Outcomes, Developmental Processes and Protective Factors in Different Conduct Problems Trajectories

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I, Leonardo Bevilacqua, 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 work.

Abstract

Conduct problems in youth are very common and have high financial and societal costs. Conduct problems can have different age of onset and developmental course and often predict later adjustment problems.

In this work, I investigated the psychosocial outcomes of different trajectories of conduct problems. Then, I examined the developmental processes underlying poor academic achievement, a common risk factor in youth with conduct problems. To do this, I tested a developmental cascade model in two early-onset subgroups of conduct problems individuals. I have also investigated whether school experience could mediate the association between conduct problems trajectories and not being in education, employment or training (NEET) at age 20. Finally, I explored a number of school-level factors that could predict the development of conduct problems in early to mid-adolescence. I used several statistical methods including meta-analysis, structural equation modelling, counterfactual-based mediation analysis and longitudinal latent growth curve modelling.

I have shown that an early-onset persistent pattern of conduct problems is associated with a greater risk of poor psychosocial outcomes compared to other trajectories (adolescent-onset and childhood-limited). The developmental cascade model I tested showed discrete differences across the two groups of early-onset conduct problems individuals, but I did not find an indirect effect carried through prenatal and postnatal risk factors that could explain poor academic achievement in adolescence. In terms of mediating factors, I found that positive school experience decreased the risk in early-onset persistent youth to become NEET in early adulthood. Finally, a positive school climate was associated with a lower risk of exhibiting persistent patterns of conduct problems in adolescence, in both males and females.

These results shed light on outcomes, processes and mediating factors that have the potential to change the development of conduct problems across life and may guide prevention and intervention programs, particularly within schools.

Impact statement

The works included in this thesis have partially answered a number of questions which had not been previously investigated. These answers have both theoretical and policy/clinical implications.

In my meta-analysis, I have shown that individuals with conduct problems are at higher risk of poor psychosocial outcomes compared to individuals with no history of conduct problems. Although this has been previously suggested by individual studies, I have shown that different trajectories of conduct problems differ in terms of risk of poor psychosocial outcomes in a hierarchical manner. Namely, the highest magnitude of risk exists in individuals with an early-onset and persistent pattern of conduct problems, followed by adolescent-onset and by childhood-limited youth. This is important because it suggests that, with varying degree of risk, all groups of youth with a history of conduct problems carry elevated risks of poor outcomes into adult life. This suggests that early intervention is needed across all groups of conduct problems individuals to minimise negative outcomes at later stages of life.

In the developmental cascade model, I have shown that males belonging to the early-onset persistent trajectory show the highest levels of risk and childhood-limited females show the lowest levels of risk across several domains (i.e. prenatal maternal psychopathology, maternal bonding, Attention Deficit Hyperactivity Disorder (ADHD) symptoms and academic achievement). I have shown that these common risk factors are longitudinally associated with one another across these two groups of conduct problems individuals. Of particular relevance, I found that ADHD symptoms in childhood-limited youth are more strongly predictive of future academic problems compared to early-onset persistent youth: this may impact the way future prevention and intervention programs are designed and delivered. For example, intervention programs that target ADHD symptoms in children with conduct problems may drastically reduce the risk of

poor academic achievement in adolescence, especially in those that are on a desisting trajectory.

To my knowledge, this is the first time that a subjective measure of quality of school experience (which includes school connectedness and school enjoyment) has been investigated as a potential mediator of the association between conduct problems trajectories and being Not in Education, Employment or Training (NEET) at age 20. I found that high school connectedness and school enjoyment decrease the risk of being NEET in the early-onset persistent group versus the low-conduct problems group by 21.1%. This finding is particularly important for schools, which generally focus on students' academic achievement over pupils' experience and feelings about the school (such as connectedness to the school and enjoyment of going to school).

In the last study, I showed that persistent patterns of conduct problems in early adolescence are associated with a number of school-level factors, specifically with poor school atmosphere/climate, which highlights again the importance of schools in protecting youth from engaging and persisting in antisocial behaviour. The last two studies are particularly relevant for guiding, designing and delivering prevention and intervention programmes for conduct problems and antisocial behaviour in school settings.

Funding and Ethics

The work presented here has been partially supported by the NIHR through a funded intervention study I worked on whilst undertaking my PhD. The Learning Together study was approved by UCL Institute of Education Research Ethics Committee (18/11/13 ref. FCL 566) and the University College London Research Ethics Committee (30/1/14, Project ID: 5248/001). All pupils signed a consent form before providing the data (please note that as pupils were under the age of 16, this in essence constitutes providing assent). Parents of all study participants were informed about the study in advance from the schools (via either email or hard copy) through a one-page parent information sheet. This was sent to schools by the research team well in advance and briefly described the study, the data collection procedure, and highlighted that the data would be kept confidential. Parents were not required to provide consent but could contact the research team if they did not want their pupils to take part in the study (passive consent). As agreed with the ethics committee given this was an opt-out consent, I did not assess whether parents had received the information.

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Published work

Chapter 4 of this thesis is based on the following peer-reviewed papers:

- Bevilacqua, L., Hale, D., Barker, E. D., & Viner, R. (2017). Conduct problems trajectories and psychosocial outcomes: a systematic review and meta-analysis. *European Child & Adolescent Psychiatry*, 1-22.

Chapter 7 of this thesis is based on the following peer-reviewed papers:

- Bevilacqua, L., Shackleton, N., Hale, D., Allen, E., Bond, L., Christie, D., & Miners, A. (2017). The role of family and school-level factors in bullying and cyberbullying: a cross-sectional study. *BMC Paediatrics*, 17(1), 160.

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Preface

There are several reasons why I have decided to research the area of developmental psychopathology and, more specifically, conduct problems: first, conduct problems is a complex and multi-determined behaviour, where genetic and environmental factors interact in a developmental fashion. In this sense, a researcher has the opportunity to focus on a large variety of aspects that characterise this behavioural manifestation, such as the impact of school, maltreatment, or the role of specific genes. Also, given the developmental nature of conduct problems, a researcher has the opportunity to look at the processes that contribute to the onset and persistence of this problem as well as its outcomes, at later stages of life. In other words, it allows an investigator to look at an exquisitely longitudinal phenomenon.

This leads to the second reason why I decided to study conduct problems which is that this area of research offers the possibility to learn many statistical techniques, which can be employed in other fields of research within psychology/psychiatry, developmental psychopathology and epidemiology (e.g. factors contributing to the onset and development of internalising behaviours or psychosis). As such, it represents a good starting point for those who want to gain statistical skills that are necessary to pursue a career in developmental psychopathology research or related fields.

Third, conduct problems and associated conditions (e.g. psychopathy and antisocial behaviour) have an extremely negative impact on society, both in terms of financial costs (e.g. damage to things, justice costs) but also in terms of damage to individuals and communities (e.g. stress and psychological damage). Trying to understand risk factors and processes that lead individuals to develop conduct problems will help to guide prevention and intervention programs that have the potential to decrease the number of people who develop conduct problems, and improve outcomes for those who have

already developed such problems. Hopefully, this will help to build a better society for future generations.

Last but not least, conduct problems are associated with antisocial behaviour and in some cases predict the occurrence of extremely violent acts. In general, human beings respond to these phenomena with fear and avoidance on one side, but also with organised actions whose aim is to repress, punish and ultimately marginalise/isolate those who commit these acts from society (e.g. prisons). Although there are some practical advantages in doing this, I support the idea that studying and understanding conduct problems and antisocial behaviour in their complexity (e.g. factors associated with it, development and consequences) will lead to better long-term outcomes for our society as a whole, including those who display such behaviours.

Chapter 1

In this chapter, I will define conduct problems and describe the associated medical conditions. I will provide epidemiological data, discuss the impact that conduct problems have on wider society, risk factors and treatment options. Towards the end of this chapter, I will describe conduct problems subtypes and trajectories. Finally, I will present the aims and research questions of this thesis in the light of current gaps in the literature.

1.1 Introduction to conduct problems: definition and measures

Conduct problems (CP) refer to a broad spectrum of behaviours seen in childhood and adolescence, which include disobeying rules, physical aggression, overt and covert bullying, stealing and property destruction. In childhood, it is more common to observe aggressive, defiant, hostile and disruptive behaviours. However, in adolescence, these behaviours may become more severe and include risk-taking, precocious sexual conduct, delinquency and more violent acts such as assault or rape[1].

These behavioural manifestations may be more or less severe and frequent and may have a range of negative consequences for the child or young person and those around him/her. These include psychological distress and concern to adult caregiver and authority figures, threats to the safety of peers, disruption of home and school environment and involvement with the criminal justice system. Many disciplines have been investigating CP, such as clinical psychology, psychiatry, education, psychometrics, sociology and behavioural genetics. This has resulted in many terms used to describe CP, which will also be used in this work to refer to CP. These are, amongst others: behavioural difficulties, under-socialised children/young people, challenging behaviours, externalising behaviours and antisocial behaviour.

There are several reasons why it is essential to recognise and intervene on CP in childhood and adolescence. First, these problems cause a great deal of stress to the young person and those involved with them including parents, teachers and classmates.

Recognition and management of CP will help to reduce the short-term stress associated with it. Another reason for recognising and managing CP is to reduce the long-term adverse outcomes associated with it. It has been suggested by several studies that CP is predictive of criminal offending, imprisonment, substance use, teen pregnancy, mental health problems, suicidal behaviour and poor physical health[2]. In addition, there is evidence for intergenerational transmission of CP. This means that those parents with a history of CP are more likely to have children who are challenging to manage and have difficult temperament (which are themselves risk factors for developing CP in childhood and adolescence). In this sense, CP is one of the childhood conditions associated with the most far-reaching and pervasive developmental and generational consequences[3].

Researchers have developed several tools to measure CP in children and young people. The Child Behavior Checklist (CBCL[4]) is a parent-administered questionnaire to screen for affective/emotional, behavioural and social problems. There is also a self-administered equivalent of this called Youth Self-report (YSR) and a teacher-administered version called Teacher-Report Form (TRF). Widely used in mental health services, schools, child and family services, as well as research settings this questionnaire has been translated into over 90 languages, and it has been cited in over 6,000 published scholarly articles[4]. Items in the CBCL are associated with problems in eight different areas: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour and aggressive behaviour. There is a CBCL version available for pre-school (one and a half to five years old) children (which contains 100 items on a three-point Likert scale) and a version for school age (six to 18 years old) children which has 118 items. The CBCL has two “broadband” scales where several of the eight syndrome scales are combined. For example, the “internalising” problems subscale sums up the anxious/depressed, withdrawn/depressed, and somatic complaints scores (e.g. “There is very little he/she enjoys”, “Feels worthless or inferior”, “Feels too guilty”, “Too fearful or anxious”). The

“externalizing” problems subscale combines rule-breaking and aggressive behaviour (e.g. “Cruel, bullying or meanness to others”, “Destroys things belonging to his/her family or others”, “Disobedient at home”, “Breaks rules at home, school or elsewhere”, “Lies or cheats”). The latter is usually employed to measure CP. Standard scores were created using a normative sample. These scores compare the raw score to what would be typical compared to responses for youths of the same gender and similar age (the school-aged version splits the age groups into 6–10 years and 11–18 years). The standard scores are standardised so that 50 is average for the youth's age and gender, with a standard deviation of 10. Higher scores indicate more problems. For each of the eight problem areas (internalising and externalising problem scales, and the total score), scores can be interpreted as “normal” (up to the 93rd percentile), borderline (93rd – 97th percentile), or clinical (above the 97th percentile) respectively. Norms take into account both age groups (6–11 and 12–18) and gender.

