoeler et al., 2019). Second, the present study utilised a more recent approach to derive polygenic scores (LDpred2-auto; Privé et al., 2020) found to be more effective at identifying associations than the method used in Armitage et al's (2022) study (PRSice-2). Therefore, previous findings that observed no association between the polygenic score for ADHD and multi-informant reported bullying victimisation may in fact be false negatives (where a true association exists).

My findings also do not support prior research showing that polygenic scores for mental health vulnerabilities are associated with self-reported (but not other informant-reported) victimisation (Armitage et al., 2022; Vrijen et al., 2023), whereas polygenic scores for cognitive and physical traits are associated with other informant-reports of victimisation, but not self-reports (Armitage et al., 2022). For example, in my study, the polygenic score for depression, educational attainment and BMI were associated with both self-reported and other-informant reported victimisation in bivariate analyses. However, there are key methodological differences between these studies to consider that may explain the divergent findings. Specifically, the present study adjusts for multi-informants when analysing polygenic predictors of self-reported victimisation. In doing so, this accounts for the residual effect of the objective (external informant) measure on the self-report measure, allowing me to improve the precision of effect estimates of the relationship between genetic predisposition to mental health vulnerabilities and self-reported victimisation. Future studies should consider

jointly modelling self- versus other-informant reported victimisation. Additionally, future research should examine whether genetic predisposition to mental health vulnerabilities also influence reporting of other adversities, such as self-reported maltreatment and neighbourhood adversity, independent of more objective measures of these adversities.

Additionally, it is worth considering whether the genetic relatedness of the mother to the study child played a role in the effect estimates observed (e.g., shared parent-offspring genetic predisposition to depression or passive r_{GE} introducing bias in mother-reported victimisation). Whilst the effect sizes were small, the present study found that the associations between the polygenic scores for mental health vulnerabilities and parent-reported bullying victimisation were slightly larger when compared to teacher-reported victimisation. For example, in the bivariate analysis, a larger association was found between the genetic predisposition to depression and parent-reported victimisation (r=0.090, 95% CI= 0.068 to 0.112; p<0.001), compared to the genetic predisposition to depression and teacher-reported victimisation (β=0.045, 95% CI= 0.026 to 0.065; p<0.001). This is important to consider in light of recent evidence indicating that genetic confounding occurs between self-reported victimisation and parent-reported child outcomes (Vrijen et al., 2023).

There are a number of limitations that should be considered. First, the findings observed in the present study may be explained by differences in the measurements used. The self-report measure of bullying victimisation comprehensively captures both occurrence and frequency of bullying (Wolke et al., 2001), whereas parent and teacher-reported bullying victimisation is obtained

via a single-item asking about the occurrence of bullying (Goodman, 2001). Therefore, it is not possible to conclude that these measures are necessarily corresponding due to parent- and teacher-report not capturing frequency which could prompt informants to acknowledge the severity of bullying and influence reporting. To address this, future research should aim to incorporate multi-informant measures that capture both occurrence and frequency in order to replicate and strengthen confidence in my findings.

Second, it is possible that self-reported bullying victimisation indexes the actual bullying experience as well as the child's perception, even after accounting for other-informant reports. This may be due to parents and teachers not witnessing or hearing about all instances of bullying. As such, even after accounting for other informants, some of the remaining associations between polygenic scores and child reported victimisation may still reflect evocative r_{GE} rather than simply an influence on perception.

Third, it should be acknowledged that parent-reports may be more prone to measurement bias than teacher reports due to the close nature of the relationship with the child and passive gene-environment correlation. Due to limited data availability, the present study did not incorporate peer reports of victimisation (Bouman et al., 2012) which could have further detailed 1) how peers of a similar age perceive the child's interactions with others and, 2) how this measure is related to the individual's genetic predisposition to mental health vulnerabilities. The inclusion of peer-reports would have allowed me to better capture an 'objective' measure of bullying victimisation and, consequently, better ascertain

which genetic predispositions specifically influence children's perception of bullying.

Fourth, the present study analysed data from ALSPAC participants restricted to European ancestry. As such, findings may not be generalisable to other groups. Finally, attrition in the ALSPAC cohort has been associated with lower socioeconomic status, genetic predisposition to adverse health outcomes therefore the study findings may not be fully representative (Howe et al., 2013; Taylor et al., 2018).

3.6 Conclusion

In conclusion, findings revealed that the polygenic score for ADHD is associated with children's self-reports of bullying victimisation, over and above reports from other informants. This suggests that children with genetic predisposition to ADHD are more likely to perceive bullying victimisation that is not apparent to parents and teachers. I also observed similar findings for the polygenic score for educational achievement, whereby children with lower genetic propensity for educational achievement were more likely to self-report victimisation, beyond other-informant reports. In contrast, polygenic scores for other mental health problems (e.g., neuroticism, anxiety) and BMI were not uniquely associated with self-reports of bullying after accounting for other-informant reports.

Chapter 4 Polygenic Scores For Psychiatric Disorders Predict Subjective Body Dissatisfaction Beyond Objective Anthropometric Measures

4.1 Summary

After examining whether the genetic predisposition to mental health vulnerabilities predicts subjective reporting of bullying victimisation over and above multi-informant reported bullying victimisation (**Chapter 3**), this chapter will explore whether these findings generalise to another subjective experience known to be a key risk factor for mental health problems in adolescence – namely, body dissatisfaction. This chapter aims to test the hypothesis that genetic predisposition to mental health vulnerabilities predict subjective weight and waist dissatisfaction, over and above objectively measured anthropometric measures (e.g., body mass index, waist circumference). Single-polygenic score models will be calculated to examine the independent effect of the individual polygenic scores on (1) weight dissatisfaction, accounting for body mass index, and (2) waist dissatisfaction, accounting for waist circumference. Multi-polygenic score models will be used to examine the unique effect of the polygenic scores for mental health vulnerabilities on (1) weight dissatisfaction, accounting for body mass index and the effects of other polygenic scores, and (2) waist dissatisfaction, accounting for

waist circumference and the effects of other polygenic scores. Supplementary material is located in **Appendix C**.

4.2 Introduction

Body dissatisfaction is characterised as a negative subjective evaluation of one's body (Grogan, 2021), and can encompass a lack of satisfaction with one's weight, shape, or specific body areas. Body dissatisfaction in adolescence has increased in recent years (Solmi et al., 2021) and, in 2019, it was reported as the most common concern among 10- to 15- year olds (The Children's Society, 2021). This is concerning because young people who experience body dissatisfaction are at a higher risk of developing poor mental health, including eating disorders (Rohde et al., 2015), psychological distress (Duchesne et al., 2017), and depressive symptoms (Sharpe et al., 2018). Notably, findings from a large longitudinal study revealed that adolescents who experienced early adolescent body dissatisfaction were likely to have later depressive symptoms, independent of body mass index (BMI) (Sharpe et al., 2018). Given the rise in body dissatisfaction and its association with later poor mental health, it is important to delineate the aetiology of body dissatisfaction.

The subjective appraisal of one's body is partly influenced by objective body characteristics. Notably, higher childhood BMI has been shown to predict higher levels of adolescent body dissatisfaction (Micali et al., 2015). However, discrepancies exist between objective body characteristics and a person's perception of their body. For example, a large, nationally representative study in England using data from the Health Survey for England (2005-2012) (Mindell et al., 2012) found that 39% of 13-15 year-olds whose weight would place them in the overweight/obese category perceived themselves to be the "right weight" (Jackson et al., 2015). In contrast, evidence from 3 UK cohorts of adolescents

(n=22,503) found that 23.8% of girls and 11.5% of boys with a normal BMI thought they were overweight (Solmi et al., 2021). Whilst there were differences across these studies in regards to the time periods they were carried out and sampling methods, they demonstrate that other factors may contribute to the development of body dissatisfaction in adolescence.

In addition to anthropometric measures, body perception could also be influenced by mental health vulnerabilities. Indeed, a meta-analysis of 23 cross-sectional studies found a cross-sectional relationship between self-reported anxiety and depression with body dissatisfaction (Barnes et al., 2020). One potential mechanism could be that individuals with mental health vulnerabilities have altered cognitive processes, such as attention biases (e.g., involving increased attention to negative stimuli; Rodgers & DuBois, 2016), which can lead to a negative perception of their body. Indeed, in an experimental task, individuals who reported higher body image concern were more likely to over-recall negative comments (Dent & Martin, 2023). This suggests that negative attentional biases involved in mental health vulnerabilities might contribute to body dissatisfaction. However, it is difficult to understand whether mental health vulnerabilities contribute to body dissatisfaction from existing cross-sectional evidence, due to the potential for reverse causality (i.e., body dissatisfaction causing mental health vulnerabilities).

A novel solution to this challenge is to examine whether genetic proxies for mental health vulnerabilities (namely, polygenic scores) are associated with later body dissatisfaction. Polygenic scores aggregate the effects of many common genetic variants associated with a particular trait (e.g., depression) from a genome-wide

association study into a single individual-level score. A key advantage of using polygenic scores for mental health vulnerabilities (instead of phenotypic measures of these symptoms), is that genetic vulnerability precedes any emergence of body dissatisfaction. Therefore, any association between polygenic scores for mental health vulnerabilities and body dissatisfaction is not likely due to reverse causation. Notably, because body dissatisfaction can also be influenced by objective body characteristics (e.g., BMI, waist circumference), these characteristics (and their respective polygenic scores) should also be accounted for, to understand the unique contribution of mental health vulnerability to perception of one's own body.

To my knowledge, only one previous study has examined whether polygenic scores for mental health vulnerabilities are associated with body dissatisfaction (Abdulkadir et al., 2022). The study found that polygenic scores for mental health vulnerabilities (e.g., depression, anxiety, schizophrenia, anorexia, neuroticism) were not associated with body dissatisfaction. However, this study was affected by key limitations which restrict the conclusions that can be drawn. First, the study did not derive polygenic scores from the most recent Genome Wide Association Study (GWAS) (e.g., for depression (Howard et al., 2019) and schizophrenia (Trubetskoy et al., 2022)), featuring larger discovery sample sizes, thus limiting statistical power to detect true effects. Second, the method used to derive polygenic scores in this study (PRSice-2) has been found to be less effective than more recent approaches (e.g. LDpred2-auto; Privé et al., 2020) in capturing genetic variance (Pain et al., 2021), further suggesting that the lack of

associations between polygenic scores for mental health vulnerabilities and body dissatisfaction may reflect false negatives.

To address these research gaps, I examined the relationships between polygenic scores for mental health vulnerabilities and body dissatisfaction, after accounting for the corresponding anthropometric measure (BMI and waist circumference). To that end, I analysed a large prospective birth cohort of adolescents who had reported on weight and waist dissatisfaction at age 13. To index genetic predisposition to mental health vulnerabilities, I derived polygenic scores from the largest and most recent GWASs, using LD-pred2 software. The aim was to determine whether (1) polygenic scores for mental health vulnerabilities predict weight dissatisfaction, beyond BMI, and (2) whether polygenic scores for mental health vulnerabilities predict waist dissatisfaction, beyond objectively measured waist circumference.

4.3 Methods

4.3.1 Participants

The present study used data from The Avon Longitudinal Study of Parents and Children (ALSPAC) study, an ongoing population-based birth cohort study (Boyd et al., 2013; Fraser et al., 2013). Pregnant women resident in Avon, UK, with expected dates of delivery between 1st April 1991 and 31st December 1992 were invited to take part in the study. From an initial 14,541 pregnancies, there were 13,988 children alive at 1 year of age. Then, an additional 913 children were recruited to the sample at age 7 years. Therefore, the total sample size available for analyses using data obtained after the age of 7 years is 15,447 pregnancies

(n=14,901 alive at age 1 year). Participants were assessed across several waves with self-report questionnaires, clinical interviews, medical records and physical examinations. The study website contains further information on study design and variables including a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data/).

Participants in the present study included those who had available genetic data, objectively measured anthropometric measures (BMI and waist circumference) and subjective self-reported measures of weight and waist dissatisfaction obtained from the age 13 study assessments. Genetic data were available for 8,842 unrelated children of European ancestry after quality control (see **Appendix C – Supplementary Methods 1**). To be included in the analyses focusing on weight dissatisfaction, participants were required to have at least genetic data (to compute polygenic score for BMI) and one or more of the following: objectively measured BMI, subjective weight satisfaction (n=5,585) (see **Figure 4.1** for overlap). For analyses focusing on waist dissatisfaction, I required participants to have at least genetic data (to compute polygenic score for Waist-to-Hip Ratio), and one or more measures of the following: objectively measured waist circumference, subjective waist satisfaction (n=5,582) (see **Figure 4.2** for overlap).

Ethical approval was obtained from the ALSPAC Ethics and Law Committee and South West– Central Bristol National Health Service Research Ethics Committee. Written informed consent was obtained from all participants for the use of data collected via questionnaires and clinics, following recommendations from the ALSPAC Ethics and Law Committee at the time. Caregivers provided consent for

child participation prior to the age of 16 years. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004).

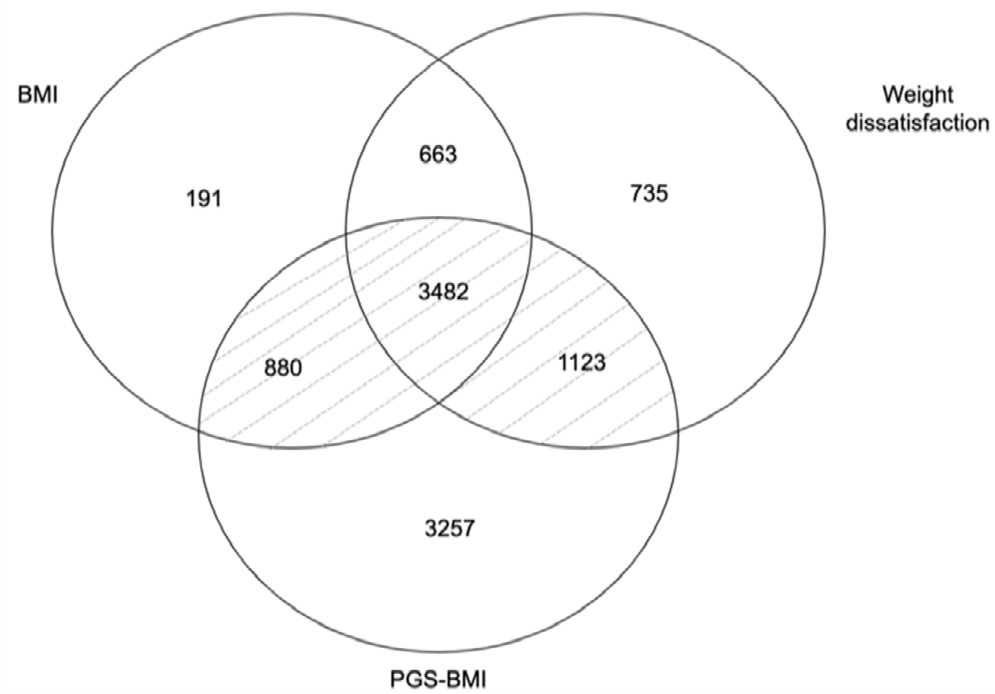


Figure 4.1. The overlap for analyses focusing on weight dissatisfaction including the polygenic score for BMI (PGS-BMI), subjective weight dissatisfaction and objectively measured BMI.

Note: Dotted lined area represents the sample used in the data analysis (n=5,585).

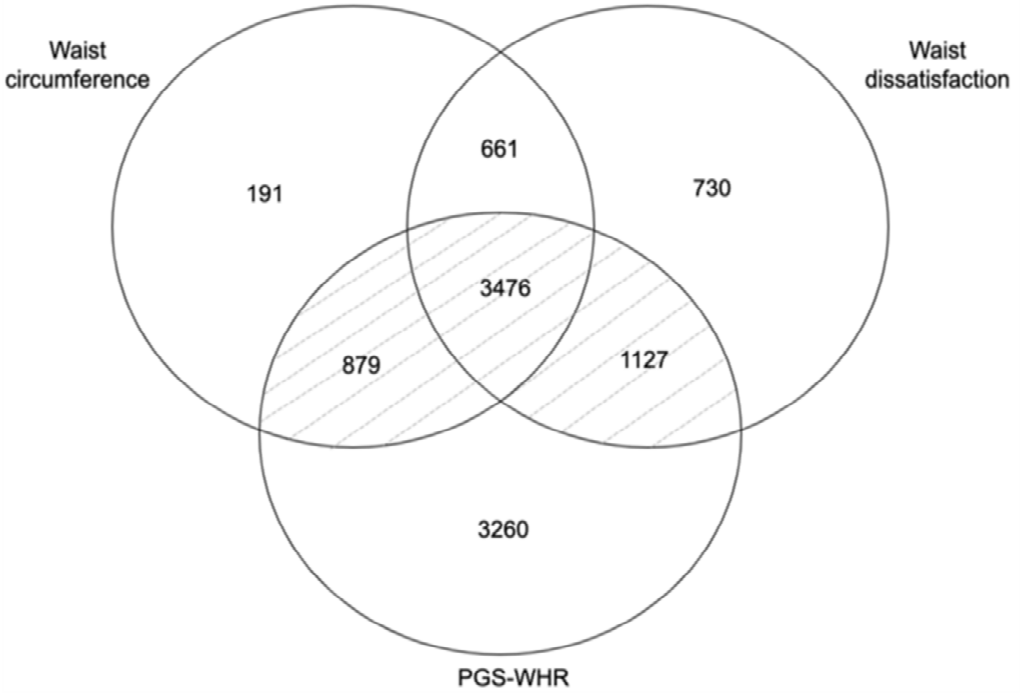


Figure 4.2. The overlap for analyses focusing on waist dissatisfaction including polygenic score for Waist-to-Hip Ratio (PGS-WHR), subjective waist dissatisfaction and objectively measured waist circumference (cm).

Note: Dotted lined area represents the sample used in the data analysis (n=5,582).

4.3.2 Measures

4.3.2.1 Subjective measures of body dissatisfaction

Participant's measures of body dissatisfaction were obtained at the age 13 study visit using the self-reported Body Dissatisfaction Scale (Calzo et al., 2012; Micali et al., 2015; Stice, 2001). This scale asked adolescents to rate their level of satisfaction with 11 body parts (weight, figure, body build or breasts, stomach, waist, thighs, buttocks, hips, legs, face and hair). For the purpose of the present study, only the items relating to weight and waist were included. This was because the corresponding objective anthropometric measures were available only for these two items (see section 4.3.2.2), which was essential to investigate the underlying aetiology of weight and waist dissatisfaction. Participants were asked to rate their responses on a six-point Likert scale: "1=Extremely satisfied", "2=Moderately satisfied", "3=Can't decide", "4=Moderately dissatisfied', "5=Extremely dissatisfied" or "6=Not an issue." The last category, "Not an issue", (comprising N=316 participants for weight dissatisfaction and N= 336 participants for waist dissatisfaction) were re-coded to missing as it does not lie naturally on the continuum from "Extremely satisfied" to "Extremely dissatisfied". As the weight and waist dissatisfaction variables were reverse coded (i.e., the more satisfied the participant the lower the number), the subjective measures are referred to as weight dissatisfaction and waist dissatisfaction throughout the present study. Both of these subjective measures were standardised (mean=0, standard deviation (SD) =1).