Another well-established tool in clinical and research settings is the Strengths and Difficulties Questionnaire (SDQ[5]). This is a short (25 items) scale for children and young people (4–17 years old). There are several versions for different informants such as parent and teacher. For each item respondents can choose to respond with “Not True” (0), “Somewhat True” (1) and “Certainly True” (2). There are five subscales in the SDQ and each of them has five items: emotional symptoms (“I worry a lot”, “I am often unhappy, downhearted or tearful”), conduct problems (“I get very angry and often lose my temper”, “I fight a lot – I can make people do what I want”), hyperactivity/inattention (“I am restless, I cannot stay still for long”, “I am easily distracted, I find it difficult to concentrate”), peer-relationships problems (“I get on better with adults than with people my own age”, “I am usually on my own. I generally play alone or keep to myself”) and prosocial behaviour which is a reversed scale, not included in the total score (“I am helpful if someone is hurt, upset or feeling ill”, “I often volunteer to help others such as parents, teachers or other children”). The subscales are combined to obtain an

“internalising problems” score (emotional symptoms plus peer-relationships problems) and an “externalizing problems” score (conduct problems plus hyperactivity/inattention). The sum of these two gives a “total problems” score. This score ranges from 0–40, with a score of 16 or above considered “abnormal”[6]. The SDQ is a versatile instrument that is widely used in a number of settings and with several populations including young people with mild learning difficulties, although some authors pointed out that it may not be appropriate for individuals with severe learning difficulties[7].

Another well-known set of instruments used to screen child behaviour is the Rutter Behaviour Scales. This set consists of Child Scale A (completed by parents) and Child Scale B (completed by teachers). Child Scale A has 31 items, 23 of which are also included in the Child Scale B. It consists of three sections. The first section states eight problems (e.g. complains of headaches, played truant), the second section asks five questions (e.g. whether the child had a speech/language problem, whether the child had an eating difficulty). The third section presents 18 descriptions of behaviour and the parent is asked to indicate whether each description “Does not apply” (0), “Applies somewhat” (1) or “Definitely applies” (2) to the child. Its range is 0–62 and a cut-off of 13 or above was chosen to identify individuals who may classify as potentially diagnosable of a psychiatric disorder. In the initial study of this measure, the authors found that this value selected over 70% of the boys and over 65% of the girls referred to the Maudsley Hospital in London[8]. Several studies where the structure of these scales was investigated suggested a three-factor structure: aggressiveness, hyperactivity and anxiety/fearfulness[9]. The 11 items that are usually employed to investigate whether CP are present belong to the “Extrovert behaviour” subscale and include, amongst others: “Bullies other children”, “Is often disobedient”, “Resentful or aggressive when corrected”, “Irritable, is quick to fly off the handle”, “Often damages or destroys own or others’ property” and “Sometimes takes things belonging to others”. These items are present also in Child Scale B.

1.1.1 Associated conditions

CP is a broad, non-diagnostic term that includes and overlaps with behaviours seen in diagnostic conditions such as Conduct Disorder (CD) and Oppositional-Defiant Disorder (ODD) in childhood and adolescence, and Antisocial Personality Disorder (APD) in adulthood. In this section, I will also describe callous-unemotional (CU) traits and psychopathy. Although these two terms refer to a similar construct, the former represents a specifier (or subgroup) of CD, while the second represents a specifier (or subgroup) of APD (which can only be given/received at age 18 or older).

CD is a mental disorder diagnosed in childhood or adolescence characterised by a pervasive, repetitive and persistent pattern of behaviours where the basic rights of others or major age-appropriate societal norms or rules are violated (such as aggression, property destruction and theft, physical harm to other people or animals). To meet DSM-V criteria for CD, at least three of the following behaviours need to be present in the past 12 months with at least one behaviour present in the past six months: often bullies, threatens, or intimidates others, often initiates physical fights, has used a weapon, has been physically cruel to people, has been physically cruel to animals, has stolen while confronting a victim, has forced someone into sexual activity, has deliberately engaged in fire setting, has deliberately destroyed others' property, has broken into someone else's house, building, or car, often lies to obtain goods or favours or to avoid obligations, has stolen items of nontrivial value, often stays out late without permission, starting before age 13, has run away from home overnight at least twice, is often truant from school, starting before age 13[10]. Children and young people with a CD diagnosis also tend to show lower levels of fear and empathy towards others.

ODD is often a precursor of CD, and it is mostly seen in children younger than age 10. ODD was introduced as a separate diagnostic category in the 1980s as part of DSM-III[11]. This happened with a certain degree of controversy and criticism because of its lack of distinctiveness from normal developmental behaviours[12]. However, with increasing

research efforts and revisions of the DSM criteria, the legitimacy of this condition was better established and the functional impairment observed in this youth is not more widely recognised[13]. ODD is a less severe condition than CD and violent, aggressive behaviours such cruelty to others and/or animals are not symptomatic of ODD. Children with ODD are defiant and disobedient, with a provocative quality to their behaviour. They tend to have frequent and/or extreme temper tantrums, and they have a confrontational, uncooperative and revengeful attitude towards others. To meet DSM-V criteria for ODD, at least four of the following behaviours need to be present in the past six months: often loses temper, often argues with adults, often actively defies or refuses to comply with adults' requests or rules, often deliberately annoys people, often blame others for his/her mistakes or behaviour, is often touchy or easily annoyed by others, is often angry and resentful, is often spiteful or vindictive.

While DSM-V includes CD and ODD as two different disorders, ICD-10 only includes a diagnosis of CD, which presents with symptoms that are similar to those seen in both DSM-V diagnoses of ODD and CD. ODD is instead treated as a subtype of CD in ICD-10. The symptom list is a combination of the eight ODD items plus the 15 CD items in DSM-V, but these are called "less severe" and "more severe" respectively. At least three or the "more severe" items are required for an ICD-10 diagnosis. A CD with ODD subtype diagnosis is made when there are four or more items from the full list of 23 but when no more than two come from the "more severe" items list.

Both DSM-V diagnosis of CD and ODD are predictive of a diagnosis of APD (which is not given before age 18), with previous CD diagnosis being a necessary condition for an APD diagnosis to be made. APD is a personality disorder characterised by pervasive and persistent disregard of moral and social norms, rights and feelings of others[10]. APD individuals typically exploit others in harmful ways for their own gain or pleasure and frequently manipulate and deceive other people. They usually display irresponsibility and arrogance and lack of remorse for their harmful actions and have a callous attitude to

those they have harmed. To diagnose APD according to DSM-V, an individual needs to be at least 18 years old and the following criteria must be met:

“A. Significant impairments in personality functioning manifest by:

1. Impairments in self-functioning (a or b):

a. Identity: Ego-centrism; self-esteem derived from personal gain, power, or pleasure.

b. Self-direction: Goal-setting based on personal gratification; absence of prosocial internal standards associated with failure to conform to lawful or culturally normative ethical behaviour.

And:

2. Impairments in interpersonal functioning (a or b):

a. Empathy: Lack of concern for feelings, needs, or suffering of others; lack of remorse after hurting or mistreating another.

b. Intimacy: Incapacity for mutually intimate relationships, as exploitation is a primary means of relating to others, including by deceit and coercion; use of dominance or intimidation to control others.

B. Pathological personality traits in the following domains:

1. Antagonism, characterised by:

a. Manipulativeness: Frequent use of subterfuge to influence or control others; use of seduction, charm, glibness, or ingratiation to achieve one’s ends.

b. Deceitfulness: Dishonesty and fraudulence; misrepresentation of self; embellishment or fabrication when relating events.

c. Callousness: Lack of concern for feelings or problems of others; lack of guilt or remorse about the negative or harmful effects of one’s actions on others; aggression; sadism.

d. Hostility: Persistent or frequent angry feelings; anger or irritability in response to minor slights and insults; mean, nasty, or vengeful behaviour.

2. Disinhibition, characterised by:

a. Irresponsibility: Disregard for – and failure to honor – financial and other obligations or commitments; lack of respect for – and lack of follow through on – agreements and promises.

b. Impulsivity: Acting on the spur of the moment in response to immediate stimuli; acting on a momentary basis without a plan or consideration of outcomes; difficulty establishing and following plans.

c. Risk taking: Engagement in dangerous, risky, and potentially self-damaging activities, unnecessarily and without regard for consequences; boredom proneness and thoughtless initiation of activities to counter boredom; lack of concern for one's limitations and denial of the reality of personal danger.

C. The impairments in personality functioning and the individual's personality trait expression are relatively stable across time and consistent across situations.

D. The impairments in personality functioning and the individual's personality trait expression are not better understood as normative for the individual's developmental stage or sociocultural environment.

E. The impairments in personality functioning and the individual's personality trait expression are not solely due to the direct physiological effects of a substance (e.g. a drug of abuse, medication) or a general medical condition (e.g. severe head trauma)."[10]

ICD-10 includes a diagnosis called "dissocial personality disorder" which includes "amoral, antisocial, asocial, psychopathic, and sociopathic personality"[14]. This condition can be diagnosed when at least three of the following are present: callous unconcern for the feelings of others; gross and persistent attitude of irresponsibility and disregard for social norms, rules, and obligations; incapacity to maintain enduring relationships, though having no difficulty in establishing them; very low tolerance to frustration and a low threshold for discharge of aggression, including violence; incapacity to experience guilt or to profit from experience, particularly punishment; marked readiness to blame others or to offer plausible rationalizations for the behaviour that has brought the person into conflict with society.

CU traits include characteristics such as lack of guilt and empathy, general affect impairment and callous use of others. Research has shown that CU traits are associated with lowered response to distress cues, impaired recognition of fearful vocal tones, impaired ability to recognise sad and fearful facial expressions, lower resting levels of

cortisol, lower arousal to distressful/unpleasant stimuli, more proneness to feel bored and lower trait anxiety levels[15]. In DSM-V, CU traits are considered a specifier of CD[10]. CP children high on CU traits show a more severe, aggressive, and stable pattern of problem behaviours. CU traits seem to show a strong genetic component. Viding et al. (2008) showed that CP in a sample of 9-year old were more heritable with the presence of CU than without CU[16]. Interestingly, authors in this study showed that a stronger difference in the magnitude of heritability estimates emerged when they controlled for hyperactivity (hence removing variance associated with hyperactivity from CP scores) in the low CU group only. In other words, this suggests that the strong heritability of CP in children high on CU traits is unlikely to be driven by hyperactivity genes.

There are also twin studies of CU traits that have been conducted in adolescence and adulthood that have found a moderate to substantial genetic influence. Blonigen et al. (2005) for example, found that approximately half of the variance in two CU traits (namely fearless dominance and impulsive antisociality) was due to genetic contributions, with heritability estimates remaining consistent from late adolescence to early adulthood (17 to 24 year)[17]. In another twin study, Larsson et al. (2006) found that two dimensions associated with CU traits and psychopathy (namely an affective disposition of callousness, lack of empathy/emotions, and behavioural impulsivity, need for stimulation, and lack of responsibility) were under strong genetic influence[18]. Some researchers[19] have suggested that specific genetic variants are involved in the development and expression of CU traits such as the oxytocin gene OXTR, the low-activity allele of the MAO-A gene and the short allele of the 5HTT gene[20], and more recently single nucleotide polymorphisms (SNPs) near the neurodevelopmental gene ROBO2[21].

There are several measures that researchers have employed to measure CU traits. One of these is the Psychopathy Checklist Youth Version (PCL-YV), suitable for adolescents[22]. This is the direct adaptation of the Psychopathy Checklist (PCL-R) which

is used to measure psychopathy in adults and will be discussed later in this section. This includes the same 20 items contained in the PCL-R apart from “parasitic way of life” and “brief marital relationships” given that these would not apply to adolescents. Items can be rated “0” (the item does not apply to the subject), “1” (the item sometimes applies to the subject) and “2” (the item fully applies to the subject). This is a two-factor scale: the first one relates to interpersonal/affective aspects and the second one related to deviant conduct. Critics highlighted however that the measure may not be particularly suitable for youth without a history of crime and also that administering the PCL-YV requires extensive training[23].

Child Problematic Traits Inventory (CPTI) is a more recently-developed scale[24]. This teacher-rated scale has 28 items rated on a four-point Likert scale and assesses psychopathic personality traits in children age 3-12 years. This tool was tested on a large population of 2056 children in Sweden. CPTI load distinctively on three different factors: a Grandiose-Deceitful Factor (items include “Lies often to avoid problems”, “Seems to see himself/herself as superior compared to others” and “To frequently lie seems to be completely normal for him/her”), a Callous-Unemotional factor (items include “Usually does not seem to share others’ joy and sorrow”, “Never seems to have bad conscience for things that he/she has done” and “Seldom remorseful when he/she has done something not allowed”) and an Impulsive-Need for Stimulation factor (items include “Likes change and that things happen all the time”, “Seems to have a great need for change and excitement” and “Seems to get bored quickly”).

Research has shown that CU traits are relatively stable across childhood and adolescence using self-report, parent-report and teacher-report and can be considered a strong precursor of adult psychopathy[25-27]. Psychopathy (which does not constitute a formal diagnosis per se in DSM-V) can be considered the adult equivalent of CU traits. Within the context of APD, psychopathy is associated with more violent and persistent patterns of criminal behaviour[28]. The core features of psychopathy according to the

triarchic model are disinhibition, which reflects a general tendency toward problems of impulse control and self-control; boldness, which is defined as the nexus of social dominance, emotional resiliency, sensation seeking and risk-taking; meanness, which is defined as aggressive resource seeking without regard for others ("disaffiliated agency")[29]. Earlier models, however, usually distinguished between a "primary" and a "secondary" psychopathy: Lykken (1995) described primary psychopaths as manipulative, planning, callous and unemotional, with low levels of anxiety and guilt while secondary psychopathy better describes individuals who are less bold and "cold-hearted" but display marked impulsivity[30]. Characteristics of primary psychopathy were thought to be highly heritable while secondary psychopathy was thought to be driven more by environmental factors, an idea that has not found strong support in recent studies, with genetic factors predicting both primary and secondary psychopathy (or related behaviours) to a similar extent[17, 18]. A two-factor framework is reflected in some of the modern tools commonly employed to measure and assess psychopathy.

The best known and commonly used scale to measure psychopathy is the Psychopathy Checklist (PCL-R)[31]. This is a 20-item clinician-administered questionnaire used in both clinical and research settings. Each item is rated on a three-point Likert scale according to the extent to which an individual shows the trait or behaviour being described. The range is 0-40, with a cut-off score of 30 or above indicating significant psychopathy in the US, and 25 in the UK[32]. Items investigate, amongst others, areas such as pathological lying, shallow affect, callousness/lack of empathy, impulsivity, irresponsibility, need for stimulation/proneness to boredom and superficial charm. The PCL-R has a two-factor structure: one reflecting interpersonal and affective features, considered the core personality traits of psychopathy, (resembling the concept of primary psychopathy) and factor two reflecting social deviance features (resembling the concept of secondary psychopathy).

The Psychopathic Personality Inventory (PPI) is also a known scale to measure psychopathy[33]. This is a 187-item (56 in the shortened version and 154 in its revised version) scored on a 4-point Likert scale, self-administered questionnaire including 8 sub-scales: Machiavellian egocentricity - the tendency to consider/give priority only personal to needs, disregarding the interests or perspective of others (e.g. "I always look out for my own interests before worrying about those of the other guy"); Social potency - the tendency to seem charming, with an ability to influence other people (e.g. " Even when others are upset with me, I can usually win them over with my charm"); Cold-heartedness - a callous orientation, absence of guilt or remorse (e.g. "When someone is hurt by something I say or do, I usually consider that to be their problem"); Carefree non-planfulness - limited willingness to formulate plans of the future (e.g. "I often make the same errors in judgment over and over again"); Fearlessness - the tendency to face risky situations without fear or anxiety (e.g. "I like my life to be unpredictable, even a little surprising"); Blame externalization - the tendency to ascribe problems, difficulties, or obstacles to other people (e.g. "A lot of people in my life have tried to stab me in the back"); Impulsive non-conformity - a neglect of social conventions, regulations, and rules (e.g. "I sometimes question authority figures "just for the hell of it"); Stress immunity - limited reaction to aversive or distressful events (e.g. "I can remain calm in situations that would make many other people panic"). The above subscales load on to two factors: fearless dominance (including social potency, fearlessness, and stress immunity – this is similar to the concept of primary psychopathy) and impulsive “asociality” or self-centred impulsivity (including Machiavellian egocentricity, impulsive nonconformity, blame externalization, and carefree non-planfulness – this is similar to the concept of secondary psychopathy). The PPI also included two special validity scales designed to identify participants who were likely to provide random, inconsistent, or insincere answers.

1.1.2 Epidemiology

CP includes several diagnoses such as ODD and CD in children and young people and APD in adulthood. There are also other concepts that relate and often overlap with CP and the diagnoses mentioned above such as CU and psychopathy. To better understand the epidemiology of CP more in general, I will draw from epidemiological data regarding these medical conditions.

CD is one of the most common mental health condition diagnosed in children and young people across the UK. The Office for National Statistics (ONS) surveys of 2017[34] reported that its prevalence was 4.6% among children and young people aged between 5 and 16 years with higher prevalence in boys (5.8%) than girls (3.4%). This survey showed that CD have a steep social class gradient, with a three to fourfold increase in more impoverished families compared to wealthier families. Interestingly, almost 40% of looked-after children, those who have been victims of abuse and/or those on child protection/safeguarding registers, between five and 17 years old, have CD. CD are observed in males more often than females, with 7% of boys and 3% of girls aged five to 10 years having a CD diagnosis. In young people aged 11 to 16 years, the proportion rises to 8% of boys and 5% of girls[34].

Maughan et al., 2004 reported that the percentage of girls with a CD was below 1% in childhood and ranged from 1.4–3.3% in adolescence, whereas for boys the rate ranged from 0.5–2.8% in childhood and from 3.2–5.4% in adolescence[35]. Other studies[36] report a threefold to fourfold difference in prevalence between children and adolescents. 46% of boys and 36% of girls with CD have at least one other mental health disorder. The comorbidity of CD with ADHD is well known and in some groups, more than 40% of young people with a diagnosis of CD also have a diagnosis of ADHD. The presence of CD in childhood is also associated with a significantly increased rate of mental health disorders in adult life, including APD (up to 50% of children and young people with CD may develop APD). The prevalence of CD varies between ethnic groups, (e.g. it seems

to be lower in Asians but higher in Black-African/Caribbean). Interestingly, previous research has shown that CP prevalence has steadily increased over the years 1974-1999 in the UK, in both boys and girls and regardless of CP levels (e.g. less severe vs more severe)[37].

In the US the prevalence of CD has been estimated to be between 12% amongst boys and 7.1% amongst girls (though other studies reported much lower numbers, i.e. 2.1% when considering boys and girls together age 8-15, and others around 6.1%). The majority of these have behavioural profiles that are consistent with “rule violation” group in the fourth version of the DSM while the smaller group is composed by those belonging to the “aggression to people and animals” profile. Having a CD diagnosis has been associated with being male and coming from an urban setting as well as a poor socioeconomic background. Other disorders were associated with a diagnosis of CD, mainly substance use disorders or impulse-control disorders[38-40].

ODD resembles CD in terms of being more prevalent amongst males compared to females (though this difference is modest) but tends to be diagnosed more often in younger children compared to older ones[35]. Like CD, it shows high levels of comorbidity with other mental health conditions (36% of girls and 46% of boys with DSM-IV ODD diagnosis meet criteria for at least one other non-antisocial DSM disorder), with ADHD being the most probable and, to a lesser extent internalising conditions (e.g. anxiety). Interestingly, individuals with ODD have a higher risk of meeting criteria for another mental health disorder in the DSM compared to CD individuals.

ODD is often diagnosed in the US with studies trying to estimate prevalence indicating that about 3-5% of the children and young people meet criteria for an ODD (with others reporting higher percentages i.e.11.2% for males and 9.2 for females)[40]. Comorbidity in ODD has been shown to be very high, with the vast majority (92.4%) of ODD individuals meeting criteria for at least one other lifetime DSM-IV disorder, including mood (45.8%),

anxiety (62.3%), impulse-control (68.2%), and substance use (47.2%) disorders. Similarly to CD, earlier onset predicts a slower speed of recovery[38].

Similarly to CD and ODD, APD prevalence varies depending on the country studied and methodology employed, but it is more often found in men. In the UK, a study conducted by Coid et al. (2006), found that antisocial personality disorder was not common, with a prevalence of 1% in men and 0.2% in women[41]. In prison settings, these percentages tend to be much higher, with a UK study reporting that an APD diagnosis was present in 63% of male remand prisoners, 49% of male sentenced prisoners and 31% of female prisoners[42]. Researchers who have attempted to provide worldwide estimates of APD reported that this condition can be found in prison settings to up to 47% in men and 21% in women[43]. Although the incidence of APD varies consistently across gender, some studies have suggested this condition may affect women more severely, with higher rates of comorbid conditions[44]. Interestingly, psychopathy was found to a much lower extent in UK prisoners: 4.5% using a PCL-R score of 30 or higher and 13% using a cut-off score of 25 or higher[45].

Two studies conducted in North America reported a higher prevalence of APD in the general population compared to the UK: Robins et al. (1991) reported APD prevalence of 4.5% in males and 0.8% in females while Swanson reported 6.8% in males and 0.8% in females[46].

Similarly to CD, APD seems to show significant comorbidity, especially with substance use disorder. One study reported that individuals with APD were three to five times more likely to drink alcohol and use illicit drugs when compared with individuals without APD[46]. Another study found that a quarter of APD individuals included in the sample had a depressive disorder[47]. Notably, in one study researchers found that 90.4% of the APD individuals sampled had at least one other psychiatric disorder[48]. Others found that over half of those with APD had co-occurring anxiety disorders during their lifetime[49]. This is somewhat inconsistent with the notion that anxiety may protect against the development

of aggressive behaviour, which is, on the contrary, associated with fearlessness and disregard of consequences related to one's own actions. This may be because anxiety negatively correlates with the primary or core aspects of psychopathy (emotional and affective), which are not so common in APD populations (similarly to CU traits in CP children and adolescent), but positively correlates with the secondary aspects (impulsive, antisocial lifestyle), which are more distinctive of APD populations[50].