4.3.2.2 Objectively measured anthropometric assessments

BMI and waist circumference were collected face-to-face at the age 13 study visit by a trained clinician and/or study researcher. BMI was calculated as weight (kilograms) divided by the square of height (metres). Weight and height were measured with the child in light clothing and without shoes. Weight was measured to the nearest 0.1 kg with Tanita Body Fat Analyser (Model TBF 305) (Tanita Europe BV, Amsterdam, Netherlands) and height to the nearest 0.1cm with a Harpenden stadiometer (Holtain Ltd, Crymych, United Kingdom). Waist circumference was measured to the nearest 1 mm at the midpoint, between the lower ribs and the pelvic bone, using a Seca 201 body tension tape and repeated twice for accuracy.

As children and adolescents are still growing, using raw BMI and raw waist circumference is not appropriate. Therefore, reference growth charts were used to derive age-and sex-adjusted z-scores. These were calculated using the LMS Method and British 1990 reference (Cole et al., 1995, 1998) by applying the sds function in the 'childsds' R package (version 0.8) (Vogel, 2022). This package is openly available from CRAN (http://CRAN.R-project.org/package=childsds). This approach allows for measures to be expressed as a standard deviation score (otherwise known as a z-score) which is considered optimal for assessing anthropometrics at a single time-point (Cole et al., 2005). The British 1990 reference features a BMI growth chart from birth to 23 years, and a waist circumference growth chart from ages 3 to 17 years.

4.3.2.3 Covariates

To improve precision in the estimates, I included age and sex as covariates. Age (years) were reported when the child attended the age 13 research clinic. Sex of the child was obtained from either the recording in the delivery room, obstetric records or birth notifications.

4.3.2.4 Polygenic score analysis

I calculated polygenic scores for mental health vulnerabilities, including for anorexia nervosa, major depressive disorder, schizophrenia, neuroticism, and lifetime anxiety disorder. Additionally, polygenic scores for anthropometric traits were also computed including for body mass index and waist-to-hip ratio (WHR). To do so, summary statistics were used from the most recent, publicly available Genome Wide Association Studies (GWAS) derived from discovery cohorts of European ancestry that did not feature ALSPAC participants (see **Table 4.1** for details) (Howard et al., 2019; Nagel et al., 2018; Purves et al., 2020; Sulc et al., 2021; Sulc et al., 2021; Trubetskoy et al., 2022; Watson et al., 2019; Yengo et al., 2018). These summary statistics were selected based on the hypothesis that mental health vulnerabilities (e.g., to depression) could drive how an individual perceives their body, while genetic influences on BMI and WHR would predict corresponding objectively measured anthropometric measures of BMI and waist circumference. The summary statistics for BMI and WHR were selected due to being closely aligned to subjective weight and waist dissatisfaction, and the objectively measured BMI and waist circumference.

Table 4.1. GWAS Summary Statistics of the 7 Included Samples.

Phenotype	Total sample size	Number of cases (affected)	Number of controls (unaffected)	Year of the publication	Link to summary statistics file	Publication DOI/URL
Body Mass Index	681275	NA	NA	2018	https://www.pgscatalog.org/score/PGS000027/	10.1093/hmg/ddy271
Waist-to-Hip Ratio	378139	NA	NA	2021	https://zenodo.org/record/5171807/	10.5281/zenodo.516756
Schizophrenia	175799	74776	101023	2022	https://pgc.unc.edu/for-researchers/download-results/	10.1038/s41586-022-04434-
Major Depressive Disorder	38695	15726	22969	2019	https://datashare.ed.ac.uk/handle/10283/3203	s41593-018-0326-7
Neuroticism	449484	NA	NA	2018	https://ctg.cncr.nl/software/summary_statistics/	10.1038/s41588-018-0151-7
Anorexia Nervosa	72517	16992	55525	2019	https://pgc.unc.edu/for-researchers/download-results/	10.1038/s41588-019-0439-2
Lifetime Anxiety Disorder (UKB)	83566	25453	58113	2020	https://drive.google.com/drive/folders/1fguHvz7I2G45sbMI9h_veQun4aXNTy1v	10.1038/s41380-019-0559-1

Abbreviation: UKB, UK Biobank.

Polygenic scores were generated using the LDPred2-auto approach, which is an extension of LDPred (Vilhjálmsson et al., 2015) with improved stability and predictive performance (Privé et al., 2020). Providing quality control is carried out on the discovery summary statistics, this Bayesian approach for computing polygenic scores automatically estimates the proportion of causal variants (p) and the SNP heritability (h^2); therefore there is no requirement for a validation dataset to tune hyper-parameters (Privé et al., 2020). This approach accounts for linkage disequilibrium between variants, and includes over 1.1 million HapMap3 variants, hence no p-value threshold is applied. All polygenic scores were standardized (mean=0, SD=1). To account for population stratification, principal components analysis was conducted retaining the top 10 principal components (Price et al., 2006). All regression models were controlled for sex, standardised age, and population stratification by including 10 principal components.

4.3.3 Statistical analysis

All analyses were conducted in R version 4.2.0 (Team, R.D.C., 2022). The analyses models are represented in **Figures 4.3** and **4.4**.

The code to run the study analysis is openly available on the following GitHub page:

https://github.com/erfrancis/PGS_Psychiatric_Traits_Body_Dissatisfaction.git.

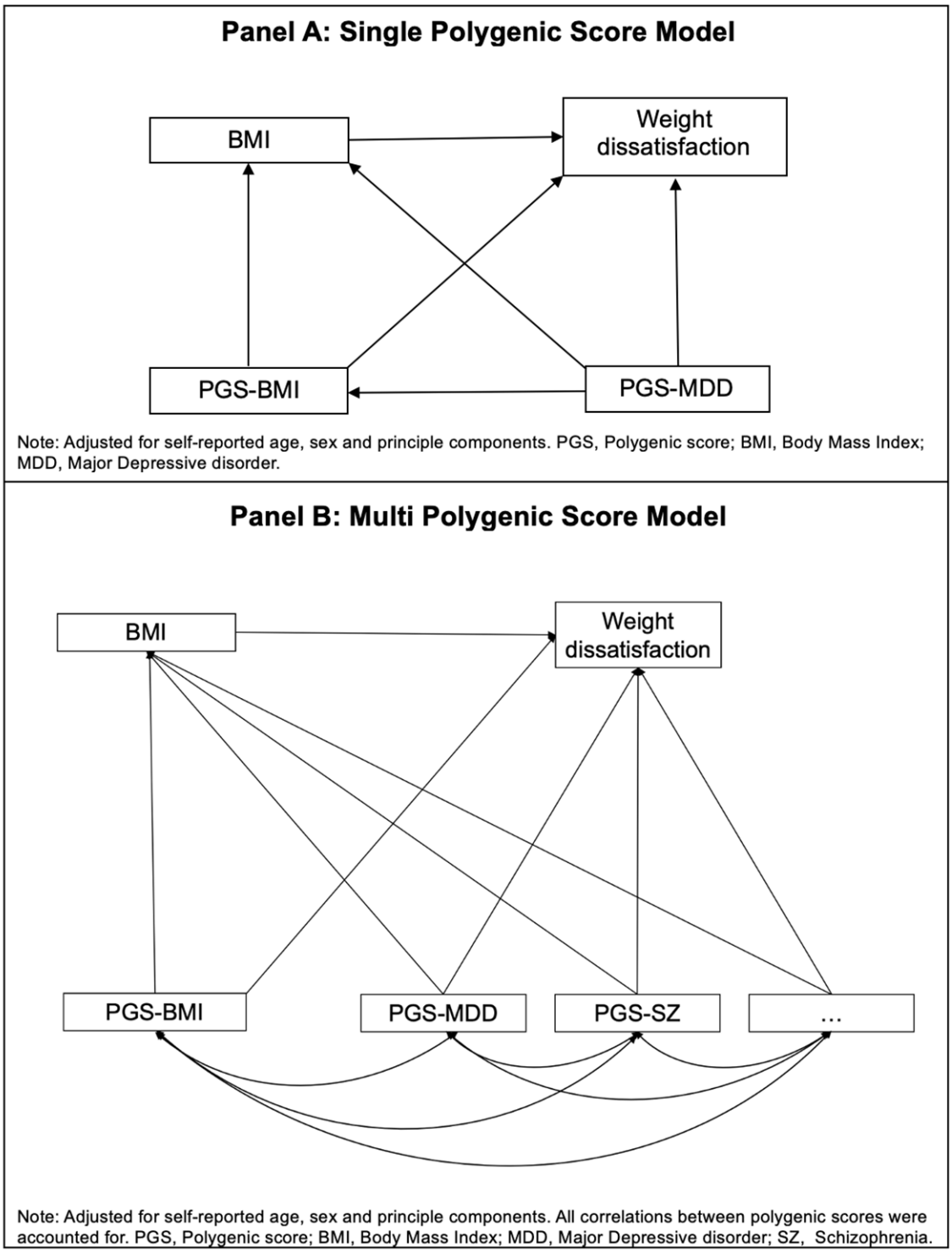


Figure 4.3. Single and Multi-PGS Models for weight dissatisfaction analyses.

The following analysis examined whether polygenic scores for mental health vulnerabilities are associated with (1) weight dissatisfaction, independent of BMI, and (2) waist dissatisfaction, independent of waist circumference. This was carried out using the structural equation modelling (SEM) package 'Lavaan' version 0.6-16 (Rosseel, 2012). Anticipating that some polygenic scores would be correlated, Single- and Multi-PGS models were run in order to examine the independent effects of polygenic scores on subjective weight and waist dissatisfaction, when adjusting for objective measures of BMI and waist circumference.

Analysis on weight dissatisfaction. First, the relationship between each polygenic score (other than polygenic score for WHR) and weight dissatisfaction, after accounting for BMI was examined ("Single-PGS" model, **Figure 4.3: Panel A**). An example of this would be assessing whether (1) the polygenic score for depression has a direct effect on weight dissatisfaction, when adjusting for BMI and the covariates (age and sex), while also testing (2) whether the polygenic score for depression has a direct effect on BMI, when adjusting for covariates. This was repeated for all polygenic scores.

Second, I estimated the independent effects of the polygenic scores for mental health vulnerabilities on subjective weight dissatisfaction, adjusting for BMI and covariates (see **Figure 4.3: Panel B**). Within this "Multi-PGS" model, all polygenic scores relating to mental health vulnerabilities and the polygenic score for BMI were included, thereby accounting for associations between polygenic scores. The main focus of this analysis was to estimate the independent effect of each mental health-related polygenic score on weight dissatisfaction, while adjusting

for BMI, the other polygenic scores (including for BMI), and covariates. In addition, objectively measured BMI was also regressed on all polygenic scores, which allowed me to test whether the putative associations between the polygenic scores for mental health vulnerabilities and weight dissatisfaction were driven by direct effects (e.g. polygenic score for depression affects weight dissatisfaction) rather than by effects via BMI (e.g. polygenic score for depression first affects BMI, which in turn affects weight dissatisfaction).

Analysis on waist dissatisfaction. Similar to the analysis on weight dissatisfaction, I applied a Single-PGS and Multi-PGS approach to understand the influence of polygenic scores for mental health vulnerabilities on waist dissatisfaction.

First, I used "Single-PGS" models to examine the relationships between each polygenic score (other than the polygenic score for BMI) and waist dissatisfaction, after accounting for objectively measured waist circumference (see **Figure 4.4: Panel A**). An example of this would be assessing whether (1) the polygenic score for depression has a direct effect on waist dissatisfaction, when adjusting for waist circumference and the covariates (age and sex), and (2) whether the polygenic score for depression has a direct effect on waist circumference, when adjusting for covariates. This was repeated for all polygenic scores.

Second, I used a "Multi-PGS" model to estimate the independent effects of the polygenic scores for mental health vulnerabilities on subjective waist dissatisfaction, adjusting for waist circumference and covariates (see **Figure 4.4: Panel B**). Within this model, all polygenic scores were included (other than the polygenic score for BMI) and all correlations were accounted for between

polygenic scores. This allowed for the estimation of the independent effect of each polygenic score for mental health vulnerabilities on weight dissatisfaction, while adjusting for waist circumference, the other polygenic scores (including for WHR), and covariates. Similar to the weight dissatisfaction analyses, the objective measure (waist circumference) was also regressed on to all polygenic scores, which allowed me to test whether the observed associations between the polygenic score for mental health vulnerabilities and weight dissatisfaction were driven by direct effects (e.g. polygenic score for depression affects waist dissatisfaction) rather than by effects via waist circumference (e.g. polygenic score for depression first affects waist circumference, which in turn affects waist dissatisfaction).

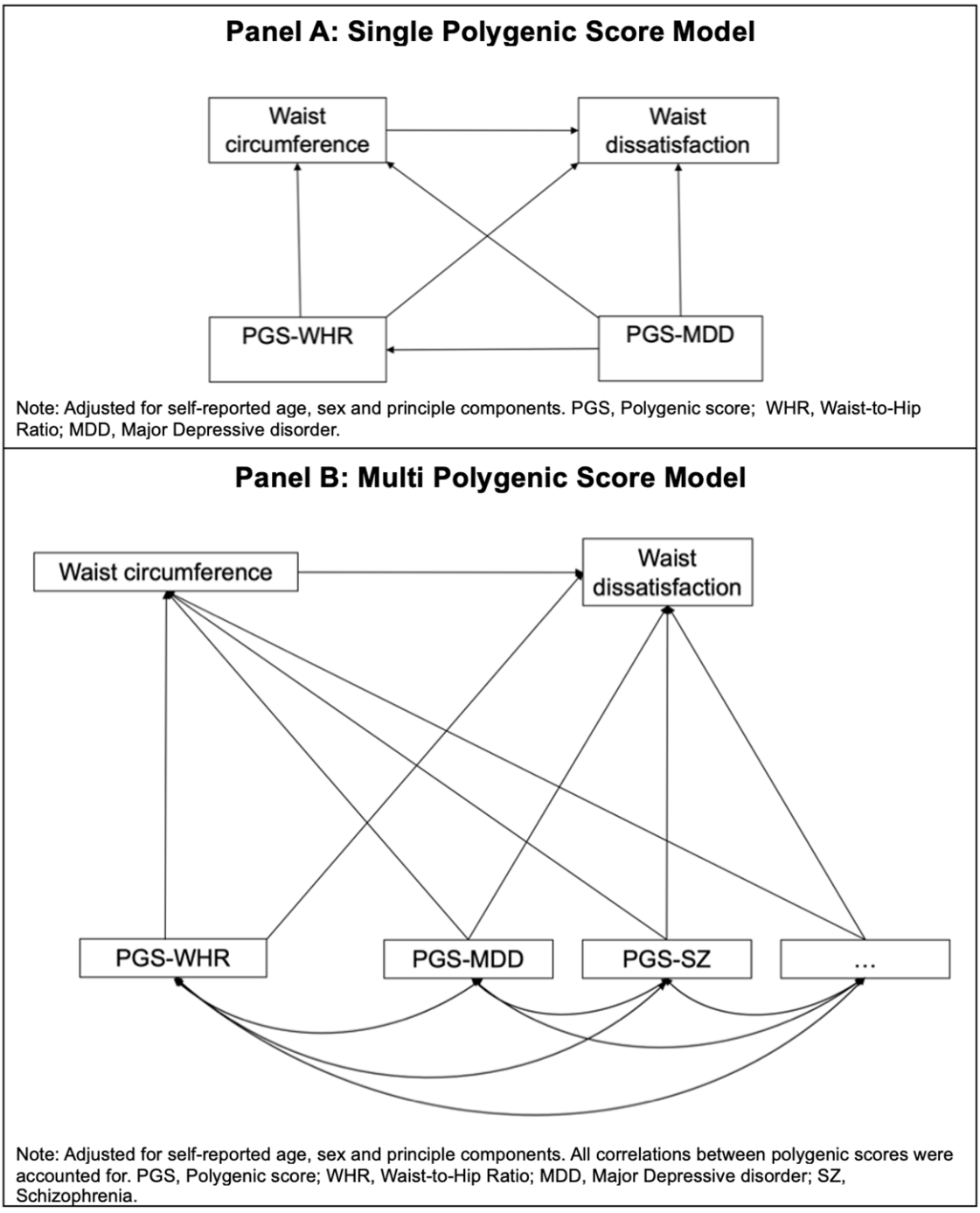


Figure 4.4. Single and Multi-PGS Models for waist dissatisfaction analyses.

Given that there is evidence of sex differences with respect to levels of body dissatisfaction (Austin et al., 2009), I carried out the following sensitivity analyses. First, within SEM, I specified a 'free model' to obtain the estimates for BMI by sex (i.e., to identify if girls/boys varied). Second, I constrained the effect of BMI on weight dissatisfaction. This allowed me to test whether the effect of BMI on weight dissatisfaction varied according to sex. To that end, I compared the free and constrained models using the anova() function in Lavaan to obtain the chi-squared, df and *p* value. Third, I then constrained the effect of the polygenic score for BMI on weight dissatisfaction. This allowed me to determine whether the effect of the polygenic score for BMI on weight dissatisfaction varied according to sex. Finally, I constrained the effect of the polygenic score for BMI on BMI. This allowed me to determine whether the effect of the polygenic score for BMI on BMI varied according to sex. I repeated these steps for each mental health polygenic score. I carried out similar analyses in the waist circumference model.

4.4 Results

4.4.1 Descriptive statistics

The mean age for the study sample was 13.23 years (SD= 0.18) (53.01% female). The study child measurements and maternal characteristics are reported in **Table 4.2**. The mean (SD), and sample size for each measurement variable are reported in **Appendix C – Supplementary Table 1**. The correlations between the 7 polygenic scores, weight and waist dissatisfaction, and raw BMI and waist circumference are depicted in **Figure 4.5**.