CU traits do not seem to be particularly common in the general population, but prevalence increases when looking at children and young people with CP. In a UK study including over 5000 children, those without CD but high on CU traits made 2.9% of the sample[51]. About 2% were diagnosed with CD, and of these, 46.1% scored high on CU traits. In a smaller US study, authors found that in their community sample, 10%-32% of those with CD and 2%-7% of those without CD met the callous-unemotional threshold specified by the DSM-V. In their clinic-referred sample, 21%-50% of those with CD and 14%-32% without CD met the CU specifier threshold by the DSM-V. Authors conclude that between 10% and 50% of youth with CD would be designated with the proposed CU specifier in their specific sample[52]. In another US study where a girl sample was employed, authors found that 65.5% of individuals in the group meeting criteria for CD had high CU scores compared to 33.8% of those who did not meet criteria for CD (at least once across multiple data collection points). To note, most of the girls who scored high on CU did not meet the criteria for CD diagnosis (65.7%). This contrasts the notion that within high CU traits individuals there will be many who also show CP but not vice-versa, which is corroborated by several studies, including longitudinal investigations[53]. However, this study employed a girls' sample only, and it could be that there are fewer girls who show CP amongst those with high CU traits compared to their male counterpart. Differences across countries and studies may also reflect differences in measuring CU traits and in defining significant cut-offs.

Psychopathy has been studied primarily in prison populations, and in association with APD. Therefore, most data regarding its prevalence comes from forensic settings. Coid et al.[54] (2009) found that in 406 prisoners across England and Wales, 7.7% of males (5.2 – 10.9) and 1.9% (0.2 – 6.9) had a PCL-R score of 30 or over. Psychopathy also showed high comorbidity with Axis two disorders (which include all personality disorders) and with substance use disorder. Few studies have also been conducted in household population and found that across England, Wales and Scotland, only 0.6% of the 638 individuals (age 16-74) surveyed scored 13 or higher on the PCL- Screening Version. Psychopathy levels in a US study including incarcerated individuals showed to be higher than those reported in the UK, but this could be because of the latter covering the entire correctional jurisdiction, compared to the former were high and medium security custody institutions only were included[31].

1.1.3 Impact

CP in childhood and adolescence are linked to not only psychiatric diagnoses such as CD, ODD and APD, but they are also associated with poor physical health. For example, in a national UK survey, parents of children with a CD were more likely to report the health of their child as “fair” or “bad” compared to parents of children without a CD (17% vs 5%). In the same study, 35% of children and young people with a CD had another main type of clinically recognisable disorder (vs 4% in those without a CD[34]). Longitudinal association between CP and physical health problems have also been extensively documented in males but also females[55]. After controlling for potentially confounding factors such as prior health, Bardone et al.[56] found that adolescent girls with a CD diagnosis were at higher risk, compared to those without a mental health condition, of more medical problems, poorer self-reported overall health, alcohol and/or marijuana dependence, tobacco dependence, sexually transmitted disease, and early pregnancy, six years later.

There is also a consistent body of evidence showing that CP are associated with poor academic achievement[57]. Hinshaw[58] (1992) proposed four potential mechanisms, such as 1) underachievement leads to problem behaviour. Here, the causal relationship might include factors such as frustration, lowered self-esteem and self-confidence and lack of attachment to school, consequences of poor school achievement that may mediate subsequent CP[59]; 2) problem behaviour leads to underachievement. Here instead, CP in the classroom may be seen as the main mediator factor from pre-existing CP and underachievement; 3) both domains lead to the other and 4) underlying predictor variables result in both CP and academic underachievement. Such antecedent factors could be individual (e.g. temperament, neuropsychological deficit) and/or environmental (e.g. family conflict).

The strongest concomitant factor associated with CP is substance use. There have been several studies linking problem behaviours with an increased likelihood of substance use and longitudinal studies support the notion that childhood CP are highly predictive of adolescent and adult substance use or substance use-related problems. For example, using data from the National Longitudinal Study of Youth, Windle (1990) found that early delinquency (unrelated to drug use) predicted later substance use, even after controlling for the effects of early substance use[60]. Lynskey and Fergusson (1995) observed that children who showed CP at age eight consumed 1.5 to 1.9 times more alcohol and had rates of alcohol-related problems, daily cigarette smoking, and illicit drug use that were 1.9 to 2.0 times higher than children with low CP scores[61].

Appears clear that the impact of CP on society is considerable, spread across domains, and is long-term. Some researchers have highlighted the extremely high impact that CP have on society, both in terms of monetary and social costs: monetary costs include those associated with incarceration to prevent further offending and costs associated to vandalism[62]. Social costs include unsafe environments e.g. schools) and damage to victims whose rights have been violated by CP individuals. Due to the impact that CP

have on several domains such as mental and physical health, education, employment, substance use and later involvement with the justice system, the overall burden has been estimated to be extremely high[63]. For example, Miller (2004) estimated that social costs associated with externalizing problems in children might be between $335 and $350 billion each year[64].

1.1.4 Risk factors

Researchers have been trying to identify factors associated with CP and related behaviours (e.g. delinquency) over the past decades and with the use of complex statistical procedures. There is now general agreement on a number of risk factors associated with CP, some of them being individual (e.g. temperament), environmental (e.g. family and socioeconomic status) and some biological (e.g. genetics).

Several individual factors have been related to CP, including low self-esteem and depression, childhood temperament, and empathy[65-67]. Impulsiveness (which include poor ability to control one's behaviour, hyperactivity and restlessness, difficulty in delaying gratification and sensation-seeking behaviours) has been shown to be a strong predictor of antisocial behaviour (ASB)[68, 69]. Low intelligence quotient (IQ) is also an important predictor of behavioural problems and delinquency. For example, in a twin study based in the UK, low child IQ predicted CP independently of socioeconomic class and of parental IQ in adolescents aged 13[70].

Family factors associated with CP have been extensively investigated. According to previous studies, poor parental supervision and harsh and punitive parenting seem to be strong predictors of CP and delinquency, as well as child abuse[71]. In a UK-based prospective study, West & Farrington (1973) found that harsh cruel, passive, or neglecting parental attitudes, and poor supervision, measured at age 8 years, all predicted later convictions and self-reported delinquency. Parental conflict and violence,

but also parental ASB have all been found to predict adolescent ASB. Having a lone parent (particularly a never-married lone mother) also increases the risk of later CP[72-74].

One of the most predictive factors of CP is low socioeconomic status (SES), regardless of whether this is measured by income, housing status or by parental occupation or education[75, 76]. Given that SES is an extremely broad domain which entails several sub-dimensions (e.g. neighbourhood and school characteristics, family practices), it is not easy to understand what aspects of low SES may better explain (or moderate/mediate) association with problem behaviours. Some researchers suggested that low SES is associated with poor childrearing practices, truancy and association with deviant peers, all factors that may explain why individuals coming from low SES families are more likely to display CP[77].

Biological risk factors for CP have been identified by previous research, and have suggested that CP and ASB are partly influenced by genes[78]. Behavioural genetics studies (e.g. twin studies) and a large meta-analysis have suggested that approximately 50% of the total variance in ASB is explained by genetic influences[79]. Candidate genes studies (in both humans and animals) have shed some lights on what specific genetic variants may be associated with CP. Researchers seem to agree the low-activity alleles of monoamine oxidase A (MAO-A) gene interact with maladaptive child environment and increases the risk of aggression and externalizing behaviour[80].

1.1.5 Treatment

Several prevention and interventions programmes have been developed for children and young people with CP. In general, the aspects that are targeted are parenting skills, family functioning, child interpersonal skills and hyperactivity.

Programs that aim to develop parenting skills usually include five elements: promoting play (e.g. teaching parents the techniques to play in a constructive and appropriate way), rewards for sociable behaviour (e.g. instead of shouting at the child not to run, they

would praise him whenever he walks quietly), clarity of rules (e.g. instead of shouting at a child to stop being naughty telling him to play quietly gives a clear instruction which makes compliance easier), consistent consequences for inappropriate behaviour (e.g. firm and calm response to aggression with light punishments such as putting the child in a room for a few minutes) and re-organising the child's day to minimise trouble (e.g. temporarily putting siblings in different rooms to avoid fights)[81].

Improving family functioning is often achieved through functional family therapy and multi-systemic therapy. In functional family therapy, the therapist works with the family in their home to improve communication between parent and young person, reduce interparental inconsistency, tighten up on supervision and monitoring, and negotiate rules the sanctions to be applied for breaking them. In multi-systemic therapy, the young person's and family's needs are assessed in their own context and in related systems such as at school and with peers. Change is achieved through implementations and use of social learning theory and cognitive therapy techniques which aim at promoting strengths within the family. Like in functional family therapy the treatment is usually delivered within the home where the person lives.

Child interpersonal skills are usually targeted and improved through the use of Cognitive-Behavioural Therapy (CBT) techniques. Usually, CP individuals are trained to control their impulsive responses, develop social interaction skills such as listening to others before talking and sharing toys/games.

Hyperactivity, which is usually associated with CP (e.g. a large number of children and young people with a CD diagnosis also have an ADHD diagnosis) is usually treated with the use of stimulants (e.g. Ritalin), which have been shown to be effective in several randomised controlled trials (RCTs)[82, 83]. However, two considerations need to be made regarding the use of stimulants for CD: first, there is not much evidence that the use of stimulants helps CD-diagnosed children and young people without comorbid ADHD. Second, pharmacotherapy is often associated with important side-effects such as sleep

problems, decreased appetite, delayed growth (especially in boys), headaches and stomach-aches[84].

1.2 Subtypes of conduct problems

Previous research has identified three main subtypes of CP: the first subtype is based on presence vs absence of callous-unemotional traits (CU traits), the second is based on the presence of physical aggression vs rule-breaking behaviour, and the third is based on the age of onset (e.g. early-onset vs adolescent-onset).

CU traits refer to limited empathy, lack of guilt, shallow affect and callous use of others. It resembles and overlaps with the construct of psychopathy, but while the latter is used to describe adults, the former refers to children and adolescents[85]. In addition, CU traits refer to the affective/interpersonal dimension of the adult construct of psychopathy[15], which is a broader concept and includes behavioural and temperamental components (particularly secondary psychopathy). Existing studies suggest that children and adolescents with severe CP and elevated CU traits show distinct genetic, cognitive, emotional, environmental, and personality characteristics that seem to indicate different aetiology underlying their behaviour problems compared to CP individuals without CU traits[86]. Research has shown that CP with CU traits are associated with an earlier onset and higher levels of proactive aggression[87]. In addition, CU traits in childhood seem to be one of the factors that, amongst others (e.g. ADHD, levels of aggression), best predict antisocial outcomes in adult age[88, 89]. On the contrary, CP children with low CU traits display better outcomes, often seem to display levels of guilt and remorse similar to their typically developing counterparts but are more prone to show threat-reactive aggression rather than proactive and premeditated aggression as seen in children with CU traits[90]. The second subtype is based on whether CP presents with mainly physical aggression or rule-breaking behaviour (e.g. the former predominantly seen in CD and latter in ODD). Although these two behavioural manifestations are correlated, there have been studies that have supported this distinction, based on factor analysis of CD symptoms,

behavioural rating scales, and more ecological observations and observer ratings[91-94]. Other studies have also highlighted the etiological and cognitive differences between these two subtypes. For example, it has been noted that physical aggression is more heritable than rule-breaking behaviour, it emerges earlier and it is linked with higher levels of emotion dysregulation and lower levels of executive functions than rule-breaking behaviour. In addition, those who appear more physically aggressive in childhood are more likely to have a continuing pattern of CP over time than those belonging to the rule-breaking subtype, which appears to be less stable and more likely to desist from displaying problem behaviours over the course of life[91].

The third subtype of CP is based on the age of onset. Moffitt (1993) differentiated between Life-Course Persistent or Early-Onset Persistent (LCP or EOP), with the onset of CP in childhood, and Adolescent-Limited or Adolescent-Onset (AL or AO) individuals displaying CP and antisocial behaviour starting in adolescence[95]. The first group would show high risk on several domains (poverty, maltreatment, family disruption, victimization) and an escalating pattern of CP and antisocial behaviour across life, with worse outcomes in adult life in terms of criminal offences, employment, mental and physical health. This group was thought to have predisposing genetic and neurocognitive factors that would result in a more pervasive and persistent pattern of antisocial behaviour. The second group was considered to be relatively “normative”, with fewer risks and transient pattern of antisocial behaviours (of less aggressive nature compared to EOP) and with desistance in early adulthood or adulthood. This way of subtyping CP individuals is particularly relevant to understand the work I have done in this thesis.

In her original taxonomy, Moffitt (1993) proposed that the two groups of individuals with antisocial behaviour, namely LCP and AL, would present with several differences (aetiology, developmental course, prognosis and classification of their behaviour as pathological or normative).

In Moffitt's theory, EOP individuals would exhibit changing manifestations of antisocial behaviour across different life-stages and contexts: kicking and hitting at age 4, truancy and bullying at age 10, selling and using drugs at age 15, robbery at age 25 (see heterotypic continuity, Kagan 1969[96]). In this sub-group of individuals, patterns of problem behaviour would originate in childhood due to neuropsychological deficits and temperamental factors which interact with a high risk environment (e.g. poor maternal bonding, harsh parenting and poverty) to potentiate a pervasive and long-lasting pattern of antisocial behaviour. Several studies have supported these hypotheses: Moffitt, Lynam & Silva[97] (1994) observed that poor neuropsychological scores predicted early-onset and persisting pattern of delinquency via multiple sources (e.g. police, courts, and self-report) and Raine et al. (2005) found that EOP individuals were more likely to have suffered a head injury, which is usually associated with cognitive impairment. Temperamental factors such as high activity levels and poor adaptability have been reported to be strongly associated with EOP trajectory group as well as familial factors such as poor SES, high levels of maternal stress and psychopathology and harsh parenting[98-100] (Barker & Maughan, 2009). The combination (and interaction) of all these factors increases risk of developmental "snares" such as incarceration, early pregnancy, or serious problems with substances which may tie CP individuals to persistent patterns of delinquency across later stages of life[101]. In terms of outcomes, this specific sub-group of CP individuals have been found to be at high risk or poor physical and mental health, low educational attainment and unemployment[55, 102, 103].

AL or AO would constitute a qualitatively different group from LCP/EOP, and in fact would include the majority of youth and be considered relatively "normative". In Moffit's theory, AL's antisocial behaviour is time-limited and discontinuous. Their pattern of CP and delinquency is inconsistent across situations: they may shoplift in stores and/or smoke illicit substances but still obey rules at school. These individuals may begin displaying antisocial and delinquent behaviour as an attempt to close the maturity gap,

show themselves and others that they are “grown-ups” and have gained their independence. Social mimicry is an important aspect that can partially explain why some adolescents start displaying problem behaviours. AO individuals may in fact mimic the behaviours of their EOP counterparts to access desirable resources such as mature status with its power and privilege. Fewer proximal risk factors have been found to be associated with AO individuals and this group, in contrast with their EOP counterpart, has lower rates of psychopathy and violent crimes[104]. Adult outcomes for this group of adolescents seem to be slightly better overall compared to EOP individuals. However, the AO group seems to still engage in behaviours such as property offenses, seems to be having poor mental health and also drug problems in adulthood[105-107].

With the development and use of more complex statistical procedures over the past years (e.g. mixture models), a third group was identified, called Childhood-Limited (CL)[98]. This group has a childhood onset but contrarily to their EOP counterpart stops performing antisocial behaviour around the time of adolescence. This group is rare and represented something of a surprise to the theory, and contrasted the notion that early CP would initiate a cascade of difficulties and disadvantages that would perpetuate disordered behaviour[105]. Previous studies found that EOP and CL groups can be differentiated to the severity of which they are exposed to prenatal (e.g. maternal anxiety and depression) and early post-natal (harsh parenting) risk factors, whereby CL present with lower risk compared to EOP[98]. Earlier works suggested that CL individuals have off-putting personality characteristics that may exclude them from groups where most delinquents operate, thus limiting their possibilities to perform delinquent behaviour in adolescence. Some evidence for this was found, with CL individuals being social isolates, often diagnosed with social phobia and schizotypal personality disorder[105]. Whether environmental factors promote CP desistance (e.g. school connectedness and academic achievement) remains unclear, but academic underachievement and school dropout seem to be often associated with the occurrence of CP, especially in

adolescence. Outcomes in adulthood for this group are generally more favourable than those in the EOP group but worse than typical individuals with no history of CP, suggesting that true recovery rarely occurs[55]. The development of CP has always been investigated in males and females together, and several authors found that the developmental course of CP may not differ substantially between males and females. However, females are less likely to display CP and also less likely to be on an EOP trajectory compared to males[108]. Also, some have found differences in terms of family predictors of childhood-onset trajectories across males and females (i.e. parenting attitudes and behaviours predict boys to be on an early-onset trajectory and not girls)[109].

Although other trajectories have been conceptualised (e.g. Adult-Onset, Abstainers)[110], in this work I will be focusing on the three trajectories of CP and antisocial behaviour described in this section: the EOP, the AO and the CL.

1.3 Gaps in the literature and research objectives

In summary, previous studies conducted in several countries on a range of life outcomes of different CP trajectories have generally found that EOP youth have the highest risk of poor outcomes in early adulthood and adulthood. However, results seem to be less clear for the AO and CL groups. Hence, this thesis aims to systematically investigate the risk of poor outcomes in different CP trajectory groups, specifically EOP, AO and CL.

Research has shown that EOP and CL (which represent the two early-onset CP trajectories) can be difficult to distinguish in terms of their behavioural manifestation in childhood, but they may also differ in terms of prenatal and postnatal risks. Although previous work has revealed similar prenatal and postnatal risk domains for CL youth as EOP children, these risk factors were present at higher levels in EOP compared to CL. For example, mothers of EOP individuals have higher levels of anxiety during the prenatal period and lower levels of enjoyment of the child in the postnatal period

compared to CL[98]. These differences at sensitive developmental periods may partially differentiate the divergent developmental trajectories of EOP and CL and also account for different educational and social outcomes in adolescence and adulthood[111]. However, there have not been many investigations into how these factors may associate longitudinally. Therefore, another aim of this thesis is to study developmental processes underlying different trajectories of early-onset CP through testing a developmental cascade model of poor academic achievement, a common risk factor in youth with CP.

Academic achievement is considered an important aspect to target in intervention and prevention programmes for youth with CP. For example, poor academic achievement has been found to be strongly predictive of poor employment outcomes and delinquent behaviour in youth displaying CP[112] (Patterson et al, 1991). Furthermore, previous studies with non-CP youth suggest that other, more subjective factors such as school connectedness promote positive youth development and that poor school connectedness in year 8 at age 12 is associated with mental health difficulties and substance use in year 10 at age 14[113]. School enjoyment may also impact these outcomes; for example, the authors of a UK study found that school enjoyment at age 7 was associated with better school engagement at age 10 and 13, which was in turn predictive of greater academic progression from Key Stage 3 to Key Stage 4 (between age 11 and 14)[109]. However, it is not clear whether school connectedness and enjoyment can mediate the association between CP and more distal outcomes such as poor educational and social outcomes (e.g. being NEET) in young adulthood. Another aim of this thesis is to investigate the role of school connectedness and enjoyment as potential mediators of the association between CP class membership and risk of being NEET in young adulthood (age 20).

Other, more structural aspects of schools have been linked to CP and other behavioural problems in adolescence. According to the theory of human functioning and school organisation[114], pedagogic practice but also structural and organisational aspects of

school (e.g. quality of relationship between students and teachers, weaker relationship between academic learning and broader student development) may contribute to produce students more likely to engage in health risk behaviours and violence. Previous studies using cross-sectional samples that structural aspects of schools (e.g. leadership and management, school overall quality and school gender) are associated with problem behaviours such as bullying and cyberbullying[115]. Tobler et al. (2011) found that value-added education was associated with a lower incidence of violent behaviours, after adjustment for individual- and school-level covariates[116]. In a review published by Sellstrom and Bremberg (2006), a number of school-level factors were associated with students' behaviour and well-being. For example, authors found that schools with low average SES had higher rates of pupil victimisation and more pupils carried weapons[117]. However, it is unclear whether these and other school factors associate with the developmental course of CP, which is a better predictor of later outcomes compared to a single-time-point indicator. Using a longitudinal, UK sample of secondary school pupils age 12-14, I aim to systematically investigate the role school-level factors in predicting different trajectories of CP, while accounting for a number of individual and family-level factors.

To achieve these aims:

1) I will conduct a systematic review and meta-analysis to investigate which psychosocial outcomes CP trajectory groups face in young adulthood and adulthood.
2) I will use Avon Longitudinal Study of Parents and Children (ALSPAC) to investigate differences in terms of prenatal and postnatal risk factors between two early-onset groups of CP, namely EOP and CL, and also across gender. In the same study, I will test a developmental cascade model to investigate whether and how these risk factors relate to each other longitudinally and contribute to poor academic achievement in these two CP groups and across gender.

3) I will use the ALSPAC cohort to investigate whether school experience in adolescence (specifically school enjoyment and school connectedness) acts as a protective factor towards later poor education and employment status (Not in Education, Employment or Training or NEET) in different trajectory groups of CP individuals.
4) I will use data from the Learning Together study to investigate what school-level factors are associated with different developmental trajectories of CP across adolescence.

The present work will address gaps that have been identified in the literature review above and will shed light on factors that have the potential to influence the course of CP across life, and thus to improve later outcomes (e.g. health, mental health, education and employment). Ultimately, this work aims to help paving the way towards identifying areas for prevention and intervention.

1.3.1 Research questions

This thesis will examine the following research questions:

1) What are the differences in psychosocial outcomes of EOP, AO and CL groups in adulthood and young adulthood?
2) Are prenatal and postnatal risk factors different for the EOP and the CL trajectory groups and across gender? Do these risk factors associate longitudinally to increase the risk of poor academic achievement in adolescence? Are these longitudinal associations different across trajectory groups and gender?
3) What is the role that school experience plays in mediating the effect of CP trajectories on later poor education and employment outcome (NEET)?
4) What is the role of structural/organisational school-factors and school atmosphere in predicting different CP trajectories from early to mid-adolescence, while controlling for individual-level factors?

Chapter 2

In this chapter, I will provide information regarding the datasets that will be used to conduct the works in this thesis. In the section below I have summarised the main characteristics of the cohorts used in the studies that have been included in the systematic review and meta-analysis. A separate section is dedicated to ALSPAC, which appears in the systematic review and meta-analysis and was used by myself and colleagues to perform original analyses. A separate and more detailed section is dedicated to the Learning Together study.

2.1 Datasets included in the meta-analysis

My meta-analysis included several papers, which made use of the following longitudinal datasets:

The Minnesota Study of Risk and Adaptation from Birth to Adulthood: this is an ongoing longitudinal study on normal and abnormal development of firstborn children of low SES women in the US. Mothers were receiving prenatal care from the Minneapolis Public Health Clinic between 1975 and 1977. At age 28, 162 (60.6%) of the initial sample of children (267) was still participating[118].