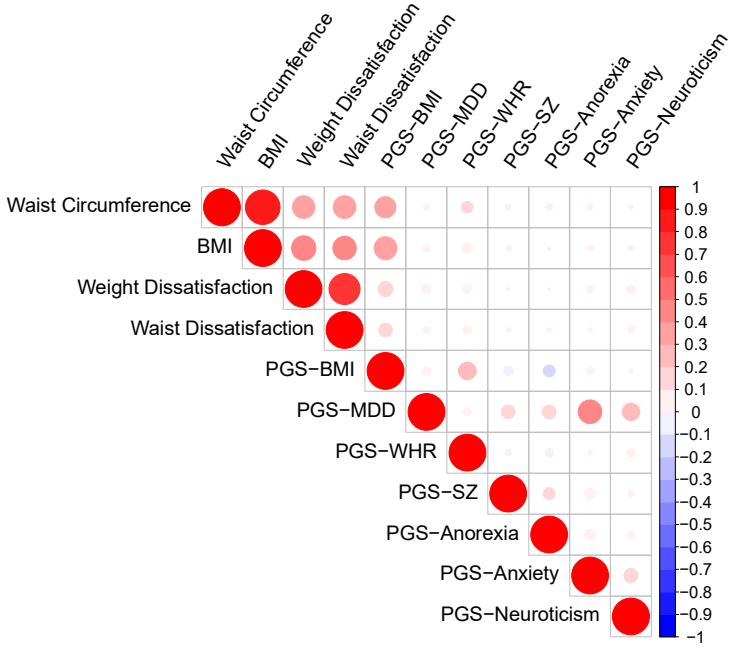


Figure 4.5. Heatmap of correlations between the weight and waist dissatisfaction, BMI and waist circumference, and polygenic scores.

Abbreviations: PGS, Polygenic Score; BMI, Body Mass Index; WHR, Waist-to-Hip Ratio; MDD, Major Depressive Disorder; SZ, Schizophrenia. Note: See **Appendix C - Supplementary Table 2** for significance (N=5,585).

Table 4.2. Descriptive statistics of the ALSPAC sample included.

Descriptive data	**N (%)**	
Maternal occupational social class (n=4,562)		
Professional	347 (7.68)	
Managerial and technical occupations	1637 (35.88)	
Skilled occupations non-manual	1884 (41.30)	
Skilled occupations manual	279 (6.12)	
Partly-skilled occupations	358 (7.85)	
Unskilled occupation	57 (1.25)	
Maternal education[a]		
University degree (n=5,237)	944 (18.03)	
A-Level (n=5,237)	1863 (35.57)	
O-Level (n=5,237)	4075 (77.81)	
CSE (n=5,237)	3050 (58.24)	
No qualification (n=5,237)	136 (2.60)	
Study child measurements at age 13 (years)	**Mean (SD)**	**Sample size**
BMI (raw score)[b]	20.31 (3.41)	4714
Waist circumference (raw score) (cm)[d]	71.98 (9.06)	4708
Weight dissatisfaction[b]	2.45 (1.17)	4463
Waist dissatisfaction[d]	2.42 (1.09)	4452
Waist-to-height ratio[b]	0.45 (0.06)	3272
BMI (z-score)[b]	0.45 (1.09)	4362
Waist (z-score)[d]	1.13 (1.05)	4355

Abbreviations: BMI, Body Mass Index; SD, Standard Deviation. [a]Not mutually exclusive i.e., study child mother can select more than one category. [b]BMI, weight dissatisfaction and waist-to-height and BMI (z-score) were calculated from the sample used for the analysis on weight dissatisfaction. [c]Waist circumference (cm), waist dissatisfaction and Waist (z-score) were calculated from the sample used for the analysis on waist dissatisfaction. Note. Occupation status by social class and education obtained at 32 weeks' gestation.

The polygenic score for BMI was strongly correlated with BMI (*r*=0.39, 95% Confidence intervals [CI]= 0.36 to 0.41) and more weakly correlated with weight dissatisfaction (*r*=0.16, 95% CI= 0.14 to 0.19). The polygenic score for WHR showed a small correlation with waist circumference (*r*=0.10, 95% CI= 0.07 to 0.13) and a very small correlation with waist dissatisfaction (*r*=0.04, 95% CI=0.01 to 0.06) (see **Appendix C – Supplementary Table 2** for further details).

4.4.2 Polygenic and anthropometric predictors of weight dissatisfaction

The largest determinant of subjective weight dissatisfaction was BMI (std.all estimate=0.285; *p*<0.001). While the polygenic score for BMI was originally correlated with weight dissatisfaction (*r*=0.16, 95% CI=0.14 to 0.19; *p*<0.001), this was no longer the case after adjusting for BMI in the Single-PGS model, and other polygenic scores in the Multi-PGS model (see **Table 4.3**). This suggests that the polygenic score for BMI influences weight dissatisfaction via BMI.

Conversely, several polygenic scores indexing mental health vulnerabilities still had direct relationships to weight dissatisfaction after adjusting for BMI (in the Single-PGS Model) including the polygenic scores for depression (std.all estimate=0.034; *p*=0.014), schizophrenia (std.all estimate=0.028; *p*=0.042), lifetime anxiety (std.all estimate=0.033; *p*=0.018), and neuroticism (std.all estimate=0.053; *p*<0.001).

After adjusting for both BMI and the effects of other polygenic sores in the Multi-PGS Model, only the polygenic score for neuroticism had a direct relationship with weight dissatisfaction (std.all estimate=0.039; *p*=0.006). The polygenic score

for anorexia was not associated with weight dissatisfaction in either the Single- or Multi-PGS model (see **Table 4.3** for further details).

Interestingly, findings revealed the polygenic score for schizophrenia was associated with BMI (std.all estimate=-0.036; p=0.018), as well as the polygenic score for neuroticism (std.all estimate=-0.028; p=0.047) but not after adjusting for correlations with other polygenic scores in the Multi-PGS model. Additionally, the polygenic score for anorexia was not associated with BMI in the Single-PGS model but it was in the Multi-PGS Model (std.all estimate=0.034; p<0.016).

I conducted sensitivity analyses to test whether the effects observed differed by sex. The relationship between BMI and weight dissatisfaction was significantly larger in girls compared to boys. The associations between polygenic scores for mental health vulnerabilities and weight dissatisfaction did not differ by sex (**Appendix C –Supplementary Table 3**).

Table 4.3. Single-PGS Model and Multi-PGS Model findings for analyses on weight dissatisfaction.

Regression	Single-PGS Model					Multi-PGS Model				
	Estimate	**Lower CI**	**Upper CI**	***p***	**Std.all Estimate**	**Estimate**	**Lower CI**	**Upper CI**	***p***	**Std.all Estimate**
Body Mass Index → Weight Dissatisfaction	NA					0.261	0.230	0.292	**<0.001**	0.285
Weight Dissatisfaction										
PGS-Body Mass Index	0.009	-0.021	0.040	0.555	0.009	0.009	-0.022	0.040	0.558	0.009
PGS-Major Depressive Disorder	0.034	0.007	0.061	**0.014**	0.034	0.014	-0.017	0.045	0.375	0.014
PGS-Schizophrenia	0.027	0.001	0.055	**0.042**	0.028	0.024	-0.003	0.051	0.087	0.024
PGS-Anorexia	0.006	-0.021	0.033	0.655	0.006	-0.001	-0.028	0.027	0.963	-0.001
PGS-Anxiety	0.033	0.006	0.060	**0.018**	0.033	0.019	-0.010	0.049	0.204	0.019
PGS-Neuroticism	0.047	0.020	0.075	**0.001**	0.053	0.039	0.011	0.067	**0.006**	0.039
Body Mass Index										
PGS-Body Mass Index	0.441	0.411	0.470	**<0.001**	0.402	0.443	0.413	0.472	**<0.001**	0.403
PGS-Major Depressive Disorder	0.029	-0.003	0.062	0.073	0.027	0.002	-0.031	0.035	0.898	0.002
PGS-Schizophrenia	-0.039	-0.071	-0.007	**0.018**	-0.036	-0.011	-0.041	0.019	0.517	-0.010
PGS-Anorexia	-0.010	-0.006	0.058	0.111	-0.010	0.037	0.007	0.066	**0.016**	0.034
PGS-Anxiety	0.026	-0.005	0.058	0.104	0.024	0.010	-0.022	0.042	0.534	0.010
PGS-Neuroticism	-0.033	-0.065	0.000	**0.047**	-0.028	-0.026	-0.057	0.004	0.091	-0.024

Abbreviations: PGS, Polygenic Score; CI, 95% Confidence Interval, Body Mass Index, Body Mass Index (z-score of BMI); Std.all, Standardised all. Single-PGS and Multi-PGS models adjusted for age, sex and 10 principle components (genetic ancestry). Multi-PGS models adjusted for the effects of other polygenic sores. Estimates for the associations between PGSs and weight dissatisfaction are standardised beta coefficients (as all variables are standardised), whereas estimates for the associations including BMI (z-score) are not equivalent to standardised beta coefficients because BMI (z-score) is not standardised within ALSPAC, but age- and sex-adjusted against the 1990 British reference panel (see **Table 4.2**).

4.4.3 Polygenic and anthropometric predictors of waist dissatisfaction

The largest determinant of subjective waist dissatisfaction was waist circumference (std.all estimate=0.25; $p<0.001$). Whilst the polygenic score for WHR was correlated with waist dissatisfaction ($r=0.04$, 95% CI=0.01 to 0.06), it was not in the Single-PGS or Multi-PGS models after adjusting for waist circumference. This suggests that the polygenic score for WHR influences waist dissatisfaction indirectly via waist circumference.

When analysing whether polygenic scores indexing mental health vulnerabilities were associated with waist dissatisfaction in either the Single or Multi-PGS model, two key findings stood out. First, the polygenic score for neuroticism had a small but direct association with waist dissatisfaction in the Single-PGS (std.all estimate=0.037; $p=0.008$) and Multi-PGS models (std.all estimate=0.036; $p=0.014$). Second, the polygenic score for anorexia also had a small direct effect on waist dissatisfaction in the Single-PGS (std.all estimate=0.030; $p=0.037$) but not after accounting for the effects of the other polygenic scores. No other polygenic score for mental health vulnerabilities was associated with waist dissatisfaction, once adjusted for waist circumference.

When analysing polygenic scores for mental health vulnerabilities associated with waist circumference, findings revealed that the polygenic scores for schizophrenia, anorexia and anxiety were associated with waist circumference in the Single-PGS model. Interestingly, the polygenic scores for anorexia, anxiety and neuroticism was associated with waist circumference in the Multi-PGS Model

only, when accounting for the effects of other polygenic scores (see **Table 4.4** for full details).

The relationship between waist circumference and waist dissatisfaction did not differ significantly by sex. Additionally, the associations between polygenic scores for mental health vulnerabilities and weight dissatisfaction did not differ by sex (**Appendix C – Supplementary Table 4**).

Table 4.4. Single-PGS Model and Multi-PGS Model findings for analyses on waist dissatisfaction.

Regression	Single-PGS Model					Multi-PGS Model				
	Estimate	**Lower CI**	**Upper CI**	***p***	**Std.all Estimate**	**Estimate**	**Lower CI**	**Upper CI**	***p***	**Std.all Estimate**
Waist Circumference →Waist Dissatisfaction	NA					0.259	0.229	0.289	**<0.001**	0.275
Waist Dissatisfaction										
PGS-Waist-to-Hip Ratio	0.004	-0.024	0.032	0.765	0.004	0.004	-0.024	0.032	0.775	0.004
PGS-Major Depressive Disorder	0.011	-0.017	0.038	0.449	0.013	-0.007	-0.038	0.025	0.679	-0.007
PGS-Schizophrenia	0.020	-0.007	0.048	0.148	0.021	0.017	-0.011	0.045	0.223	0.018
PGS-Anorexia	0.029	0.002	0.057	**0.037**	0.030	0.026	-0.001	0.054	0.063	0.027
PGS-Anxiety	0.013	-0.015	0.040	0.371	0.013	0.007	-0.023	0.037	0.660	0.007
PGS-Neuroticism	0.037	0.010	0.065	**0.008**	0.037	0.036	0.007	0.064	**0.014**	0.036
Waist Circumference										
PGS-Waist-to-Hip Ratio	0.111	0.081	0.142	**<0.001**	0.106	0.110	0.079	0.140	**<0.001**	0.104
PGS-Major Depressive Disorder	0.020	-0.010	0.051	0.195	0.019	0.016	-0.018	0.050	0.355	0.015
PGS-Schizophrenia	-0.031	-0.061	0.000	**0.048**	-0.029	-0.030	-0.061	0.001	0.054	-0.029
PGS-Anorexia	-0.036	-0.067	-0.006	**0.019**	-0.035	-0.031	-0.061	-0.001	**0.046**	-0.030
PGS-Anxiety	0.034	0.004	0.064	**0.028**	0.033	0.035	0.002	0.069	**0.036**	0.034
PGS-Neuroticism	-0.025	-0.056	0.005	0.105	-0.024	-0.037	-0.069	-0.006	**0.020**	-0.035

Abbreviations: PGS, Polygenic Score; CI, 95% Confidence Interval; Waist circumference, Waist circumference (z-score); Std.all, Standardised all. Single-PGS and Multi-PGS models adjusted for age, sex and 10 principle components (genetic ancestry). Multi-PGS models adjusted for genetic correlation with other PGSs. Estimates for the associations between PGSs and waist dissatisfaction are standardised beta coefficients (as all variables are standardised), whereas estimates for the associations including waist circumference (z-score) are not equivalent to standardised beta coefficients because waist (z-score) is not standardised within ALSPAC, but age- and sex-adjusted against the 1990 British reference panel (see **Table 4.2**).

4.5 Discussion

This study aimed to examine whether polygenic scores relating to mental health vulnerabilities were (1) associated with weight dissatisfaction beyond objectively measured BMI, and (2) associated with waist dissatisfaction beyond objectively measured waist circumference. The following discussion will address (1) novel insights into the role of mental health vulnerabilities in the aetiology of weight and waist dissatisfaction, (2) insights into the role of objective body characteristics in body dissatisfaction, and (3) directions for future research.

Findings revealed that adolescents with greater genetic predisposition to mental health vulnerabilities are more likely to experience weight and waist dissatisfaction, even after accounting for objectively measured body characteristics. Specifically, the polygenic scores for depression, anxiety, and neuroticism were associated with weight dissatisfaction, independently of BMI. I also found that the polygenic scores for neuroticism and anorexia were associated with waist dissatisfaction, independent of waist circumference. Given that these polygenic predictors were partially different for each phenotype, it could be hypothesised that slightly different mental health vulnerabilities play a role in these specific body-related perceptions. Notably though, genetic predisposition to neuroticism was consistently associated with both waist and weight dissatisfaction across all models. Conceptually, neuroticism is commonly defined as a tendency to experience negative emotions. It is likely that adolescents who are predisposed to neuroticism may be more self-conscious and have a tendency to negatively perceive their bodies, leading to weight and waist dissatisfaction. Individuals who are susceptible to neuroticism may also ruminate (i.e., think

frequently) in a negative way about their appearance, contributing to body dissatisfaction. Indeed, these genetically informed findings are consistent with observational research indicating the importance of neuroticism in the development of body dissatisfaction. For example, a meta-analysis of 26 studies found that among all personality traits, neuroticism was most strongly associated with body dissatisfaction, when adjusted for BMI (r=0.26, 95% CI=0.20-0.29; p<0.001) (Allen & Robson, 2020). However, previous studies are susceptible to reverse causation as it is conceivable that negative perception of one's body may exacerbate neuroticism. In contrast, because the polygenic score for neuroticism precedes any phenotypic manifestation of neuroticism or body dissatisfaction, present findings are less susceptible for such reverse causation. Therefore, the present study implicates neuroticism more directly in the aetiology of body dissatisfaction. As the genetic predisposition to neuroticism appears to be associated with weight dissatisfaction and is known to be associated with mental health outcomes, this suggests there is a risk of genetic confounding when assessing the causal contribution of body-related dissatisfaction to later mental health. As a result, future studies examining the link between the trait neuroticism and body dissatisfaction should adopt a genetically informed design.

The present study findings may have important clinical implications as they highlight a potential target for intervention. Children presenting with weight and waist dissatisfaction may be assessed for neuroticism and benefit from psychological treatment that targets these thoughts and feelings. Given neuroticism is often considered a transdiagnostic factor underlying emotional disorders, it could be considered that interventions that target neuroticism (i.e.,

anxiety sensitivity) (Cassiello-Robbins et al., 2020) may improve not only body dissatisfaction but also reduce overall psychopathology. Further to this, interventions for anxiety and depression may be fruitful in reducing body dissatisfaction, such as cognitive behavioural therapy. Here, negative thoughts about one's appearance could be challenged through various approaches such as cognitive restructuring (Lewis-Smith et al., 2019). Or perhaps, instead of targeting maladaptive cognitions, a clinician could adopt a neuroticism-focused approach and target the child's negative body perception and other negative biases present in neuroticism. In fact, there is preliminary evidence in adults to indicate those with neurotic tendencies benefit from a trait-focused approach in order to reduce harmful outcomes (Carl et al., 2014).

Greater polygenic risk for anorexia nervosa was also associated with waist dissatisfaction, after accounting for waist circumference. This is likely to be because adolescents at risk of anorexia are prone to be highly self-critical about their physical body shape. Interestingly though, adolescents with greater polygenic risk for anorexia did not report higher levels of weight dissatisfaction, possibly suggesting that their concern lies more specifically with their body shape rather than weight. Although this effect was not observed when accounting for the effects of other polygenic scores, namely the influence of the polygenic score of neuroticism. An unexpected finding was that the polygenic score for anorexia nervosa was associated with higher BMI in the Multi-PGS model. While this may seem counterintuitive (as anorexia leads to low BMI), cases included in the GWAS for anorexia nervosa may have experienced a range of symptoms including not only restrictive eating, but also binge eating which could increase

BMI. Accordingly, future research should aim to incorporate polygenic scores derived from larger discovery sample sizes, featuring different 'sub-types' of anorexia nervosa, which may yield different findings. As the present study finding linking the polygenic sore for anorexia with increased BMI was limited only to the Multi-PGS model (with opposite findings in the Single-PGS model) these findings should be interpreted with caution.

This study's findings are contrary to previous research in the ALSPAC dataset which found that polygenic scores for mental health difficulties (e.g., neuroticism, depression, anxiety, anorexia) were not associated with body dissatisfaction in adolescence (Abdulkadir et al., 2022). The conflicting findings could be due to three reasons. First, the present study utilised a more powerful polygenic score method, which has been shown to outperform the methodology used in the previous study (Pain et al., 2021; Privé et al., 2020). As more robust polygenic score methods are developed with the goal of improving predictive accuracy, it is not surprising that this may have led to novel associations that otherwise would not have been detected, even within the same datasets. Second, the present study derived polygenic scores from more recent GWASs for certain mental health disorders (e.g., for depression; Howard et al., 2019) increasing power to detect true effects.