The Mater-University of Queensland Study of Pregnancy (*MUSP*): this is a longitudinal study following up a cohort of 7223 infants and mothers from antenatal care to the child's 21st year which was started in 1981. The sample is representative of public obstetrical patients (who are different compared to private obstetrical patients in that they come from generally lower social class, have lower education levels, are more likely to be smokers and tend to have more health problems). Although attrition was relatively high at later follow-up stages (i.e. 72% responded at 14 year follow-up and 52% at 21 year follow-up), one advantage of this dataset is that a lot is known about those lost (e.g. lower birthweight, lower maternal educational levels, more likely to be smokers and have poorer mental health)[119].

T*he Dunedin Multidisciplinary Health and Development Study* (or Dunedin Study): this is an ongoing longitudinal study of the health and mental health, development and behaviours of a general sample of New Zealanders. The initial sample had 1037 participants, who were studied from birth (1972-73), and followed up at the age of three when the longitudinal study was established. Since then they have been assessed every two years until the age of 15, then at ages 18, 21, 26, 32 and 38 (2010-2012). Study participants are currently being assessed at age 45 (2017-2019). In this study, the sample retention has been very high, with 961 (95%) of participants taking part in the 2010-2012 follow-up[120].

The California Longitudinal Study: 220 study participants were first seen in 4th grade when their mean age was 10.2 years (SD=0.56). 15% of the sample was African American while the remaining 85% was European American. The retention rate ranged from 87% to 99% across the study's data collection points and 99% of the original sample was assessed at the end of high school (17-18 years old)[121].

Flemish Study on Parenting, Personality, and Development (*FSPPD*): this an ongoing longitudinal study that started in 1999. In this study, data were collected at seven different time points in 1999, 2000, 2001, 2004, 2007, 2009, and 2012. Study participants were 599 families (92.5% two-parent families) with an elementary school-aged child. Children were 304 boys and 295 girls, age range 5 - 11 years (M= 7 years 10 months, SD= 1.16). At latest data collection point data was available for 434 (72.4%) individuals (age range 17–20 years, 47% males)[122].

2.2 ALSPAC

ALSPAC is an ongoing prospective transgenerational study investigating development across the life course. A distinctive feature of ALSPAC is the breadth of repeated measures assessments conducted frequently over the duration of the study[123]. The dataset contains plenty of information including but not limited to health (e.g. whether

informants were diagnosed with a medical condition, treatments and medication regimes, self-reported general health) and mental health (e.g. externalizing and internalising behaviours, formal psychiatric diagnoses, parental mental health), health risk behaviours (e.g. risk-taking behaviour, drinking, smoking and substance use), physiological and biological indicators of health (e.g. Genome-wide data), diet, household and social context (e.g. crowding and pets, social class based on parental occupation, type of neighborhood), school and academic achievement, employment and criminal convictions. ALSPAC also benefits from having eligible participants' information available through the Office of National Statistics (around 99% coverage of the eligible sample), National Pupil Database (around 82% coverage of the eligible sample) and General Practice Research Database (around 4% coverage of the eligible sample).

The original sample included all women residents in the old county of Avon, whose expected delivery was estimated to be between the 1st of April 1991 and 31st of December 1992. All resulting children from these pregnancies were eligible to be part of the study. The eligible sample comprised 20248 pregnancies. 14541 (71.8%) were recruited antenatally and resulted in 14062 live-born children and of these, 13988 were still alive at 12 months of age. With additional participants enrolled at postnatal recruitment phase 2 and 3, ALSPAC dataset counted a total of 14775 children (enrolled sample).

Data collection points are numerous (68 in 2012) and have been grouped by the ALSPAC team retrospectively in six phases: "infancy" (>4 weeks and <2 years of age), "early childhood" (>2 years and <7 years), "childhood" (7 years of age), "late childhood" (>7 years and <13 years), "adolescence" (>13 years and <16 years) and "transition to adulthood" (>16 years and <18 years). More recently, ALSPAC has released age 20 and 23 data. Age 25 data has been collected and it is now being cleaned and prepared for publication by the research team.

A core sub-sample of over 3000 families have responded to all the 55 assessments open to the "full" sample and 5777 have responded to 75% or more of these assessments (541 individual assessments). Figure 1 shows attrition rates of the years in ALSPAC. Participants in ALSPAC showed higher educational attainment compared to the national average at age 16. This difference increases with increasing completeness of participation in the study over time. Conversely, those who were lost to follow-up had lower educational attainment compared to the national average. In addition, those lost to follow-up were more likely to be male, to be non-White and to receive free school meal[123].

Similar to all studies where a representative sample has been attempted, this study had a slight shortfall in the less affluent families (those living in rented accommodation, not having a car or being single or unmarried cohabiting). The study had a shortfall in ethnic minority mothers too. Figure 1 shows attrition rates of the years in ALSPAC. Participants in ALSPAC showed higher educational attainment compared to the national average at age 16. This difference increases at later follow-ups. Conversely, those who were lost to follow-up had lower educational attainment compared to the national average. In addition, those lost to follow-up were more likely to be male, to be non-White and to receive free school meal[123].

An advantage of ALSPAC is that variables created by authors are kept in the dataset and researchers can request them like any other variables contained in the dataset. For example, I have used latent classes of CP that were previously created by other researchers (see Barker and Maughan 2009) to perform original analyses[98]. Details of how these trajectories were created are reported later in this chapter.

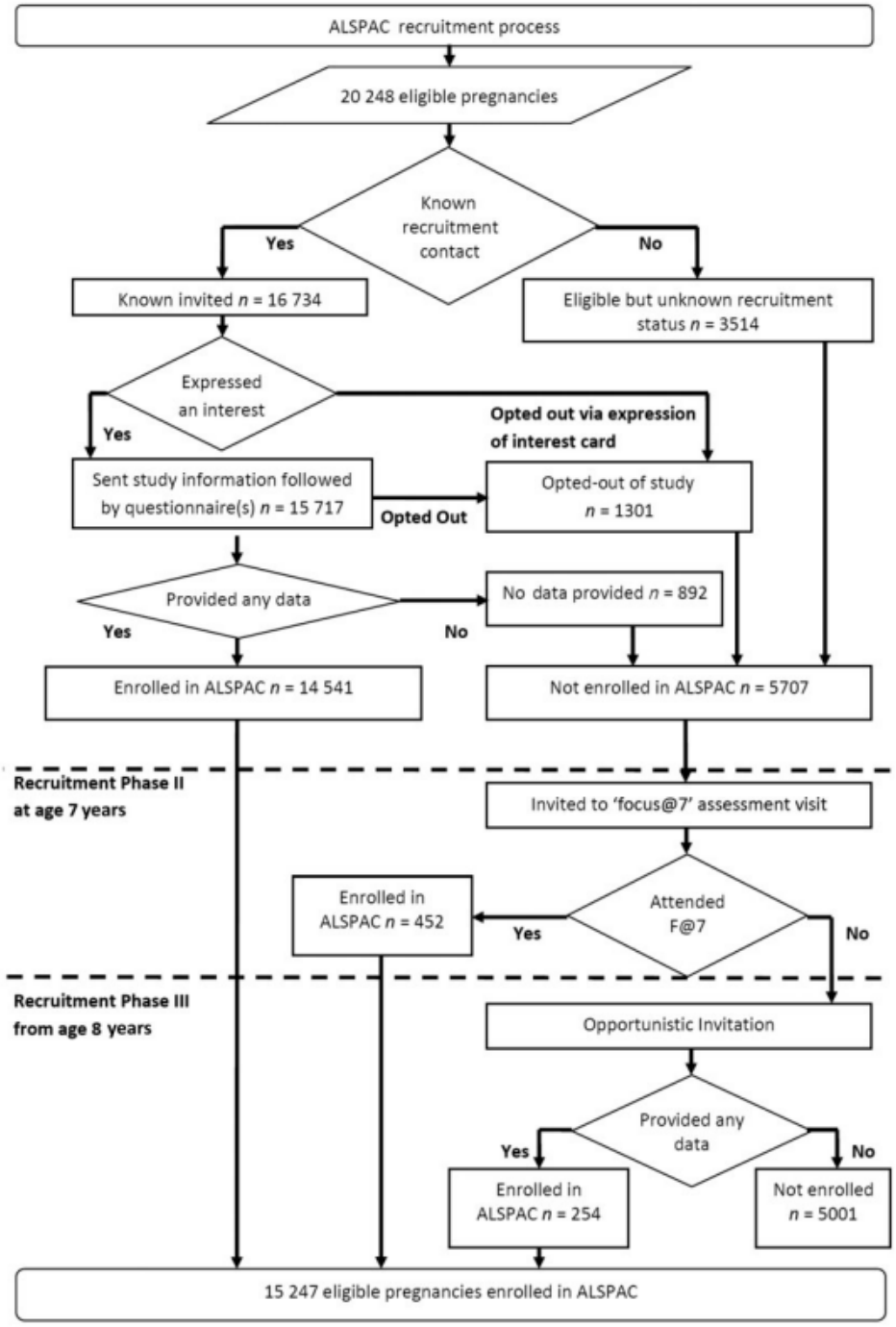


Figure 1 ALSPAC enrolment campaign flow diagram (taken from Boyd et al., 2013)

2.3 Learning Together study

The Learning Together trial is a three-year cluster randomised controlled trial with integral economic evaluation and process evaluation in 40 schools across south-east England, with schools as the unit of allocation[124]. The aim of this trial is to evaluate the cost-effectiveness of a whole-school intervention called INCLUSIVE to decrease bullying and antisocial behaviour (as primary outcomes) and a range of mental health, health and health risk-behaviours (secondary outcomes) in adolescents aged 11-16 in secondary schools.

Schools were recruited from secondary schools in Greater London and the surrounding counties (Surrey, Kent, Essex, Hertfordshire, Buckinghamshire, and Berkshire) with a maximum travel time estimated to be one hour from the study centres in London. Inclusion criteria include: secondary schools within the state education system (including community, academy or free schools, and mixed or single sex) in south-east England. Exclusion criteria include: private schools, schools with an Ofsted rating (most recent) of "Inadequate/poor". We aided recruitment by collaborating with existing school networks such as the UCL Partners Schools Network, the UCL Institute of Education Teaching Schools and schools that are part of Challenge Partners. 500 eligible schools were approached, initially by letter and Email with a telephone follow-up, complying with good practice and research governance for undertaking studies within the education system.

Schools whose head-teacher gave informed written consent to take part in the study were allocated to either intervention or control arms. Stratified randomisation was conducted by the Clinical Trials Unit (CTU) at the London School of Hygiene & Tropical Medicine (LSHTM). To promote baseline equivalence, we stratified by key school-level determinants of misbehaviour. These are: single-sex versus mixed-sex school; school-level deprivation, as measured by percentage of students eligible for free school meals (low/moderate 0 to 23%; high >23%, with 23% being the median for England); school

"best eight value-added" (VA) in GCSE exams (above and below median for England of 1000). This is a school-level measure of students' academic progress.

The intervention theory of change is based on the theory of human functioning and school organisation and postulated that intervention inputs would increase student commitment to learning/academic values and sense of belonging to the school community[114]. This is achieved by improving relationships between and among staff and between students' academic education and broader development. Increased school commitment would then discourage students from engaging in anti-school behaviours such as bullying, aggression and substance use as alternative ways to achieve a sense of identity and status.