Third, there are other methodological differences between the present study and Abdulkadir et al's (2022) study, such as this study's specific focus on weight and waist dissatisfaction. Using a global sum score across dissatisfaction items may have introduced heterogeneity in the body dissatisfaction measure hampering the ability to detect specific effects. Using a global sum score also means that there

is no exactly matching corresponding objective measure, which means that the outcome does not appropriately capture the subjective element in body dissatisfaction, limiting the ability to find true associations.

Another notable finding related to the role of objective body characteristics (and corresponding genetic predisposition) in body dissatisfaction. First, adolescents with greater BMI and waist circumference were more likely to be dissatisfied with their weight and waist, respectively. Second, the polygenic score for BMI was associated with weight dissatisfaction via BMI, and the polygenic score for WHR influenced waist dissatisfaction via waist circumference. This indicates that the relationships between genetic predisposition to BMI and waist-hip ratio with body dissatisfaction are mediated by the corresponding anthropometric measures. Indeed, this finding supports previous research that indicates BMI is on the causal pathway between genetic predisposition to anthropometric measures and disordered eating (Abdulkadir et al., 2020). Interestingly, there were no residual effects of the polygenic scores for BMI and waist-hip ratio on body dissatisfaction measures, which means that genetic predisposition to these anthropometric measures do not directly contribute to subjective processes, in contrast to polygenic predisposition to mental health disorders.

The present study findings should be viewed in light of several limitations. First, the present study tested whether polygenic scores for mental health vulnerabilities were associated with weight and waist dissatisfaction reported at age 13 years. Whilst an individual's genetic predisposition to mental health vulnerabilities is fixed from conception, the associations between polygenic scores and outcomes such as body dissatisfaction may vary across

developmental periods. Future research should therefore use genetically informed designs to assess whether the predisposition to mental health vulnerabilities are informative at different time-points for self-reported body dissatisfaction. This could shed light on (1) whether underlying genetic variants for mental health vulnerabilities influence body perception over-time, and (2) if there are key ages whereby interventions to target negative body perceptions may be most beneficial for those with mental health vulnerabilities. This may also provide supporting evidence for previous meta-analytical findings that indicated age may be a modifying factor in the relationship between the trait neuroticism and body dissatisfaction (Allen & Robson, 2020).

Second, the weight and waist dissatisfaction measures were assessed through single items, which may not comprehensively capture an adolescent's overall levels of body dissatisfaction (i.e., an adolescent may not be satisfied with their waist size, but may be happy with the rest of their appearance). However, these measures were selected in order to further understand the underlying aetiology, and additionally allowed for the inclusion of corresponding objectively measured assessments (BMI and waist circumference), and polygenic scores of the corresponding anthropometric measures (BMI and WHR). This allowed me to delineate the specific mechanisms that may contribute to weight and waist dissatisfaction which may otherwise not have been possible.

Third, whilst the present study finds evidence to implicate the genetic predisposition to mental health vulnerabilities in the development of body dissatisfaction, it should be acknowledged that there may be other aetiological factors involved. Notably, societal pressures (De Coen et al., 2021) and parental

attitudes (Michael et al., 2014) may influence a young adolescents' perception of what they consider an ideal body shape, size and weight. Further to this, there may be a number of potential mediators of the effect between genetic predisposition to neuroticism and body-related dissatisfaction that were not measured, such as frequent comparison with others (Pedalino & Camerini, 2022).

Finally, similar to other longitudinal studies, the ALSPAC sample is affected by attrition over time, leading to missing data at the age 13 assessment and a sample with higher levels of socioeconomic advantage than the original cohort (Wolke et al., 2009). To account for missing data, the present study incorporated the full information maximum likelihood method which has been shown to be comparable to other approaches (Dong & Peng, 2013). However, future studies should test whether these findings replicate in higher-risk and population-representative samples.

4.6 Conclusion

In conclusion, the present study found evidence to partially support my hypothesis that genetic predisposition to mental health vulnerabilities predicts weight and waist dissatisfaction, beyond anthropometric measures. Findings revealed susceptibility to neuroticism was directly associated with both weight and waist dissatisfaction, after adjusting for the corresponding anthropometric measures and the effects of other polygenic scores. Future studies should investigate the underlying aetiology of body-related dissatisfaction by adopting a genetically informed approach and explore potential mediators of the effects observed, as well as examine whether the effect observed changes over-time from early childhood to late adolescence.

Chapter 5 Discussion

5.1 Summary

This PhD thesis consisted of three studies that sought to better understand (1) the relationship between subjective and objective measures of adverse experiences in mental health and (2) whether genetic predispositions to mental health vulnerabilities might affect the child's subjective experience of mental health risk factors. The concluding chapter of this thesis summarises the main findings of each study, discusses the potential aetiological mechanisms underlying the stronger associations between subjective experiences of adversity and psychopathology, and considers implications for future research and clinical interventions.

5.2 Summary of the studies and main findings

5.2.1 Subjective and objective measures of childhood adversity and their associations with psychopathology: a meta-analysis

Chapter 2 examined the agreement between subjective and objective measures of childhood adversities (childhood maltreatment, bullying victimisation and neighbourhood adversity), and their independent associations with psychopathology, through a meta-analysis.

First, I found only modest associations between subjective self-reports of childhood adversities and the corresponding objective measures. Second, results revealed that subjective measures of adversities were associated with psychopathology, independent of corresponding objective measures. In contrast, objective measures of adversities had null or minimal independent associations with psychopathology. These meta-analytic results were broadly consistent across different types of childhood adversity (child maltreatment, bullying victimisation, and neighbourhood adversity) assessed through different types of objective measures (e.g., child protection or legal records for maltreatment, peer nominations for bullying victimisation, and crime records for neighbourhood adversity). Third, moderation analyses revealed that the relationship between subjective measures of childhood adversity and psychopathology was moderated by (i) the informant for psychopathology (with larger associations when psychopathology was self-reported versus reported by another informant), and (ii) study type (with larger associations when psychopathology was assessed concurrently to adversity measures [i.e., in cross-sectional analyses] versus later

on [i.e., in longitudinal analyses]). Notably, the relationship between objective measures of childhood adversity and psychopathology was also moderated by the informant for psychopathology, with larger associations found when psychopathology was reported by other informants rather than self-reported.

Given that subjective and objective measures of childhood adversity only moderately agree, this supports the notion that these measures should not be used interchangeably to capture such experiences. Findings of this meta-analysis suggest that the effects of childhood adversity on psychopathology are primarily driven by the individual's subjective experience. This may indicate that the effect of objective adverse childhood experiences on psychopathology may be driven by the perception and memories of the childhood adversity. However, there are also several alternative explanations for the stronger association between subjective measures of childhood adversity and psychopathology, such as confounding, shared method variance, and reverse causation (e.g., individuals with psychopathology may be more prone to perceive experiences as more negative due to cognitive biases).

5.2.2 Identifying genetic predictors of self-reported bullying victimisation: a multi-informant, multi-polygenic score approach

Chapter 3 aimed to investigate whether genetic predisposition to mental health vulnerabilities might affect a person's subjective experience of bullying victimisation. To do so, I examined whether polygenic scores for mental health vulnerabilities influenced self-reported bullying victimisation, after accounting for other-informant reports (from parents and teachers). This approach enabled me

to understand whether children with particular genetic predispositions were more likely to perceive (and self-report) higher levels of bullying than what was reported by parents and teachers. I hypothesised that genetic predisposition to mental health vulnerabilities (as indexed by polygenic scores for depression, anxiety, schizophrenia, ADHD and neuroticism) would predict self-reports of bullying victimisation, when adjusted for other-informant reports. Using data from a prospective UK birth cohort (ALSPAC), the study results partially supported my hypothesis, as the polygenic score for ADHD was associated with self-reported bullying victimisation, after accounting for parent and teacher reports. However, while polygenic scores for other mental health vulnerabilities (e.g., depression, anxiety, and neuroticism) were associated with self-reported bullying victimisation in unadjusted analyses, these associations no longer remained after accounting for other-informant reports and the effect of other polygenic scores. Further analysis also showed that children with lower polygenic scores for educational attainment were more likely to self-report victimisation, after accounting for other-informant reports.

These results extend current understanding by testing for the first time whether polygenic scores for mental health vulnerabilities are associated with self-reports of bullying victimisation, after accounting for multi-informant reports of victimisation and the effects of other correlated polygenic scores. These findings suggest that children with genetic vulnerability to ADHD are likely to perceive exposure to bullying victimisation, beyond experiences apparent to their parents and teachers. This is in line with prior research that found individuals with mental health vulnerabilities may be more prone to reporting harmful experiences

(McQuade et al., 2011). In the context of the present study, this means children with vulnerabilities to ADHD may self-report bullying victimisation due to being more prone to perceiving experiences as negative due to cognitive biases. However, it is also possible that self-reported bullying victimisation indexes the actual bullying experience as well as the child's perception, even after accounting for other-informant reports (as parents and teachers may not witness or hear about all instances of bullying). Therefore, another explanation could be that children with mental health vulnerabilities (e.g., ADHD) may be more likely to be bullied due to exhibiting symptoms (e.g., hyperactivity) that result in being targeted by bullies.

5.2.3 Polygenic scores for psychiatric disorders predict subjective body-related dissatisfaction beyond objective anthropometric measures

To further test the hypothesis that genetic predisposition to mental health vulnerabilities influence a person's subjective experience, in **Chapter 4**, I tested whether polygenic scores for mental health vulnerabilities are associated with adolescent perceptions of body image. Using data from ALSPAC, I examined whether polygenic scores for mental health problems (and other related traits) were associated with adolescent weight and waist dissatisfaction, over and above objective anthropometric measures (BMI and waist circumference). First, I found that the polygenic score for neuroticism was associated with (i) weight dissatisfaction, independent of objectively measured BMI, and (ii) waist dissatisfaction, independent of objectively measured waist circumference, and after accounting for the effect of other polygenic scores. Second, the polygenic score for anorexia was associated with waist dissatisfaction, independent of

objectively measured waist circumference. Finally polygenic scores for BMI and Waist-to-Hip Ratio were associated with weight and waist dissatisfaction, respectively, but these associations were entirely mediated by the corresponding objectively measured body characteristics (BMI and waist-circumference).

Overall, the study findings only partially support my hypothesis as not all polygenic scores relating to mental health vulnerability were associated with weight and waist dissatisfaction, after accounting for anthropometric measures and the effect of other correlated polygenic scores. Despite this, the study extends current knowledge of genetic predictors of subjective body perception.

First, it provides evidence indicating that the genetic predisposition to neuroticism influences body dissatisfaction in early adolescence, when accounting for anthropometric measures of BMI and waist circumference and the effects of other polygenic scores. This is likely to be because adolescents who are predisposed to neuroticism may be more self-conscious and have a tendency to negatively perceive their bodies, leading to weight and waist dissatisfaction. Second, it provides evidence suggesting that adolescents with genetic predispositions to anorexia are more likely to be dissatisfied with their waists, regardless of their objective waist circumference. This is likely to be because adolescents at risk of anorexia are prone to be highly self-critical about their physical body shape. Third, the results presented provide corroborative evidence that indicates that there is a relationship between the polygenic score for BMI and subjective body dissatisfaction, via the objective measure of BMI.

Taken together, these studies provide insights into the role of subjective appraisal of experiences in mental health (when compared to objective experiences), and

the influence of genetic predisposition to mental health on children and adolescents' subjective perceptions of adverse events (bullying victimisation) and their physical appearance (body dissatisfaction). Below, I will discuss the potential explanations for the stronger associations between subjective experiences (including adversities) and psychopathology.

5.3 Stronger associations between subjective (versus objective) experiences of adversity and psychopathology: generalisability and potential mechanisms

Generalisability to wider experiences. As discussed, my thesis provides evidence indicating that subjective self-reports of adverse childhood experiences are more strongly associated with mental health problems than corresponding objective measures. This is consistent with wider literature which shows that perceptions of other childhood experiences (e.g., income inequality, Piera Pi-Sunyer et al., 2023; family social status, Rivenbark et al., 2020) are more strongly linked to psychopathology than corresponding objective measures. Notably, recent evidence obtained from a prospective cohort study (N=12,995) found that adolescents who perceived themselves as poorer than their friends reported more social difficulties and adverse mental health, than adolescents who perceived themselves as richer or equal, independent of objective measures (Piera Pi-Sunyer et al., 2023). Whilst findings showed both the adolescents' perceived income inequality and the objective family income played a role in how the adolescent perceived themselves, it was the perception of economic disadvantage that predicted worse outcomes (i.e., for internalising and externalising problems) (Piera Pi-Sunyer et al., 2023). Similarly, in a longitudinal

twin-based study (Rivenbark et al., 2020), results revealed that the adolescents' perception of social status was associated with experiencing poorer health and wellbeing (e.g., depression and anxiety), over and above shared family socioeconomic status (accounting for in twin-difference analyses). Taken together, as perception of experiences is emerging as a potential predictor of psychopathology, beyond the objective experience, it is important to explore the potential mechanisms by which this could occur.

5.4 Potential mechanisms underlying the stronger associations between subjective (versus objective) experiences of adversity and psychopathology

Mediation. First, the relationship between objective measures of adverse experiences and psychopathology may be explained by the subjective self-report measure being a potential mediator of the relationship (see **Figure 5.1**).

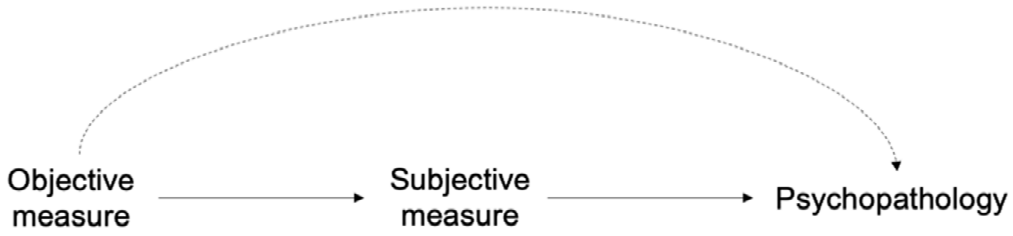


Figure 5.1. Mediation.

In **Figure 5.1**, the directed arrows trace a path that goes from the objective experience of adversity to psychopathology via the subjective self-report measure. Here, the subjective measure can be referred to as a mediator, as it is

a mechanism on the causal pathway between the objective experience and psychopathology. In this figure, the assumption is made that the subjective experience of adversity (mediator) is caused by the objective experience (exposure), and as a result causes psychopathology (outcome/consequence). For example, this would represent a scenario in which objective experiences of childhood adversity affect a person's memories and perceptions of that experience, which in turn drive risk for psychopathology (e.g., perhaps due to evoking negative feelings about themselves and others). Note that there is a dotted curved arrow from the objective measure to psychopathology, indicating there may be either no direct effect of the objective measure on psychopathology, or a residual effect that is not captured by the subjective experience.

This model may explain my findings from **Chapter 2**, as I found that objective measures of childhood adversities were not associated with psychopathology after accounting for subjective self-report measures. Because previous evidence has shown that objective measures of childhood adversities are associated with psychopathology before accounting for subjective measures (Cutajar et al., 2010; Mills et al., 2016; Widom et al., 2007), this could indicate that the subjective experience acts as a mediator between objective measures (exposure) and the psychopathology (outcome). However, other mechanisms might also explain the stronger associations between subjective – versus objective - measures with psychopathology.

Genetic confounding. The stronger association between subjective measures of adversities and psychopathology may be explained by genetic confounding – whereby individuals with genetic predispositions to mental health vulnerabilities might perceive experiences in a more negative way, and also develop psychopathology (see **Figure 5.2**).

Figure 5.2. Genetic confounding.

In **Figure 5.2**, there are two directed arrows from genetic predispositions to mental health vulnerabilities to (1) the subjective measure, and (2) psychopathology. The dotted arrow from the subjective measure to psychopathology indicates that the association between the subjective measure and psychopathology may be (at least partly) spurious and explained by genetic confounding. This could be due to the genetic predisposition to mental health vulnerabilities influencing both the subjective perception of adverse experiences (exposure) and psychopathology (outcome).

In **Chapter 2,** for example, I cannot rule out that the relationship found between subjective self-reported childhood adversities and psychopathology may be confounded by the individual's pre-existing mental health vulnerability. To be specific, an individual's genetic predisposition to depression may have (1) directly

increased their risk of psychopathology, and (2) led to becoming more prone to perceiving their experiences as negative, and thereby reporting experiences of adversity. The role of genetic confounding has previously been explored by research examining adolescents' self-reported bullying victimisation and later self-reported internalising problems (Vrijen et al., 2023). Using data from a prospective cohort study (N=1,604), authors found that the relationship between self-reported bullying victimisation and internalising problems (i.e., depression) was confounded by the genetic predisposition to internalising problems. That is to say that the same genes that influence self-reported bullying victimisation in adolescence, also influence internalising problems later experienced (Vrijen et al., 2023). This evidence shows that genetic confounding is a potential etiological mechanism that explains why subjective self-reported experiences have stronger associations with psychopathology.

My findings from **Chapters 3 and 4** highlight the importance of considering genetic confounding when incorporating self-reported measures. For instance, in **Chapter 3**, I found that higher genetic susceptibility to ADHD is associated with adolescents self-reporting greater levels of bullying victimisation than the amount reported by parents and teachers. This indicates that genetic predisposition to ADHD may affect an adolescent's perception of bullying victimisation, above and beyond actual victimisation experiences captured by parents' and teachers' reports. In turn, this suggests that the associations between self-reported bullying victimisation and ADHD might be partly confounded by genetic vulnerabilities contributing to ADHD and perceptions of victimisation. Similarly, in **Chapter 4**, I found that the genetic predisposition to neuroticism was associated with

adolescents' experiences of body dissatisfaction, when adjusted for objective anthropometric measures. In other words, this provides evidence that a pre-existing mental health vulnerability influences the subjective experience of weight and waist dissatisfaction, beyond the objective assessment. It is therefore possible that associations between body-related dissatisfaction and psychiatric disorders involving neuroticism (e.g., depression, anxiety), might be confounded by genetic predisposition to neuroticism.

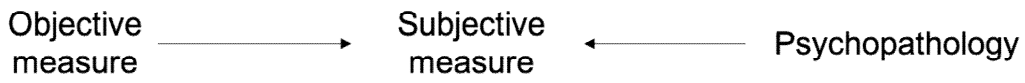


Figure 5.3. Reverse causation.

Reverse causation. A stronger association between subjective measures of adversities and psychopathology could also be attributable to reverse causation, in which psychopathology precedes self-reports of adversity, which is particularly relevant for retrospective assessments of adversities. In other words, findings may be partially explained as individuals with psychopathology may be more prone to self-report exposure to adversity, due to recall bias (i.e., arising from a negative bias in autobiographical memory; Colman et al., 2016) or a greater tendency to interpret experiences as adverse. In **Figure 5.3**, the directed arrow from psychopathology to the subjective measure represents this phenomenon, whereby instead of the subjective measure (reported exposure) causing the psychopathology (outcome), the "reverse" has occurred so that psychopathology precedes the subjective measure. Notably, in this figure there is an effect of the objective measure on the subjective measure, indicating that the self-report

measure is informed both by the objective exposure and the bias in perception due to reverse causation.

Recall bias has been found to partially explain findings from a recent study examining the associations between subjective self-report and objective measures (court records) of childhood maltreatment in relation to emotional disorders (Danese & Widom, 2023). The study found that subjective measures of maltreatment were associated with later emotional disorders, but this association was attenuated by psychopathology at the time of self-report. This supports that recall bias may contribute to the effects that I observed in **Chapter 2** and supports the need for longitudinal studies with repeated measures of both subjective and objective measures and psychopathology, to disentangle the direction of effects (i.e., whether subjective reports precede psychopathology or vice versa).

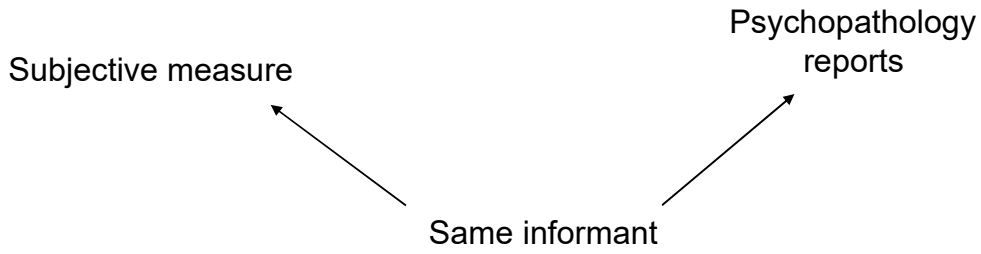
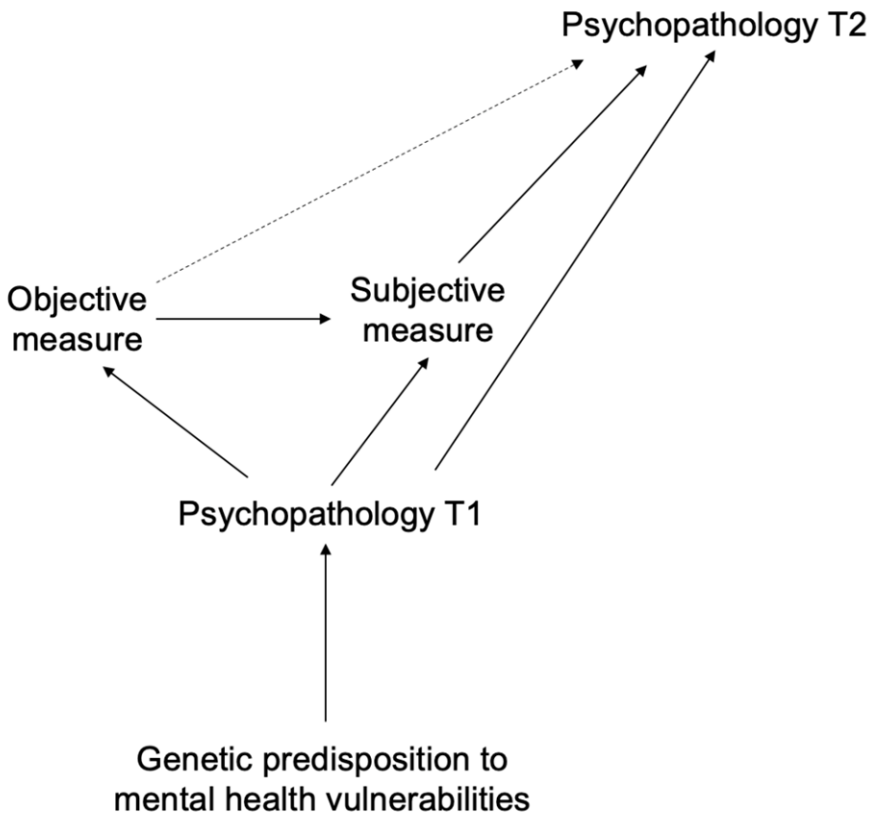


Figure 5.4. Shared method variance.

Shared method variance. Another alternative explanation for the stronger associations between subjective measures of adversity and psychopathology is shared method variance (see **Figure 5.4**). This implies that the association between the exposure (e.g., subjective measures of adversity) and the outcome (e.g., psychopathology) may be artificially inflated due to both measures being

reported by the same individual (i.e., self-reported). This may explain the moderation findings from **Chapter 2**, given that I found subjective self-report measures of adversities were more strongly associated with psychopathology that was self-reported, versus reported by other informants. In contrast, objective measures (that do not rely on self-report) showed minimal associations with self-reported psychopathology, and stronger associations with psychopathology reported by another informant. Interestingly, previous research using retrospective self-reports of childhood adversity found evidence of shared method variance. Authors determined this influenced the predictive capacity of retrospective reports with participants underestimating the impact of adversity on objective life outcomes and overestimating the impact of adversity on self-reported outcomes (Reuben et al., 2016).



Note: Psychopathology T1 refers to the first instance of symptoms (i.e., in early childhood), Psychopathology T2 refers to symptoms that are persistent or new that are reported at a later time-point (i.e., late childhood or early adolescence).

Figure 5.5. Diagram showing the potential aetiological mechanisms and biases that may explain findings reported in this thesis.

Altogether, there are several aetiological mechanisms and biases that may explain observed stronger associations between subjective measures and psychopathology. These are important to acknowledge when interpreting findings from this thesis. **Figure 5.5** represents a potential causal framework by which the subjective and objective measures are associated with psychopathology.

First, there is a directed arrow from genetic predisposition to mental health vulnerabilities to psychopathology at time-point 1 (T1). This indicates that there

is a causal effect of the underlying predisposition of mental health vulnerabilities toward the emergence of psychopathology (outcome). Second, the direction of effect indicates that psychopathology at T1 precedes the subjective self-report measure (reverse causation). This explains how genetic predisposition to mental health vulnerabilities can indirectly impact subjective reporting via early symptoms of mental health difficulties. This is evidenced by my finding in **Chapter 4** showing that the genetic predisposition to neuroticism is associated with body-related dissatisfaction, beyond objectively assessed anthropometric measures. Third, there is a direct causal effect from the objective measure to the subjective measure. Here, the objective measure has an indirect effect on later psychopathology T2 (via the subjective self-report), consistent with the pattern of findings in **Chapter 2**. Fourth, there is an indirect arrow from genetic predisposition to mental health vulnerabilities to objective measures via psychopathology at T1. This can be explained by considering that evocative gene-environment correlations may influence objective reports of experiences (Pingault et al., 2022). For instance, as found in **Chapter 3**, the genetic predisposition to ADHD was associated with multi-informant reported victimisation. This could be explained by the adolescents' underlying genetic variants attributed to ADHD influencing their behaviour (e.g., hyperactive-impulsivity). In turn, this may lead to more attention from teachers and parents whom may be more likely to identify if the adolescent is experiencing bullying victimisation. Finally, the dotted arrow suggests that the objective measure may still have a direct partial effect on psychopathology at T2.

5.5 Future implications

5.5.1 Research implications

As underlying aetiological mechanisms and biases may explain the stronger association between subjective measures and psychopathology, it is imperative that future research tests and addresses these alternative explanations.

First, to address reverse causation and recall bias (i.e., earlier psychopathology biases the perception of the environment), longitudinal studies with repeated measures of subjective and objective experiences and psychopathology should employ models (e.g., cross-lagged models) to test the direction of effects between subjective and objective measures and psychopathology. Second, shared method variance could be minimised by using multi-informant reports (i.e., clinical records, parent or teacher reports) to capture psychopathology, as opposed to relying on the subjective self-report alone. This does not necessarily mean that reports from other individuals are superior to self-report. Instead, by incorporating measures of psychopathology that are not self-reported, this would allow researchers to rule out findings being due to shared method variance. Third, it is imperative that researchers test for the independent contribution of subjective versus objective measures by incorporating both measures in study designs. To enable this, cohort data could be linked to administrative data, for example child protection records that detail child maltreatment, and crime records that capture neighbourhood violence.

Finally, due to the potential for genetic confounding in observational studies, it is important to account for genetic predisposition and traits that may confound associations between subjective reporting of the individual's experience and

psychopathology. Here, the use of genetically informed approaches would allow researchers to further interrogate the causal mechanisms that influence the subjective experience (Baldwin & Degli Esposti, 2021; Pingault et al., 2022). Examples include, but are not limited to (1) accounting for polygenic scores for mental health vulnerabilities in analyses on the associations between subjective measures with psychopathology, (2) integrating polygenic scores with heritability estimates of psychopathology to account for greater genetic variance in mental health outcomes and test whether effect estimates between subjective reports and psychopathology are confounded by genetics (Pingault et al., 2022; Vrijen et al., 2023), (3) mendelian randomisation to interrogate causal effects between risk factors (i.e., self-reported childhood maltreatment) and psychopathology (Warrier et al., 2021) and (4) within-family comparisons that allow for shared genetics between siblings/co-twins to be accounted for, so any difference in psychopathology may be attributed to the twin differences in perception of the environment; Rivenbark et al., 2020). Whilst no single approach will be free from bias, applying multiple approaches with different assumptions (triangulation; Baldwin & Degli Esposti, 2021; Munafò et al., 2021), will improve researchers' ability to identify the underlying aetiological mechanisms that may explain why stronger associations occur between subjective experiences and psychopathology.

5.5.2 Implications for interventions

My thesis findings have implications for prevention and intervention that warrant further discussion.

First, it is of ethical importance to prevent objective experiences of childhood adversity from occurring, regardless of the long-term mental health consequences of objective experiences. However, if it is the case that subjective experiences mediate the effects of objective adverse experiences on psychopathology (**Figure 5.1**), then preventing adversity could also help to prevent mental health problems in the population. For instance, anti-bullying interventions have been developed to stop, reduce and prevent school-based bullying. For example, KiVa is a research-based anti-bullying intervention program first developed in Finland for children aged 7 to 15 (Kärnä, Voeten, Little, Poskiparta, Alanen, et al., 2011), that has since expanded to Italy and the UK (Axford et al., 2020; Nocentini & Menesini, 2016). This involves children being given material to promote anti-bullying, as well as encouraged to partake in a unique video game in which the child is required to recognise instances of bullying prior to passing through to the next level. Another dimension to this program, is that as well as targeting peers, the intervention provides information to teachers and parents. For teachers, a web-based discussion forum is open to all participating in order to seek advice and share experiences. For parents, they receive a guide on how to reduce bullying (Kärnä, Voeten, Little, Poskiparta, Kaljonen, et al., 2011). A recent meta-analysis evaluating the effect of 100 bullying intervention programs, including those similar to KiVa, found that they significantly reduced the incidence of both bullying perpetration and bullying victimisation (Gaffney et al., 2021). However, despite proving effective, these interventions appear to only have a small impact on reducing internalising symptoms (Guzman-Holst et al., 2022). This may in part be explained due to the bullying intervention programme targeting the occurrences of bullying within

schools and therefore only indirectly targeting mental health outcomes. In addition to such interventions targeting occurrences of victimisation, additional interventions supporting children who report being bullied may improve the effects of such interventions by addressing several pathways depicted in **Figure 5.5**: (i) potentiating the effect of interventions by addressing the mediating pathway between objective exposure and later psychopathology; (ii) address underlying mental vulnerabilities which may be manifested in both increased reporting and later psychopathology; (iii) help break the path between early and later psychopathology that can be strengthened by perception processes (e.g. perceiving bullying may increase rumination, which may feed into later psychopathology).

Additional support for the prevention of objective exposure to harmful childhood experiences can be obtained from evidence examining the effectiveness of child maltreatment prevention programs. For instance, previous research has examined the impact of the Nurse Family Partnership, a home visitation programme involving nurses visiting high-risk families (e.g., children born to women who were either teenagers, unmarried or were from a lower socioeconomic background) on maltreatment (Olds et al., 1998). Findings indicated that more frequent nurse visits led to fewer instances of abuse and neglect in the first 15-years of the child's life (Olds et al., 1998). Importantly, due to being under close observation by the nurse, the child was less likely to be restricted in homes and punished (i.e., physically abused) (Olds et al., 1998). This suggests that the exposure to childhood maltreatment can be modified through targeting the environment and in effect the potential perpetrators' behaviour.

However, such primary prevention programmes cannot prevent children already exposed to adverse experiences from the harmful effects (i.e., psychopathology). Therefore, secondary interventions that aim to prevent risk of psychopathology in individuals already exposed to adversity should also be considered.

If it is indeed the case that subjective experiences contribute to the risk of psychopathology (and this association is not fully explained by alternative sources of bias; **Figures 5.1-5.5**), clinical interventions that target the exposed individual's perception and memory of their experiences may reduce psychopathology. Therapeutic intervention for young people who have experienced adversities often involve models that adapt existing cognitive therapies that are typically administered to individuals with psychopathology (Cohen et al., 2010). For instance, trauma-focused cognitive behavioural therapy (trauma-focused CBT) is recognised as one of the most effective interventions to reduce psychopathology in children and adolescents who have experienced trauma (Leenarts et al., 2013). A key component of trauma-focused CBT is perceptual bias modification. This involves the therapist enabling the child to identify the link between how they feel, think and behave with inaccurate memory recall. For example, by challenging memory distortions and unhelpful trauma-related cognitions (i.e., shame) (Leenarts et al., 2013). Additionally, it also incorporates the family of the child by facilitating healthy communication that involves providing the child opportunities to discuss thoughts and emotions in a safe and therapeutic environment.

However, trauma-focused CBT is not appropriate to administer when the perpetrator is a family member (Cohen & Mannarino, 2015). Additionally, other

barriers to a child's progress include family or social problems. Indeed, a recent meta-analysis (n=8 studies) examined the risk factors that predict drop out from trauma-focused CBT and found that family income and parental education predicted drop-out (van der Hoeven et al., 2023). Importantly, there is limited research assessing the longer term treatment effects of trauma-focused CBT (Thielemann et al., 2023), and evidence indicating it may benefit older adolescents as opposed to children (Hoogsteder et al., 2022). Therefore, it remains unclear as to whether this approach effectively targets the perceptions and memories of harmful experiences for all individuals.

My findings also suggest that clinical interventions that support children with pre-existing mental health vulnerabilities may lead to a reduction in both perceived negative experiences, and eventual psychopathology. For instance, I found that genetic predisposition to ADHD is associated with children's reports of bullying victimisation, and genetic predisposition to neuroticism influences body dissatisfaction. This indicates that supporting children with early signs of ADHD and neuroticism may be a worthwhile avenue. However, clinical implementation of polygenic scores in clinical practice (i.e., to identify at-risk individuals) is yet to be applied in practice due to polygenic scores only capturing a small proportion of heritability (Lewis & Vassos, 2020), although with increased precision and performance, this may change. Instead, children with a genetic predisposition to neuroticism and ADHD could be identified if they exhibit early symptoms of these conditions. Meanwhile, one approach to alleviate body dissatisfaction may be to enhance the bond and level of open communication between parent and child (Laporta-Herrero et al., 2021). Here, trust may build and therefore the child could

feel more supported to disclose if experiencing body dissatisfaction warranting intervention. Additionally, the child could be taught to develop the capability to critically analyse media information to pre-empt risk for developing body dissatisfaction as a result of induced low self-esteem.

5.6 Conclusion

This PhD thesis aimed to better understand (i) the relationship between subjective and objective experiences and their associations with mental health, and (ii) the role of genetic predisposition to mental health vulnerabilities in subjective experiences.

The findings presented in this thesis show that the subjective appraisal of experiences is more strongly associated with psychopathology than objective measures of such experiences. By capitalising on the most recent GWAS summary statistics and leveraging a more powerful polygenic score approach than used in previous research, I was able to identify that the genetic predisposition to mental health vulnerabilities may contribute to young people's subjective experiences. As such, my thesis findings could potentially impact prevention programs and clinical interventions for children and adolescents. This is due to novel insights gained as to the importance of targeting perception and memories of experiences in those reporting harmful experiences and feelings. Nonetheless, future research should aim to replicate findings in independent samples and consider whether using different genetically informed approaches may help in further understanding the underlying aetiological mechanisms that explain why subjective measures are associated with psychopathology, beyond objective measures.

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Appendices

Appendix A – Supplementary material for Chapter 2. Subjective and objective experiences of childhood adversity: a meta-analysis of their agreement and relationships with psychopathology.

Supplementary Method 1. Search terms to identify eligible studies.

"child* trauma" OR "child* advers*" OR "maltreatment" OR "child* abuse" OR "child* neglect" OR "victim*" OR "bully*" OR "bullie*" OR "neighbourhood viol*" OR "neighborhood viol*" OR "neighbourhood advers*" OR "neighborhood advers*"] AND ["subjective*" OR "perceived" OR "perception*" OR "self-report*"] AND ["objective*" OR "record" OR "agency-notified" OR "peer nom*" OR "peer report*" OR "peer reputation"] AND ["mental health" OR "mental illness" OR "psychopathol*" OR "psychiatric" OR "depress*" OR "anxi*" OR "panic" OR "obsessive compulsive" OR "self inj*" OR "self harm*" OR "suicid*" OR "eating disorder*" OR "schiz*" OR "psychotic" OR "psychosis*" OR "bipolar" OR "attention deficit hyperactivity disorder" OR "conduct" OR "substance abuse" OR "alcohol" OR "drug" OR "cannabis".

Supplementary Method 2. Variables extracted.