The INCLUSIVE intervention is based on three promising approaches to reduce bullying and other antisocial behaviours. The first is the idea of intervening at the level of the whole school to modify the systemic operations of schools and consequently impact on a range of health outcomes and risk behaviours[125]. A key element of such interventions appears to be increasing student engagement with school (including a sense of belonging and commitment to academic values) particularly in students who are most disadvantaged, and present with a higher risk for poor health and educational outcomes[126]. The INCLUSIVE intervention does not radically change existing activities in intervention schools. However, it is intended to replace existing non-restorative disciplinary school practices with restorative approaches where the action group convenes this to be more appropriate. The second approach is restorative practices, a notion that developed in part from the concept of restorative justice. Restorative practices refer to a range of methods and strategies that seek to repair relationships that have been damaged, including those damaged through bullying, rather than assign blame and enact punishment. This is usually done by bringing about a sense of remorse and restorative action in the offender and forgiveness in the victim. In other words, restorative practices aim to enable those who have been harmed to convey the impact of

the harm to those responsible, and for those responsible to acknowledge this impact and take action to put it right[127]. The third approach is social and emotional education. Modules in the social and emotional skills curriculum cover: developing and establishing respectful relationships in the classroom and the wider school, managing emotions, understanding and building meaningful and trusting relationships, exploring others' needs and avoiding conflict and maintaining and repairing relationships. There is evidence that classroom curricula teaching young people the skills needed to manage emotions and relationships can enhance the quality of social relationships, improve mental health and significantly reduce bullying[128].

The INCLUSIVE trial involved two years of facilitated intervention and a final year without facilitation. In all three years, intervention schools were expected to convene an action group, consisting of a minimum of six students and six members of staff, including at least one senior leadership team member and one member of each of the teaching, pastoral and support staff six times per school year. Schools were encouraged to include a broad range of students in the action groups, including those involved previously with behavioural problems. Action groups were tasked with developing action plans to coordinate delivery of the intervention outputs including 1) reviewing and revising school rules and policies and staff-student interaction to incorporate restorative practices and principles; 2) implementing restorative practices throughout the school to prevent and address episodes of bullying and antisocial behaviour; 3) delivering a student socio-emotional skills curriculum for years eight to ten; and 4) additional tailored actions to address specific local priorities. These actions were informed by the findings about their students' subjective experiences of bullying, aggression, and the school environment from our baseline survey (before randomisation) and from a 12-month survey of students at the end of year 8 (age 12-13 years) in intervention schools only as well as from the 24-month trial survey. In the first two years, action groups received support from external facilitators with previous experience in whole-school change who attended all action

groups meetings. In year three, facilitation was led by the action groups themselves (more specifically by a senior leadership team member or another experienced member of staff).

To facilitate restorative practices, an introductory training was given to all staff in the 40 schools, alongside an enhanced three-day training course targeting five-ten members of staff in each school. Restorative practices included “circle-time” (which brings students and teachers together in the attempt to maintain positive relationships, and deal with specific but not major problems) and “conferencing” (used to deal with more serious incidents and can include, where necessary, parents and external agencies).

2.3.1 Outcomes

The primary outcomes were self-reported experience of bullying victimisation (including both physical and relational bullying) and perpetration of aggressive/antisocial behaviour measured at 36 months. Bullying victimisation was assessed by the Gatehouse Bullying Scale (GBS), a 12-item validated self-report measure of being the subject of teasing, name calling, rumours, being left out of things and physical threats or actual violence from other students, including face-to-face and cyberbullying, within the last three months[113]. Students report the frequency and upset related to each experience. Items are summed to make a total bullying score (a higher score represents more frequent upsetting bullying). Perpetration of aggressive/antisocial behaviour was measured using the Edinburgh Study of Youth Transitions and Crime (ESYTC) school misbehaviour scale, a 13-item validated tool that measures self-reported aggression towards students and teachers. Items include “Fight in or outside the classroom”, “Refuse to do homework or classwork”, “Be cheeky to a teacher”, “Hit or Kick a teacher” and “Threaten another student”. Each item was coded from “hardly ever” or “never”; “less than once a week”; “at least once a week”; to “most days”. Items are summed to provide a total score and higher scores indicate greater aggressive/antisocial behaviour.

Secondary outcomes include quality of life, measured using the Paediatric Quality of Life Inventory (PedsQL) version 4.0, a 30-item reliable and valid measure of the quality of life in normative adolescent populations[129].

Wellbeing, measured using the Short Warwick-Edinburgh Mental Well-Being Scale (SWEMWBS), a validated 7-item scale designed to capture positive emotional well-being[130].

Psychological difficulties were measured using the Strengths and Difficulties Questionnaire (SDQ): a validated and widely used instrument that detects behavioural, emotional and peer problems, and pro-social strengths in children and adolescents[6]; two subscales (internalising and externalising problems) are summed to provide a "total difficulties/problems" score where a higher number indicates greater problems.

Bullying perpetration was measured using the bullying subscale of the Modified aggression scale, a 5-item measure of bullying perpetration. Higher scores indicated greater bullying[131].

Substance use was measured using validated age-appropriate questions taken from national surveys (e.g. "smoking in previous week", "ever smoked regularly"), alcohol use ("use in previous week", "number of times got really drunk") and illicit drug use (last month, lifetime use).

Sexual risk behaviour was assessed by asking the age of sexual debut and use of contraception at Use of NHS health services was assessed by asking about use of primary care, accident & emergency, other services in past 12 months.

Contact with police was assessed by asking the question "Have you been stopped, told off or picked up by the police in the last 12 months?"

2.3.2 Sample characteristics

At baseline, data were available for 6667 (3103 males, 47%) Year 7 students (mean age = 11.8, SD = 0.4) in 40 schools in south-east England. Of these, 39.4% were White British, 25.0% were Asian or Asian British, 14.0% were Black or Black British, 8.5% were White (other), 7.0% reported having mixed ethnicity, 1.0% were Chinese or Chinese British, and 5.1% were from other ethnic groups. Participation rate was 93.6% (92.9% in the intervention arm and 94.3% in the control arm). At first follow-up (24 months), data were available for 6290 Year 9 students in all the 40 schools (5295 original, 995 new and 1372 lost to follow-up), with an overall participation rate of 89.35% (90.4% in the control arm and 88.3% in the intervention arm). At second follow-up (36 months), data were available for 5960 Year 10 students (4766 original, 624 new at 24 months, 570 new at 36 months and 1308 lost to follow-up) with an overall participation rate of 83.1% (85% in the control arm and 81.2% in the intervention arm). The 40 participating schools did not differ significantly from 450 non-recruited schools in terms of size, population, deprivation, or gross or value-added attainment, but participating schools were more likely to have an Ofsted rating of good or outstanding. Student and school characteristics and outcomes at baseline were well balanced across arms.

Further details are provided in Figure 2.

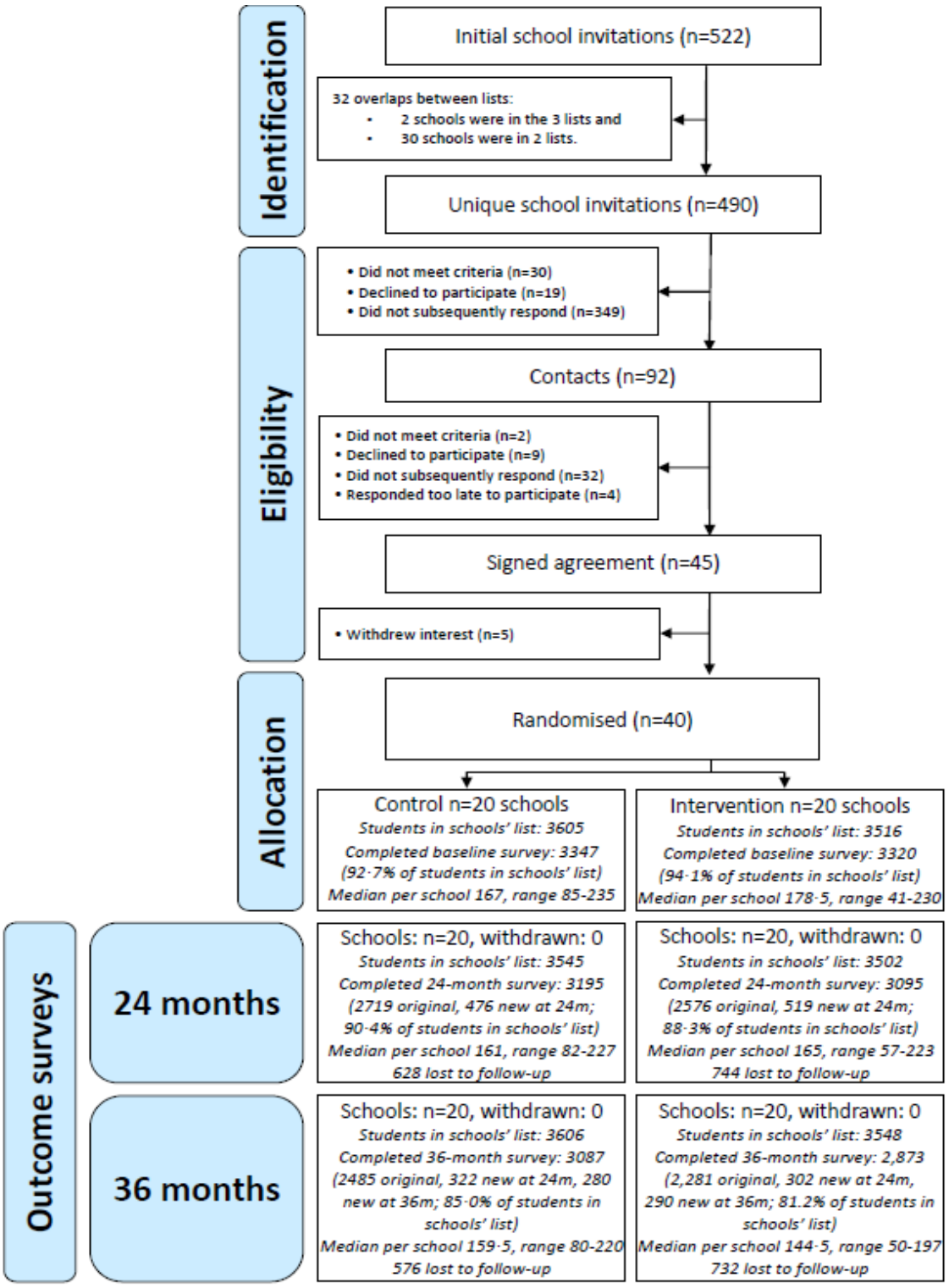


Figure 2 Consort diagram showing the Learning Together trial profile

2.3.4 Variables

The analyses were carried out using only pupils in the control arm, across the three time points, to avoid the confounding effect of the intervention. The resulting sample consisted of 4039 participants (2026 girl and 2013 boys). The self-reported measure of CP and antisocial behaviour was the ESYTC (described in "Outcomes" section above) and the school-level factors that I investigated as potential predictors of CP class membership were:

-School-level deprivation: proportions of students eligible for free school meal (FSM): this is a widely used proxy measure for economic deprivation in the UK[132]. In England and Wales, local education authority-maintained schools must provide a free meal to students if they or their parents receive specific benefits. We used the percentage of students eligible for FSM at any time during the past six years, obtained from publicly accessible data from Department of Education school performance tables[133]. The proportion of students eligible for FSM in our sample schools ranged from 3.0% to 79.2% (mean=36.4%, SD=19.6).

-The Income Deprivation Affecting Children Index (IDACI) score of the schools' postal address: the IDACI scores deprivation that measures the proportion of children in a small area under the age of 16 who live in low-income households. It is supplementary to the Indices of Multiple Deprivation and is used for calculation of the educational contextual value added score, measuring children's educational progress[134].