- First author name
- Year of publication
- Cohort name
- Country of study origin
- Percentage female of analytic sample
- Sample size for analysis
- The type of exposure reported by the objective measure
- The type of exposure reported by the subjective measure
- The type of objective measure
- The type of subjective measure
- Observational period for Adverse Childhood Experiences (ACE) reported using objective measure
- Observational period for ACE reported using subjective measure
- The age when subjective measure was obtained
- Variable type for the objective measure
- Variable type for the subjective measure
- The mental health outcome being studied
- The assessment being used to measure mental health outcome
- The informant reporting mental health outcome
- The age when mental health was assessed
- The variable type of psychopathology measure
- Type of effect size reported for the objective measure
- The reported effect size for the association between objective measure and the mental health outcome, controlling for subjective measure
- The standard error reported for the association between objective measure and the mental health outcome, controlling for subjective measure
- The standard deviation reported for the association between objective measure and the mental health outcome, controlling for subjective measure

- The 95% confidence interval reported for the association between objective measure and the mental health outcome, controlling for subjective measure
- The p value reported for the association between objective measure and the mental health outcome, controlling for subjective measure
- Type of effect size reported for the subjective measure
- The reported effect size for the association between subjective measure and the mental health outcome, controlling for objective measure
- The standard error reported for the association between subjective measure and the mental health outcome, controlling for objective measure
- The standard deviation reported for the association between subjective measure and the mental health outcome, controlling for objective measure
- The confidence interval reported for the association between subjective measure and the mental health outcome, controlling for objective measure
- The p value reported for the association between subjective measure and the mental health outcome, controlling for objective measure
- Type of effect size agreement
- Effect size agreement between the subjective and objective measures
- The standard error reported for agreement between the subjective and objective measures
- Number of participants in the total sample that have each measure
- Number of participants who report the objective measure only
- Number of participants who report the subjective measure only
- Number of participants who report the subjective and objective measure only
- Number of participants that have none of the measures reported
- Representativeness of participants classified as exposed to adversity on the objective measure
- Selection of participants classified as not exposed to adversity on the objective measure
- Quality of the subjective assessment of ACE
- Whether the objective and subjective assessments measure exactly the same experiences
- Whether the objective and subjective assessments cover the same time period of exposure

- Demonstration that the mental health outcome was not present before exposure to adversity
- Whether relevant confounding factors controlled for
- Whether subjective measures were administered prior to mental health measures

Supplementary Method 3. Converting unadjusted correlations to partial correlations.

Step 1: Specify correlation matrix with correlations between (i) outcome and the subjective measure, (ii) outcome and the objective measure, and (iii) subjective and the objective measure

Step 2: Generate a covariance matrix from the correlation matrix by specifying standard deviations of the (i) outcome, (ii) objective measure, and (iii) subjective measure*

Step 3: Fit a structural equation model on the covariance matrix, in which the psychopathology outcome is regressed on subjective measures and objective measures of childhood adversity

Step 4: Extract partial correlations and standard errors for the (i) association between the psychopathology outcome and the subjective measure, adjusting for the objective measure, and (ii) association between the psychopathology outcome and the objective measure, adjusting for the subjective measure.

*If the standard deviations were not available, the structural equation model was fitted on the correlation matrix.

Supplementary Table 1. PRISMA Checklist.

Section and Topic	Item #	Checklist item	Location where item is reported (page)
TITLE			
Title	1	Identify the report as a systematic review/meta-analysis	34
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	NA
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	36-38
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	38
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	38-39, 187
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	39
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	39, 187
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	38-39
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	39-40
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	188-190
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	188-190

Section and Topic	Item #	Checklist item	Location where item is reported (page)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	40, 196-198
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	40-41
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	38-39
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	41-43
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	41-43
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	41-43
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	42-43
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	44, 205

Section and Topic	Item #	Checklist item	Location where item is reported (page)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	45
Study characteristics	17	Cite each included study and present its characteristics.	45
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	199
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	45, 59
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	196-199
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	49-58
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	49-58
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	NA
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	61-67
	23b	Discuss any limitations of the evidence included in the review.	61-67
	23c	Discuss any limitations of the review processes used.	61-67
	23d	Discuss implications of the results for practice, policy, and future research.	66-67

Section and Topic	Item #	Checklist item	Location where item is reported (page)
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	38
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	38
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	38
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	NA
Competing interests	26	Declare any competing interests of review authors.	NA
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	43

Supplementary Table 2. The Description of Bias Assessment**.**

The following table corresponds to the description of the information that was extracted in order to assess the bias of included studies. I adapted the Newcastle-Ottowa scale (Wells et al, 2000) with relevant items to assess the quality of studies in examining the associations between subjective and objective measures of childhood adversity with psychopathology. For example, I added items on whether the subjective and objective measures capture exactly the same experience and cover the same time period, and whether psychopathology was assessed longitudinally or cross-sectionally. These additional questions resulted in a 9-point scale ranging from 0 (indicating very high bias) to 8 (indicating very low bias).

Bias assessed	Description	Assignment of score
Exposed group is representative	*Representativeness of participants classified as exposed to adversity on the objective measure*	A score of 0 or 1 (as outlined below) depending on whether participants classified as exposed to adversity on the objective measure are: a) truly representative of the average cohort in the community (1) b) somewhat representative of the average cohort in the community (1) c) selected group: e.g. children selected because of exposure to maltreatment/other adversity (0) d) no description of the derivation of the exposed group (0)
Selection of controls	*Selection of participants classified as not exposed to adversity on the objective measure*	A score of 0 or 1 depending on whether participants classified as unexposed on the objective measure are: a) drawn from the same community as those classified as "exposed" on the objective measure or matched to ensure comparability (1). b) drawn from a different source (0). c) No description of the derivation of the unexposed group (0).
Quality of subjective measure	*Quality of the subjective assessment of ACE*	A score of 0 or 1 depending on whether the self-report assessment of adversity was based on a:

Bias assessed	Description	Assignment of score
		a) Interview or questionnaire tested for validity and reliability (1). b) non-validated self-report questionnaire/interview or no description (0).
Comparison of ACE measures	*Whether the objective and subjective assessments measure exactly the same experiences.*	A score of 0 or 1 (as outlined below): a) The subjective and objective measures assess exactly the same ACE experiences i.e., child maltreatment, bullying victimisation (1). b) The subjective and objective measures do not assess different ACE experiences i.e., objective = neighbourhood crime records, subjective = neighbourhood disorder (0). c) It is unclear whether the subjective and objective measures assess the same thing (0).
Comparison of exposure time	*Whether the objective and subjective assessments cover the same time period of exposure*	A score of 0 or 1 (as outlined below: a) The time-period of exposure to adversity covered by the objective and subjective measures was exactly the same (e.g., court records and self-reports measured adversity between birth and age 12) (1) b) The time-period of exposure to adversity covered by the objective and subjective measures was different (e.g., court records assessed adversity between birth and age 12; self-reports assessed adversity between birth and age 18) (0)
Control for mental health	*Demonstration that the mental health outcome was not present before exposure to adversity*	A score of 0 or 1 (as outlined below: a) Pre-existing mental health outcomes were controlled for in the analysis (or participants with pre-existing mental health problems were removed) (1) b) Mental health outcome(s) was not controlled for (0).
Confounding	*Whether relevant confounding factors controlled for.*	A score of 0 or 1 (as outlined below: a) The study controlled for any of the following confounders: - socioeconomic status - parental education - family income - other adversities (e.g., poverty, bullying, maltreatment, victimisation) - genetic risk for mental health problems (family history of psychopathology, polygenic score) (1). b) Did not control for any of the above (0).

Bias assessed	Description	Assignment of score
Longitudinal	*Whether subjective measures were administered prior to mental health measures*	A score of 0 or 1 (as outlined below): a) Subjective measures (e.g., self-reports) of adversity were collected prior to mental health outcomes (e.g., if self-reports were measured at age 8 and mental health was measured at age 10) (1). b) Subjective measures were administered at the same time or after the assessment of mental health measures (0). c) It is unclear when subjective measures were administered (0).

Supplementary Table 3. Risk of Bias for All Included Studies (agreement and main meta-analysis).

	Exposed group is representative	Selection of controls	Quality of subjective measure	Comparison of ACE measures	Comparison of exposure time	Control for mental health	Confounding	Longitudinal	Total risk of bias score*
Bouman et al., 2012	1	1	1	1	1	0	0	0	5
Cho & Jackson., 2016	0	1	1	1	1	0	0	0	4
Danese & Widom., 2020	0	1	1	1	1	0	1	0	5
De Los Reyes & Prinstein., 2014	1	1	1	1	1	0	0	0	5
Everson et al., 2008	0	0	0	1	1	0	1	0	3
Flanagan et al., 2008	1	0	1	1	1	0	0	0	4
Graham, et al., 2003	1	1	0	1	1	0	0	0	4
Graham & Juvonen., 1998	1	1	1	1	1	0	0	0	5
Goldman-Mellor et al., 2016	1	1	0	0	1	0	1	0	4
Gromann et al., 2013	1	1	1	1	0	0	0	0	4
Havlicek & Courtney., 2016	0	0	0	1	1	0	0	0	4
Kochel et al., 2017	1	1	0	1	1	0	0	1	5
McClain et al., 2020	1	1	1	0	1	1	0	1	6
McGee et al., 1995	0	1	1	1	1	0	0	0	4
Mulder et al., 2017	1	1	1	1	1	0	0	1	6
Negriff et al., 2017	0	1	1	1	1	0	0	0	4
Newbury et al., 2017	1	1	0	0	0	1	1	0	4
Rigby & Slee., 1999	1	1	1	1	1	0	0	0	5
Sierau et al., 2017	0	0	1	1	1	0	0	0	3
Smith et al., 2008	1	1	0	1	0	1	1	0	5
White et al., 2016	0	0	1	1	1	0	0	1	4
Zimmer-Gembeck & Pronk., 2012	1	1	0	1	1	0	0	0	4

*Risk of bias total scores ranged from 3 to 6 out of 8, with 0 being the highest risk of bias.

Supplementary Table 4. Formulae for conversion to correlation**.**

Raw effect size type	Formula for conversion to *r*	Reference
Cohen's *d*	$r = \frac{d}{\sqrt{d^2 + a}}$	Borenstein et al.,2021
Log odds ratio	Step 1: $d = LogOddsRatio\ x\ \frac{\sqrt{3}}{\pi}$ Step 2: $r = \frac{d}{\sqrt{d^2 + a}}$	Borenstein et al, 2021
Risk Ratio (RR)	Step 1: $LogOddsRatio = \frac{\log(1-p) * RR}{1 - RR * p}$ Step 2: $d = LogOddsRatio\ \times \frac{\sqrt{3}}{\pi}$ Step 3: $r = \frac{d}{\sqrt{d^2 + a}}$	Grant, 2014
Unstandardised beta $(\boldsymbol{\beta})$	$r\ = \beta\ \left(\frac{sd\ exposure}{sd\ outcome}\right)$	Cross Validated, 2022

RR= Risk Ratio; *p*= the control event rate (prevalence in unexposed population)*; d*= Cohen's d*; se*= standard error; a is the correction factor for cases where $n_1 \neq n_2$. If n_1 and n_2 are not precisely known, then $a = 4$*;* OR= Odds Ratio; CI= Confidence Interval; $\beta = Unstandardised\ Coefficient$; $\mathrm{r} = \mathrm{Correlation\ Coefficient}$; sd= Standard Deviation; sd exposure = Standard Deviation of the Exposure Variable Reported; sd outcome = Standard Deviation of the Outcome Variable Reported.

Supplementary Table 5. Egger's Test and leave-one-out analysis for studies examining the agreement between subjective and objective measures of childhood adversity.

Agreement meta-analysis	Egger's Test	Leave-one-out analysis*		Meta-analytic effect size for comparison
	Q_mod (*p*)	Smallest effect size *r* (95% CI)	Largest effect size *r* (95% CI)	
Maltreatment (meta-analysis of correlations)	2.59 (0.11)	0.29 (0.22-0.35)[a]	0.34 (0.25-0.43)[b]	0.32 (0.23-0.41)
Maltreatment (meta-analysis of kappas)	0.46 (0.50)	0.13 (0.09-0.17)[a]	0.17 (0.10-0.24)[c]	0.16 (0.10-0.22)
Bullying (meta-analysis of correlations)	7.80 (0.0052)	0.32 (0.26-0.38)[d]	0.36 (0.28-0.44)[e]	0.35 (0.27-0.42)

*****Letters next to each estimate correspond to the study reference removed:
[a]McGee et al., 1995; [b]White et al., 2016;[c]Cho & Jackson, 2016; [d]Gromann et al., 2013; [e]De Los Reyes & Prinstein, 2004.

Supplementary Table 6. Egger's Test and leave-one-out analysis for studies assessing whether subjective and objective measures of childhood adversity independently predict psychopathology.

Main meta-analysis	Egger's Test	Leave-one-out analysis*		Meta-analytic effect size for comparison *r* (95% CI)
	Q_mod (*p*)	Smallest effect size *r* (95% CI)	Largest effect size *r* (95% CI)	
Maltreatment (subjective measure)	0.02 (0.89)	0.14 (0.07- 0.20)[a]	0.18 (0.13-0.23)[b]	0.16 (0.09-0.22)
Maltreatment (objective measure)	0.01 (0.93)	0.02 (-0.02-0.07)[a]	0.08 (-0.00-0.15)[c]	0.06 (-0.02-0.13)
Bullying (subjective measure)	1.54 (0.21)	0.11 (0.07-0.14)[d]	0.13 (0.09-0.17)[e]	0.12 (0.08-0.17)
Bullying (objective measure)	4.81 (0.03)	0.02 (-0.02-0.06)[f]	0.04 (-0.00-0.09)[g]	0.03 (-0.01-0.08)

*****Letters next to each estimate correspond to the study reference removed:
[a]Cho & Jackson, 2016; [b]White et al., 2016;[c]Danese & Widom, 2020; [d]Bouman et al., 2012; [e]Kochel et al., 2017; [f]Mulder et al., 2017;[g]McClain et al., 2020.

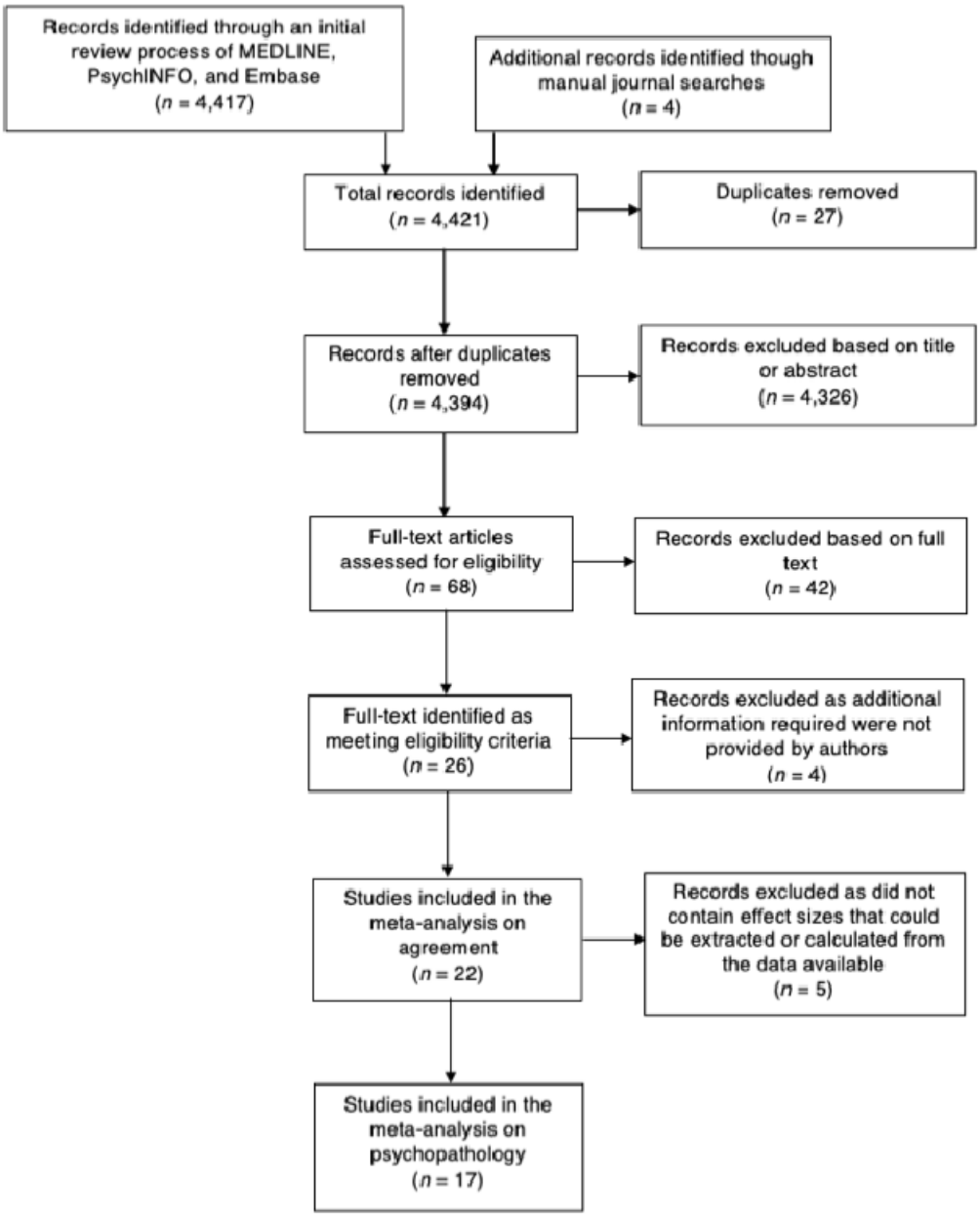
Supplementary Table 7. Moderators of the Association Between Subjective and Objective Measures of Adverse Childhood Experiences and Psychopathology.

Moderators by adversity type	No of studies reporting each outcome	No. of effect sizes	Effect Size Estimate, *r* (95% CI)	QM	*QM P* value
Childhood maltreatment					
Subjective measure					
Informant for psychopathology				1.93	0.16
Self-report	5	88	0.14 (0.07-0.20)		
Other	1*	6	0.26 (0.10-0.41)		
Study type				7.15	**0.0075**
Cross-sectional	5	82	0.18 (0.13-0.23)		
Longitudinal	1*	12	0.03 (-0.07-0.14)		
Type of psychopathology[a]				0.09	0.77
Externalising problems	4	36	0.15 (0.06-0.24)		
Internalising problems	5	45	0.16 (0.07-0.24)		
Sex (percent female)	6	94	-0.02 (-0.03-0.01)	30.34	**<0.0001**
Study quality	6	94	0.02 (-0.07-0.12)	0.28	0.60
Objective measure					
Informant for psychopathology				9.62	**0.0019**
Self-report	5	88	0.02 (-0.02-0.07)		
Other	1*	6	0.21 (0.10-0.32)		
Study type				0.005	0.95
Cross-sectional	5	82	0.05 (-0.03-0.13)		
Longitudinal	1*	12	0.01 (-0.16-0.17)		
Type of psychopathology[a]				0.09	0.76
Externalising problems	4	36	0.05 (-0.03-0.14)		
Internalising problems	5	45	0.06 (-0.02-0.14)		
Sex (percent female)	6	94	-0.01 (-0.03-0.01)	1.34	0.25
Study quality	6	94	-0.03 (-0.12-0.05)	0.62	0.43
Bullying victimisation					
Subjective measure					
Informant for psychopathology				20.37	**<0.0001**
Self-report	8	30	0.15 (0.11-0.20)		
Other	3	15	0.03 (-0.04-0.09)		
Study type				1.58	0.21
Cross-sectional	9	31	0.13 (0.08-0.17)		
Longitudinal	3	14	0.09 (0.03-0.16)		
Type of psychopathology				0.21	0.64
Externalising problems	1*	1*	0.08 (-0.07-0.24)		
Internalising problems	8	43	0.12 (0.07-0.17)		
Study quality	9	45	-0.00 (-0.05-0.04)	0.01	0.92
Sex (percent female)	9	45	0.00 (-0.00-0.00)	0.14	0.71

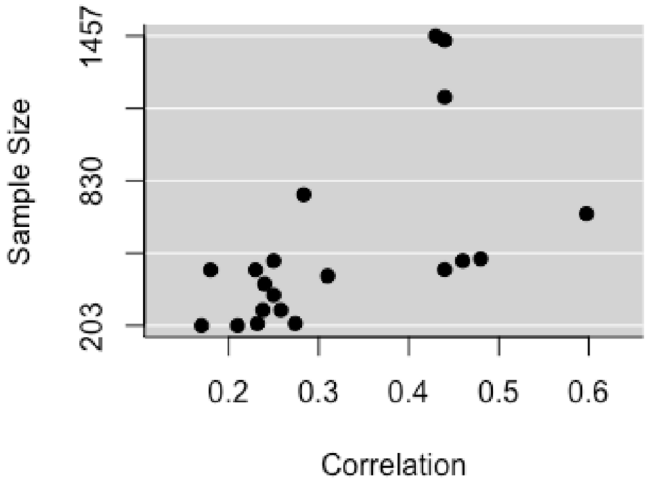
Moderators by adversity type	No of studies reporting each outcome	No. of effect sizes	Effect Size Estimate, *r* (95% CI)	QM	*QM P* value
Objective measure					
Informant for psychopathology				3.30	0.07
Self-report	8	30	0.02 (-0.04-0.07)		
Other	3	15	0.08 (0.01-0.15)		
Study type				0.06	0.81
Cross-sectional	9	31	0.03 (-0.01-0.08)		
Longitudinal	3	14	0.03 (-0.04-0.09)		
Type of psychopathology				145.01	**<0.0001**
Externalising problems	1*	1*	0.47 (0.40-0.53)		
Internalising problems	8	43	0.02 (-0.02-0.07)		
Study quality	9	45	-0.00 (-0.05-0.04)	0.03	0.87
Sex (percent female)	9	45	-0.00 (-0.00-0.00)	1.11	0.29

* These estimates are based on only a single study and/or single effect size and are presented for transparency, but should be interpreted with caution. Everson et al., 2008 not included in the analysis for moderation by mental health outcome as "psychological adjustment" outcome reported was a positive indicator of wellbeing rather than mental ill health.

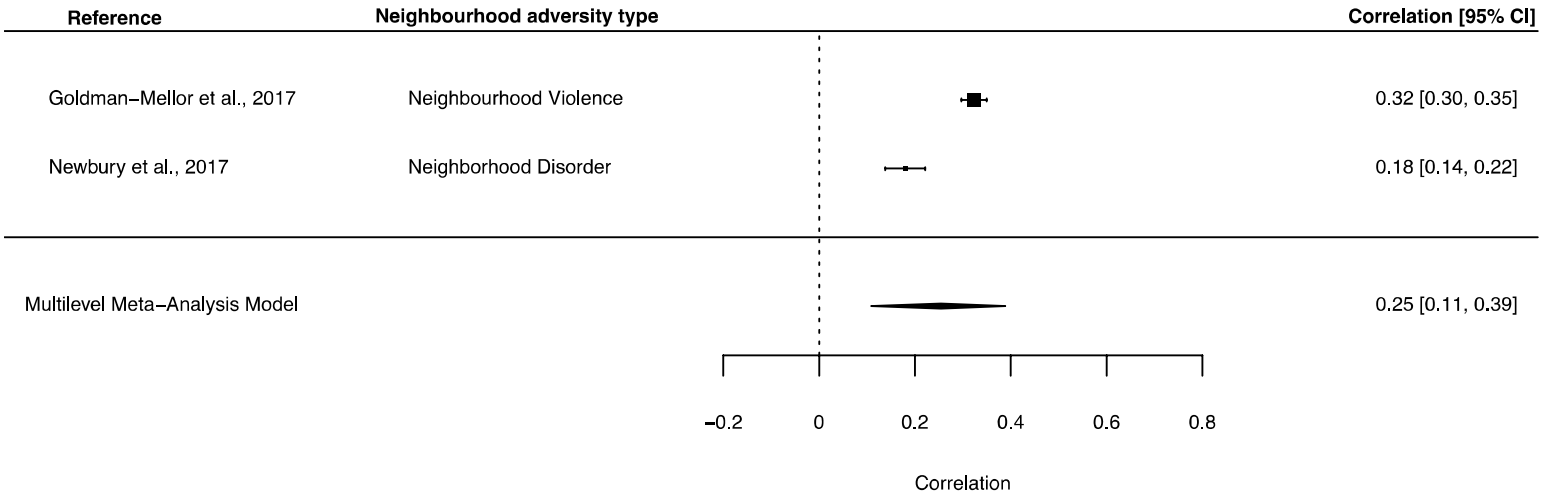
Supplementary Figure 1. PRISMA flow diagram for the study inclusion process.



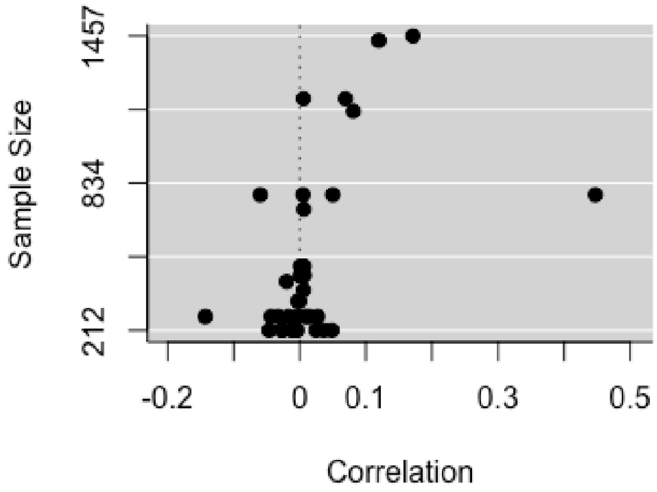
Supplementary Figure 2. Correlation between subjective and objective measures of bullying victimisation, according to study sample size.



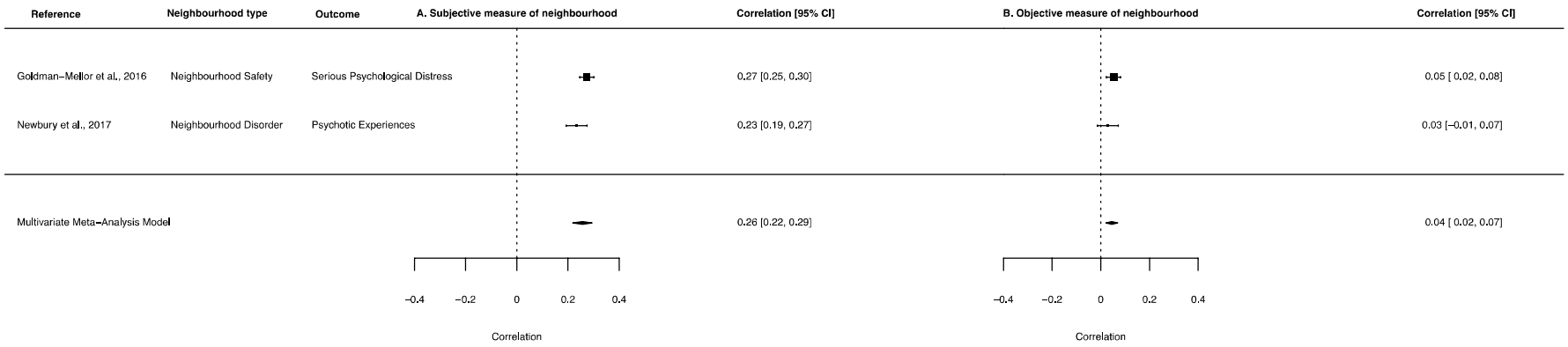
Supplementary Figure 3. Forest plot for studies examining the correlation between subjective and objective measures of neighbourhood adversity.



Supplementary Figure 4 Correlation between objective measures of bullying victimisation with psychopathology independent of subjective measures, by study sample size.



Supplementary Figure 5. Forest plot showing the meta-analytic associations between subjective measures of neighbourhood adversity and psychopathology, independent of objective measures (Panel A), and objective measures of neighbourhood adversity and psychopathology, independent of subjective measures (Panel B).



Appendix B – Supplementary material for Chapter 3. Identifying Genetic Predictors of Self-reported Bullying Victimisation: a Multi-Informant, Multi-Polygenic Score Approach.

Supplementary Methods 1. Quality Control Procedures.

Quality control was carried out on the GWAS Summary statistics and the ALSPAC genetic data to derive polygenic scores. This was carried out within the same syntax that computed the LDpred2-auto. Example code is available on GitHub: https://github.com/erfrancis/genetic_predictors_bullying_multi-informant

First, to carry out appropriate quality control on the GWAS summary statistics, when the information was provided by GWAS authors, SNPs with INFO scores below 0.6 and Minor Allele Frequency below 0.01 were excluded, along with ambiguous and duplicate SNPs.

Second, genetic data was obtained from ALSPAC children (Boyd et al., 2013; Fraser et al., 2013). Data were genotyped using the Illumina HumanHap550 quad chip genotyping platforms. The resulting raw genome-wide data were subjected to standard quality control methods. Individuals were excluded on the basis of gender mismatches, minimal or excessive heterozygosity, disproportionate levels of individual missingness (>5%) and insufficient sample replication (IBD<0.8). Population stratification was assessed by multidimensional scaling analysis and compared with Hapmap II (release 22) European descent (CEU), Han Chinese, Japanese and Yoruba reference populations; all individuals with non-European ancestry were removed. SNPs with a minor allele frequency of <0.01%, and evidence of violations of Hardy Weinberg equilibrium (p<1E-7) were removed leaving 4,886,821 SNPs.

Supplementary Methods 2: Inclusion criteria for additional analysis

The following details the inclusion criteria for the additional analysis to examine whether the effect of the polygenic scores on self-reported victimisation would differ when informants were included in separate models as opposed to adjusted for multi-informants.

To be included in the analysis featuring parent-report of bullying victimisation, participants were required to satisfy the following: have available genetic data (to compute polygenic scores), at least one time-point whereby the parent-reported bullying victimisation was obtained (study child age 9 and 10), and at least one time-point whereby the self-reported bullying victimisation was obtained (study child age 8 and 10) (n=7,441; see the supporting Supplementary Figure 1 in Appendix B).

To be included in the analysis featuring teacher-report of bullying victimisation, participants were required to satisfy the following: have available genetic data (to compute polygenic score), at least one time-point whereby the teacher-reported bullying victimisation was obtained (study child age 7 and 10 years), and at least one time-point whereby the self-reported bullying victimisation was obtained (study child age 8 and 10) (n=8,110; see the supporting Supplementary Figure 2).

Supplementary Table 1. Sample Overlap of Participants Included in the Main Data Analysis.

Genetic Data	Teacher-Report	Parent-Report	Self-Report	Included (n=8,319)
1	1	0	0	878
1	0	1	0	209
1	0	0	1	228
1	1	1	0	502
1	1	0	1	545
1	0	1	1	1624
1	1	1	1	4333

Note. 1=variable present, 0= variable not present. Inclusion criteria for the main model required that participants have genetic data and at least one or more of the phenotypes (teacher-report, parent-report, self-reported bullying victimisation) (n=8,319).

Supplementary Table 2. Sample Overlap of Participants Not Included in the Main Data Analysis.

Genetic Data	Teacher-Report	Parent-Report	Self-Report	Not included (n=7,450)
1	0	0	0	647
0	1	0	0	2035
0	0	1	0	264
0	0	0	1	112
0	1	1	1	963
0	1	1	0	514
0	1	0	1	229
0	0	1	1	399
0	0	0	0	2287

Note.1=variable present, 0= variable not present. Participants were not included in the main model if they did not satisfy conditions to be included (n=7,450).

Supplementary Table 3. Bullying and Friendship Interview Schedule.

Items relating to exposure to bullying	Dimension	Scoring	Age assessed*
Had personal belongings taken Been threatened/blackmailed Been hit/beaten up Been tricked in a nasty way Been called bad/nasty names	Overt	0 = None 1 = 1-3 times in the past 6 month 2 = 4+ times in the past 6 months but < once a week 3= At least once per week	8, 10
Others wouldn't play [hang out] with them to upset them Been made to do things didn't want to Had lies/told nasty things said Had games spoilt	Relational	0 = None 1 = 1-3 times in the past 6 month 2 = 4+ times in the past 6 months but < once a week 3= At least once per week	

*Included in the present study.

Supplementary Table 4. Pearson Correlation Matrix of Phenotypes and Polygenic Scores (PGS) in the Analytic Sample.

Measurement Variables	Self-Report	Parent-Report	Teacher-Report	PGS-MDD	PGS-SZ	PGS-ADHD	PGS-Anxiety	PGS-Neuro	PGS-Education	PGS-BMI
Self-Report	1.00									
Parent-Report	0.28***	1.00								
Teacher-Report	0.19***	0.29***	1.00							
PGS-MDD	0.06***	0.10***	0.06***	1.00						
PGS-SZ	-0.00^{ns}	0.01^{ns}	0.00^{ns}	0.15***	1.00					
PGS-ADHD	0.11***	0.10***	0.09***	0.25***	0.05***	1.00				
PGS-Anxiety	0.03*	0.04***	0.05***	0.42***	0.09***	0.12***	1.00			
PGS-Neuro	0.02*	0.03*	0.02^{ns}	0.22***	0.04**	0.05***	0.15***	1.00		
PGS-Education	-0.08***	-0.05***	-0.05***	-0.13***	0.03**	-0.31***	-0.07***	-0.06***	1.00	
PGS-BMI	0.06***	0.07***	0.06***	0.06***	-0.06***	0.17***	0.04***	-0.01^{ns}	-0.24***	1.00

Abbreviations: PGS, Polygenic Score; MDD, Major Depressive Disorder; SZ, Schizophrenia; ADHD, Attention Deficit/Hyperactivity Disorder; Neuro, Neuroticism; Education, Educational Attainment; BMI, Body Mass Index.
p value thresholds: <0.001***; <0.01**; <0.05*; ns=not significant (*p*>0.05)

Supplementary Table 5. Single-PGS Model and Multi-PGS Model findings for Parent Reported Bullying Victimisation.

Regression	Single-PGS Model					Multi-PGS Model				
	b	Lower CI	Upper CI	*p*	β	b	Lower CI	Upper CI	*p*	β
Parent-Report → Self-Report	NA					0.305	0.278	0.333	**<0.001**	0.279
Self-reported victimisation[a]										
PGS-Major Depressive Disorder	0.034	0.011	0.057	**0.003**	0.035	0.013	-0.013	0.039	0.339	0.013
PGS-Schizophrenia	-0.006	-0.028	0.017	0.630	-0.006	-0.008	-0.031	0.015	0.514	-0.008
PGS-Attention Deficit/Hyperactivity Disorder	0.085	0.062	0.107	**<0.001**	0.086	0.068	0.043	0.092	**<0.001**	0.068
PGS-Anxiety	0.014	-0.008	0.037	0.211	0.015	-0.003	-0.028	0.022	0.819	-0.003
PGS-Neuroticism	0.018	-0.005	0.041	0.124	0.018	0.011	-0.012	0.034	0.352	0.011
PGS-Educational Attainment	-0.063	-0.086	-0.041	**<0.001**	-0.064	-0.036	-0.060	-0.012	**0.004**	-0.036
PGS-Body Mass Index	0.041	0.018	0.064	**<0.001**	0.042	0.021	-0.003	0.044	0.082	0.021
Parent-reported victimisation										
PGS-Major Depressive Disorder	0.086	0.065	0.107	**<0.001**	0.096	0.066	0.042	0.091	**<0.001**	0.074
PGS-Schizophrenia	0.008	-0.013	0.030	0.446	0.009	-0.001	-0.022	0.021	0.954	-0.001
PGS-Attention Deficit/Hyperactivity Disorder	0.086	0.064	0.107	**<0.001**	0.095	0.059	0.036	0.083	**<0.001**	0.066
PGS-Anxiety	0.040	0.018	0.061	**<0.001**	0.044	0.002	-0.021	0.025	0.861	0.002
PGS-Neuroticism	0.022	0.001	0.044	**0.044**	0.025	0.004	-0.018	0.026	0.715	0.005
PGS-Educational Attainment	-0.044	-0.066	-0.022	**<0.001**	-0.049	-0.007	-0.030	0.016	0.558	-0.008
PGS-Body Mass Index	0.060	0.039	0.082	**<0.001**	0.067	0.045	0.023	0.067	**<0.001**	0.050

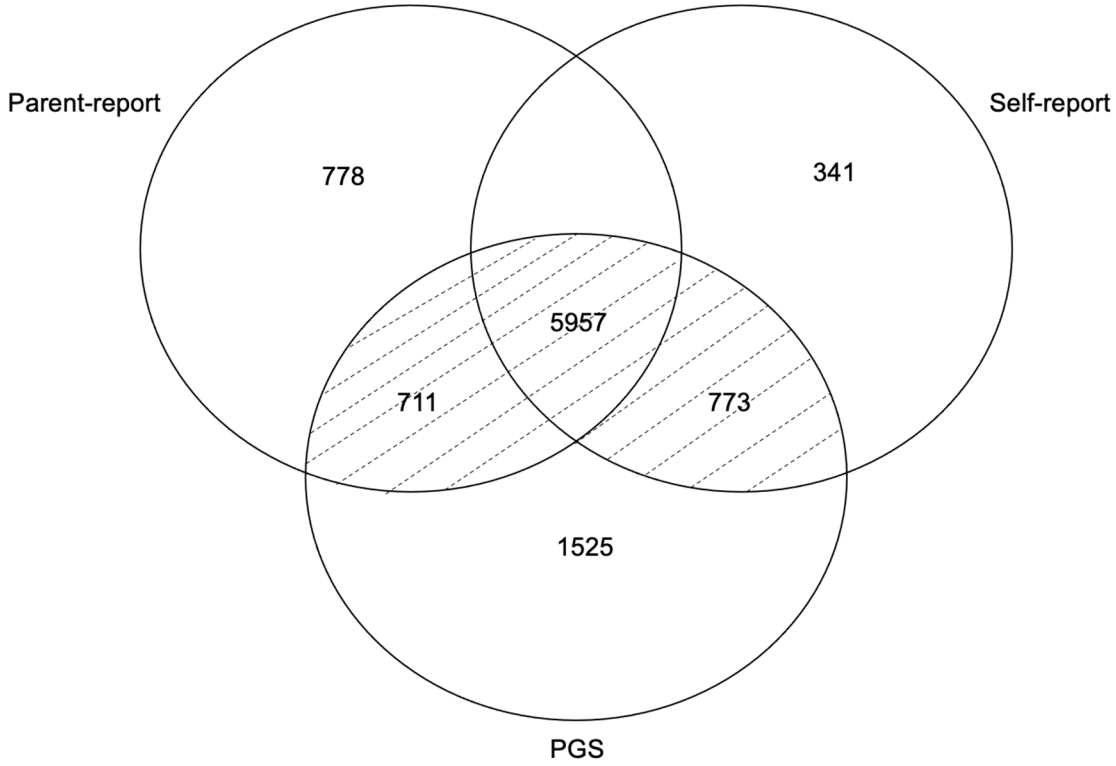
[a]Adjusted for parent-reported bullying victimisation. Abbreviations: b, unstandardised coefficient betas; β, standardised coefficient betas; PGS, Polygenic Score; CI, 95% Confidence Interval; MDD, Major Depressive Disorder; SZ, Schizophrenia; ADHD, Attention Deficit Hyperactivity Disorder; BMI, Body Mass Index. Single-PGS and Multi-PGS models adjusted for age, sex and 10 principal components (genetic ancestry). Multi-PGS adjusted for genetic correlations. Bold P-value represents significant (<0.05). N=7,441.

Supplementary Table 6. Single-PGS Model and Multi-PGS Model findings with Teacher Reported Bullying Victimisation.

Regression	Single-PGS Model					Multi-PGS Model				
	b	Lower CI	Upper CI	*p*	β	b	Lower CI	Upper CI	*p*	β
Teacher-Report → Self-Report	NA					0.238	0.199	0.276	**<0.001**	0.276
Self-reported victimisation[a]										
PGS-Major Depressive Disorder	0.051	0.028	0.075	**<0.001**	0.052	0.029	0.002	0.055	**0.033**	0.029
PGS-Schizophrenia	-0.003	-0.026	0.020	0.807	-0.003	-0.007	-0.030	0.017	0.564	-0.007
PGS-Attention Deficit/Hyperactivity Disorder	0.096	0.073	0.120	**<0.001**	0.098	0.074	0.049	0.099	**<0.001**	0.075
PGS-Anxiety	0.019	-0.004	0.042	0.102	0.020	-0.006	-0.031	0.020	0.658	-0.006
PGS-Neuroticism	0.021	-0.002	-0.045	0.074	0.021	0.011	-0.013	0.035	0.368	0.011
PGS-Educational Attainment	-0.069	-0.093	-0.046	**<0.001**	-0.070	-0.036	-0.061	-0.011	**0.005**	-0.036
PGS-Body Mass Index	0.051	0.027	0.074	**<0.001**	0.051	0.028	0.004	0.052	**0.020**	0.029
Teacher-reported victimisation										
PGS-Major Depressive Disorder	0.043	0.025	0.061	**<0.001**	0.058	0.019	-0.002	0.040	0.077	0.026
PGS-Schizophrenia	0.000	-0.019	0.018	0.971	0.000	-0.006	-0.024	0.013	0.551	-0.008
PGS-Attention Deficit/Hyperactivity Disorder	0.068	0.050	0.086	**<0.001**	0.092	0.054	0.034	0.073	**<0.001**	0.072
PGS-Anxiety	0.033	0.015	0.051	**<0.001**	0.044	0.016	-0.004	0.036	0.109	0.022
PGS-Neuroticism	0.012	-0.006	0.031	0.185	0.017	0.002	-0.016	0.021	0.807	0.003
PGS-Educational Attainment	-0.035	-0.054	-0.017	**<0.001**	-0.047	-0.007	-0.027	0.013	0.487	-0.009
PGS-Body Mass Index	0.045	0.027	0.063	**<0.001**	-0.116	0.032	0.013	0.051	**0.001**	0.043

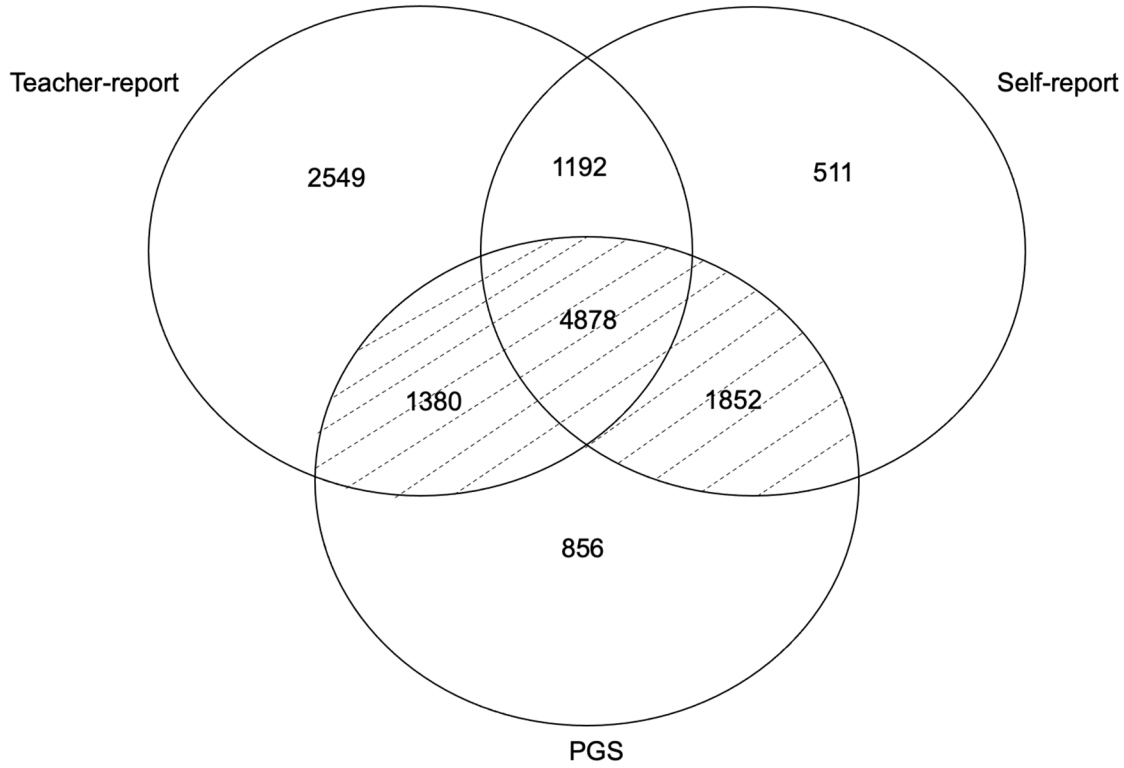
[a]Adjusted for teacher-reported bullying victimisation. Abbreviations: b, unstandardised coefficient betas; β, standardised coefficient betas; PGS, Polygenic Score; CI, 95% Confidence Interval; MDD, Major Depressive Disorder; SZ, Schizophrenia; ADHD, Attention Deficit Hyperactivity Disorder; BMI, Body Mass Index. Single-PGS and Multi-PGS models adjusted for age, sex and 10 principal components (genetic ancestry). Multi-PGS adjusted for genetic correlations. Bold *p* value represents significant ($p<0.05$). N=8,110.

Supplementary Figure 1. Overlap for the phenotypes self-report bullying victimisation, parent-reported bullying victimisation and polygenic scores.



Total meeting inclusion criteria indicated by shaded region (n=7,441).

Supplementary Figure 2. Overlap for the phenotypes self-report bullying victimisation and teacher-reported bullying victimisation and polygenic scores.



Total meeting inclusion criteria indicated by shaded region (n=8,110).

Appendix C – Supplementary material for Chapter 4 Polygenic Scores For Psychiatric Disorders Predict Subjective Body Dissatisfaction Beyond Objective Anthropometric Measures

Supplementary Methods 1. Quality Control Procedures

Quality control was carried out on the GWAS Summary statistics and the ALSPAC genetic data to derive polygenic scores. This was carried out within the same syntax that computed the LDpred2-auto. Example code is available on GitHub:

https://github.com/erfrancis/PGS_Psychiatric_Traits_Body_Dissatisfaction

GWAS Summary statistics

First, to carry out appropriate quality control on the GWAS summary statistics, when the information was provided by GWAS authors, SNPs with INFO scores below 0.6 and Minor Allele Frequency below 0.01 were excluded, along with ambiguous and duplicate SNPs.

Second, genetic data was obtained from ALSPAC children (Boyd et al., 2013; Fraser et al., 2013). Data were genotyped using the Illumina HumanHap550 quad chip genotyping platforms. The resulting raw genome-wide data were subjected to standard quality control methods. Individuals were excluded on the basis of gender mismatches, minimal or excessive heterozygosity, disproportionate levels of individual missingness (>5%) and insufficient sample replication (IBD<0.8). Population stratification was assessed by multidimensional scaling analysis and compared with Hapmap II (release 22) European descent (CEU), Han Chinese, Japanese and Yoruba reference populations; all individuals with non-European ancestry were removed. SNPs with a minor allele frequency of <0.01%, and evidence of violations of Hardy Weinberg equilibrium (p<1E-7) were removed leaving 4,886,821 SNPs.

Supplementary Table 1. Mean (SD) Body Mass Index and Waist Circumference for Subjective Measures by Group.

Subjective Measure	Group*	N	Mean (SD) BMI	Mean (SD) Waist Circumference (cm)
Weight Dissatisfaction	1	892	18.6 (2.02)	68.0 (5.71)
	2	2047	19.6 (2.74)	70.4 (7.5)
	3	387	20.7 (3.42)	73.0 (9.8)
	4	903	22.2 (3.62)	76.1 (9.9)
	5	234	24.1 (4.5)	80.1 (11.5)
	NA	1066	20.5 (3.62)	72.7 (9.72)
Waist Dissatisfaction	1	788	18.8 (2.24)	67.8 (5.77)
	2	2121	19.6 (2.74)	70.3 (7.34)
	3	633	20.8 (3.5)	73.2 (9.68)
	4	708	22.3 (3.88)	76.8 (10.5)
	5	202	23.9 (4.24)	80.2 (11.1)
	NA	1130	20.5 (3.58)	72.7 (9.59)

*Groups: 1="Extremely satisfied"; 2="Moderately satisfied"; 3="Can't decide"; 4="Moderately dissatisfied"; 5="Extremely dissatisfied"; NA= missing data, and "Not an issue" group. "Not an issue" does not lie naturally on the continuum from extremely satisfied to dissatisfied and was re-coded as missing. Mean (SD) BMI and waist circumference reported for those meeting criteria for the subjective measures (1) weight dissatisfaction analyses (n=5,585) and (2) waist dissatisfaction (n=5,582) analyses.

Supplementary Table 2. Correlation Matrix of Measurement Variables and Polygenic Scores (PGS) in the Adolescent ALSPAC Sample.

Variables	BMI	Waist	Weight Dissatisfaction	Waist Dissatisfaction	PGS-BMI	PGS-WHR	PGS-MDD	PGS-SZ	PGS-Anorexia	PGS-Anxiety	PGS-Neuro
BMI	1.00										
Waist Circumference	0.87***	1.00									
Weight Dissatisfaction	0.44***	0.38***	1.00								
Waist Dissatisfaction	0.29***	0.29***	0.63***	1.00							
PGS-BMI	0.39***	0.33***	0.16***	0.10***	1.00						
PGS-WHR	0.09***	0.10***	0.05***	0.04*	0.23***	1.00					
PGS-MDD	0.04*	0.03*	0.06***	0.02^{ns}	0.06***	0.06***	1.00				
PGS-SZ	-0.02^{ns}	-0.02^{ns}	0.01^{ns}	0.01^{ns}	-0.07***	-0.03*	0.14***	1.00			
PGS-Anorexia	-0.01^{ns}	-0.03*	0.01^{ns}	0.02^{ns}	-0.10***	-0.05***	0.14***	0.10***	1.00		
PGS-Anxiety	0.03^{ns}	0.03*	0.04*	0.02^{ns}	0.04**	0.02^{ns}	0.41***	0.09***	0.08***	1.00	
PGS-Neuroticism	-0.01^{ns}	-0.01^{ns}	0.06***	0.04*	-0.01^{ns}	0.05***	0.23***	0.03*	0.04***	0.15***	1.00

Abbreviations: BMI, Body Mass Index; Waist, Waist circumference (cm); WHR, Waist Hip Ratio; PGS, Polygenic Score; MDD, Major Depressive Disorder; SZ, Schizophrenia; Neuro, Neuroticism.
Note: The analytical sample for Supplementary Table 2 is the sample included in the weight dissatisfaction analyses (n=5,585) due to the larger sample size (waist dissatisfaction analyses: n=5,582).
p value thresholds: <0.001***; <0.01**; <0.05*; ns=not significant (p>0.05)

Supplementary Table 3. Sex Group Differences in the Analyses on Weight Dissatisfaction.

Polygenic score	Effect Estimate Boys (95% CI)	Std.all Estimate	Effect Estimate Girls (95% CI)	Std.all Estimate	Chi-squared	df	*p*
BMI → Weight dissatisfaction	0.205 (0.159 to 0.252)	0.232	0.303 (0.262 to 0.344)	0.332	9.463	1	**0.002**
PGS-BMI → Weight dissatisfaction	-0.004 (-0.050 to 0.041)	-0.004	0.024 (-0.018 to 0.065)	0.023	0.77572	1	0.3785
PGS-BMI → BMI	0.442 (0.400 to 0.483)	0.405	0.441 (0.400 to 0.482)	0.400	0.00040072	1	0.984
PGS-MDD → Weight dissatisfaction	0.032 (0.009 to 0.072)	0.033	0.037 (0.001 to 0.074)	0.037	0.041272	1	0.839
PGS-MDD →BMI	0.053 (0.007 to 0.098)	0.048	0.007 (-0.038 to 0.052)	0.007	1.8958	1	0.1686
PGS-SZ →Weight dissatisfaction	0.047 (0.006 to 0.087)	0.048	0.014 (-0.022 to 0.051)	0.014	1.3575	1	0.244
PGS-SZ → BMI	-0.027 (-0.073 to 0.019)	-0.025	-0.051 (-0.096 to -0.006)	-0.047	0.52473	1	0.4688
PGS-Anxiety → Weight dissatisfaction	0.020 (-0.020 to 0.061)	0.021	0.043 (0.006 to 0.079)	0.044	0.63942	1	0.4239
PGS- Anxiety → BMI	0.021 (-0.024 to 0.067)	0.020	0.031 (-0.013 to 0.076)	0.029	0.09006	1	0.7641
PGS-Anorexia →Weight dissatisfaction	0.019 (-0.021 to 0.060)	0.020	-0.001 (-0.037 to 0.035)	-0.001	0.52764	1	0.4676
PGS-Anorexia → BMI	0.002 (-0.044 to 0.048)	0.002	-0.022 (-0.045 to 0.018)	-0.021	0.55095	1	0.4579
PGS-Neuroticism → Weight dissatisfaction	0.031 (-0.009 to 0.071)	0.032	0.060 (0.022 to 0.097)	0.059	1.0857	1	0.2974
PGS-Neuroticism → BMI	-0.044 (-0.090 to 0.001)	-0.041	-0.019 (-0.065 to 0.026)	-0.017	0.57594	1	0.4479

Abbreviations: CI, Confidence Interval; Std.all; Standardised all; df, degrees of freedom; BMI, Body Mass Index; MDD, Major Depressive Disorder; SZ, Schizophrenia.
Note: Bold *p* value represents significant ($p<0.05$).

Supplementary Table 4. Sex Group Differences in the Analysis on Waist Dissatisfaction.

Polygenic score	Effect Estimate Boys (95% CI)	Std.all Estimate	Effect Estimate Girls (95% CI)	Std.all Estimate	Chi-squared	df	*p*
Waist circumference → Waist dissatisfaction	0.231 (0.179 to 0.282)	0.219	0.269 (0.232 to 0.306)	0.304	1.3999	1	0.2367
PGS-WHR → Waist dissatisfaction	0.000 (-0.043 to 0.044)	0.000	0.005 (-0.032 to 0.041)	0.005	0.02254	1	0.8807
PGS-WHR → Waist circumference	0.081 (0.040 to 0.121)	0.084	0.137 (0.092 to 0.182)	0.124	3.2691	1	0.0706
PGS-MDD → Waist dissatisfaction	0.011 (-0.031 to 0.053)	0.011	0.011 (-0.025 to 0.048)	0.011	7.5928e-07	1	0.9993
PGS-MDD → Waist circumference	0.039 (-0.001 to 0.079)	0.041	0.004 (-0.042 to 0.050)	-0.025	1.2988	1	0.2544
PGS-SZ → Waist dissatisfaction	0.032 (-0.009 to 0.074)	0.033	0.012 (-0.025 to 0.049)	0.012	0.51905	1	0.4712
PGS-SZ → Waist circumference	-0.001 (-0.042 to 0.039)	-0.002	-0.060 (-0.105 to -0.014)	-0.054	3.5132	1	0.06088
PGS-Anxiety → Waist dissatisfaction	0.018 (-0.024 to 0.061)	0.019	0.008 (-0.028 to 0.044)	0.008	0.13174	1	0.7166
PGS- Anxiety → Waist circumference	0.033 (-0.007 to 0.073)	0.035	0.039 (-0.007 to 0.084)	0.035	0.036764	1	0.8479
PGS-Anorexia →Waist dissatisfaction	0.046 (0.004 to 0.088)	0.046	0.017 (-0.019 to 0.053)	0.017	1.0501	1	0.3055
PGS-Anorexia → Waist circumference	-0.013 (-0.054 to 0.027)	-0.014	-0.059 (-0.104 to -0.014)	-0.054	2.2323	1	0.1352
PGS-Neuroticism → Waist dissatisfaction	0.028 (-0.013 to 0.070)	0.029	0.046 (0.008 to 0.083)	0.045	0.36672	1	0.5448
PGS- Neuroticism → Waist circumference	-0.035 (-0.074 to 0.005)	-0.037	-0.015 (-0.061 to 0.032)	-0.013	0.40427	1	0.5249

Abbreviations: CI, Confidence Interval; Std.all; Standardised all; df, degrees of freedom; WHR, Waist-to-hip ratio; MDD, Major Depressive Disorder; SZ, Schizophrenia.