-School type: Our sample includes of five different types of schools: community (n=5), where premises and funding are provided by local authorities; foundation (n=6), where the school owns its own premises but funding comes from the local authority; voluntary-aided (n=4), where the premises are owned by a charity but funding is at least partly from the local authority; sponsor-led academy (n=6) which are usually created from an underperforming school which obtained an independent business or charitable sponsor and where funding comes directly from central government; and converter academy

mainstream (n=18), which are successful schools which have opted to gain more autonomy and have funding directly from central government. Voluntary-aided, community and foundation schools follow the National Curriculum and are supervised by the local authority. In our sample, all voluntary-aided schools were faith schools. Academies do not have to follow the National Curriculum except for core subjects. In addition, they have more freedom in setting their own term times and changing the length of school days[135].

-School size: the total number of students in the school[133].

-Sex composition: mixed sex or single sex.

-School quality most recent overall Ofsted rating: in England, schools are inspected by a statutory body, the Office for Standards in Education, Children's Services and Skills[133]. Ofsted inspections are carried out every 2–5 years, depending on inspection outcomes and all schools had data from 2011 to 14[136]. Schools were classified as 1= "Outstanding", 2= "Good", 3= "Requires improvement" or 4= "Inadequate" based on the quality of teaching, leadership and management, achievement of students, and behaviour and safety of students at the school. Our sample did not include schools with a rating of "Inadequate."

-Value added (VA) score: a second school quality rating was the VA score, an official measure of the progress students make between different stages of education. To calculate this, a median line approach is used whereby the VA score for each student is the difference (positive or negative) between their own output point score (end of Key Stage 4) and the median output point score achieved by others with the same or similar starting point (Key Stage 2 or 3), or input point score[133]. Scores for VA were given, with schools that neither added nor subtracted value being given a score of 1000.

Chapter 3

In this chapter, I will describe what statistical methods have been employed to carry out the analysis for each of the works presented here. Some of the information presented here will also be present in the individual chapters (chapters 4-7) but here I will report not only more details, but I will also provide a general theoretical framework for each of the analytical approaches I employed.

3.1 Systematic review and meta-analysis

To investigate research question number 1 (What are the differences in psychosocial outcomes of EOP, AO and CL groups in adulthood and young adulthood?) I have conducted a systematic review and meta-analysis.

A systematic review is a type of literature review that allows a researcher to identify all relevant studies in a specific field through a systematic and rigorous process. This process includes defining a research question and performing a search to retrieve all relevant data, extracting the data, assess the quality of the data, critically appraise and synthesise the data. Data are usually synthesised in a narrative way but sometimes, if data allow this (e.g. the evidence is consistent across studies), a formal statistical procedure is employed, called meta-analysis.

A meta-analysis is a quantitative method used to synthesise information (e.g. effect sizes such as ORs) from related studies; it helps to summarise data in a specific area of research by producing a summary effect. A meta-analysis is often used to add information or clarify the effectiveness of a specific treatment (e.g. a drug or a particular psychological treatment to help people with a certain difficulty) vs another (e.g. placebo) but more broadly, a meta-analysis provides a summary measure of the association of an exposure with a specific outcome, even when the contributing studies are observational, as long as they are deemed to be controlled for all relevant confounders.

3.2 Search strategy

The search strategy was implemented across two search engines and the details are reported below.

PsycINFO:

1. exp Conduct Disorder/

2. conduct disorder.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]*

3. conduct problem.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]*

4. 2 or 3

5. 1 or 4

6. drug abuse/

7. (antisocial behavio?r or substance related disorder$ or substance use$ or substance abuse or outcome$ or antisocial personality disorder).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]

8. exp Antisocial Personality Disorder/

9. 6 or 7 or 8

10. exp Longitudinal Studies/

11. (trajector$ or developmental or childhood or pathway$ or longitudinal or prospective or continuity or follow up or consequence$ or developmental or pathway or longitudinal or early onset or late onset or adolescent onset or childhood onset or age of onset or adult or continuity or follow up or consequence or adulthood or prospective).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]

12. 10 or 11

13. 9 or 12

14. 5 and 13

MEDLINE:

("Substance-Related Disorders"[Mesh]) OR "Antisocial Personality Disorder"[Mesh] OR antisocial behavior OR antisocial behaviour OR substance related disorder OR substance use OR substance abuse OR outcome* OR antisocial personality disorder)) OR (("Longitudinal Studies"[Mesh]) OR "Prospective Studies"[Mesh] OR trajector* OR developmental OR pathway* OR longitudinal OR prospective OR continuity OR follow up OR consequence*))) AND ("Conduct Disorder"[Mesh] OR conduct disorder* OR conduct problem*).*

The search yielded a total of 10415 studies. All abstracts were screened using EPPI reviewer software[137]. EPPI reviewer is a web-based application for managing and analysing data for use in research synthesis. After performing the searches in PsycINFO and MEDLINE described above, I have imported search results into EPPI reviewer. I set a similarity threshold to exclude duplicates and then screened all abstract. Each abstract was either included or excluded. When excluded, a specific reason was provided (see PRISMA Flow Diagram). When included, it was screened at full-text level. Here it could be then excluded (providing again a specific reason for exclusion) or included for review and meta-analysis.

3.2.1 Quality and risk of bias in included studies

A modified version of the Newcastle-Ottawa scale was used to perform quality assessments for the included studies[138]. This assessed the representativeness of the CP population and non-exposed population and the comparability of these samples, the reliability and validity of measurement variables and attrition. Total scores range from

zero to six. For more details, a template is can be found below and quality data for included studies is shown in the next chapter.

Newcastle-Ottawa Scale (amended version)

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Selection

1) Representativeness of the exposed cohort

a) truly or somewhat representative of the average conduct problems trajectory in the community ★

b) selected group, unrepresentative of the total group (e.g. prison sample)

c) no description of the derivation of the cohort

2) Selection of the non exposed (Low trajectory)

a) drawn from the same community as the exposed cohort ★

b) drawn from a different source

c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

a) Use of validated tools at different time points ★

c) self/maternal/other report (non standardised) or retrospective recollection

d) no description

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for any of gender, SES, ethnicity and other factors usually associated with mental health ★

b) study controls for any other factors ★

c) no mention of control variables

Attrition

1) Adequacy of follow up of cohorts

a) less than 20% attrition, or description provided of those lost ★

b) follow-up rate less than 80% and no description of those lost

c) no statement

3.2.2 Mixed effects meta-analysis

There are usually two types of meta-analysis employed to produce a summary effect when a summary measure is thought to be appropriate: fixed-effect and random-effects meta-analysis. The main difference is that in a fixed-effect meta-analysis the basic assumption is that exposure (or treatment in cases of RCTs) effect is the same across all studies considered. In the random-effects meta-analysis treatment effects are allowed to vary across studies. In other words, in a fixed-effect model, we assume that all studies share a common true effect and that the relative effect of a specific exposure compared to the reference group is the same in all study settings. Differences in effects sizes across multiple studies are assumed to be due to sampling error only (or sampling error). Hence, if all studies had an infinitely large sample size then the effect size would be equal to the “true” exposure effect and equal to the mean of all studies’ effect sizes considered. The systematic reviewer who employs this approach will have to clearly state that it is assumed that all studies considered are functionally identical. In a random-effects approach to meta-analysis, the exposure effect is not assumed to be invariant

across studies, with the different effects sizes accounting for different study features (e.g. setting and participants' characteristics). In other words, we are allowing for extra variability across studies. This is due not only to sampling error, as in fixed-effects meta-analysis, but also due to study characteristics (which may not be functionally identical, as in more realistic scenarios). Following the example given above, if we had infinite large sample sizes in a random-effect meta-analysis, the effect sizes of different studies would still vary because of real differences in study settings and participant characteristics. A measure of this variation is also of interest and reported together with the overall mean.

Until the mid-2010s, the fixed-effect approach was employed more commonly in psychology and some estimated that more than three-quarters of meta-analyses in this field were conducted using this approach[139]. More recently, however, the advantages of using a random-effects approach were recognised: one can rarely assume that in a realistic scenario the studies in the meta-analysis are estimating the same common effect. Also, compared with the fixed-effect model, the weights assigned under random-effects are more balanced. This is due to the fact that under the random-effects model researchers try to estimate the mean of a distribution of true effects: large studies may yield more precise estimates than small studies, but each study is estimating a different effect size, and each of these effect sizes serve as a sample from the population whose mean we want to estimate. To summarise, random-effects models represent a more conservative test and are preferable over fixed-effects models where there is significant or unexplained heterogeneity[140]. Also, a random-effects approach allows for the calculation of measures of heterogeneity across studies (I-square) for each meta-analysis, with the recommendation that summary values should not be computed if the heterogeneity exceeds a pre-specified value.

I used random-effects meta-analyses to compute pooled effect sizes and confidence intervals when comparing the odds ratios of various outcomes across CP trajectories. To test for significant differences in effect sizes across trajectories, I observed whether the

confidence intervals for effect sizes overlapped; non-overlap was interpreted as a significant difference between effect sizes. This is a conservative estimate of significant differences [ref] which is appropriate given the multiple comparisons being made.

I used Odds Ratios (ORs) as my main summary statistics to perform the meta-analyses. If ORs were not available in the paper, they were calculated from available information (i.e. mean and standard deviation or mean and standard error) using the Campbell Collaboration Effect Size calculator[141]. I analysed data using the METAN command for STATA 13[142] and the syntax can be found below:

```
gen logOR = ln(OR)

gen logOR_LowCI = ln(OR_LowCI)

gen logOR_HighCI = ln(OR_HighCI)

metan logOR logOR_LowCI logOR_HighCI, random eform lcols(Sample)
xlabel(.2, .5, 1, 2, 5) boxsca(0) favours(Reduced risk  #
Increased risk) astext(60) textsize(152) effect(Odds Ratio)
```

3.2.3 Developmental Cascade Model

To investigate research question number 2 (Are prenatal and postnatal risk factors different for the EOP and the CL trajectory groups and across gender? Do these risk factors associate longitudinally to increase the risk of poor academic achievement in adolescence? Are these longitudinal associations different across trajectory groups and gender?) I have tested a developmental cascade model using ALSPAC data collected at multiple time points.

A developmental cascade is a theoretical model which aims to identify the relationship between multiple risk factors (or domains) that may contribute to the development of

mental or behavioural difficulties over time. In other words, developmental cascades refer to the longitudinal causal effect that certain events or characteristics (individual or environmental) may have on later life and at the level of several domains. For example, Van Lier and Koot[143] (2010) tested a developmental cascade model that began with externalising behaviours in primary school, moved through multiple dimensions of peer problems in first through third grades, and resulted in multiple problems in fourth grade. Another example is the work of Dodge et al. (2008) who tested a cascade model of the development of serious violence in adolescence[144]. Authors looked at the cumulative impact that adverse social context at the time of birth has on early harsh parenting, which in turn will negatively affect school readiness, which will lead to CP, which in turn will lead to school failure, which will increase risk of low parental monitoring, which will increase risk of affiliation with deviant peers and which will ultimately result in violent behaviour in adolescence. They also investigated whether each of these risk factors independently increased the risk of adolescence violence and whether each predictor mediated the association between the previous and the following one.

3.2.4 Structural equation modelling (SEM)

Developmental cascade models are usually tested within a structural equation modelling (SEM) framework. SEM is a powerful multivariate analytical approach which allows to understand complex and dynamic relationships among a set of observed and/or unobserved variables. Differently from basic regression where there is a clear distinction between dependent and independent variables, in SEM a variable can have a reciprocal role and be considered independent in one portion of the equation, but dependent in another one[145]. SEM includes confirmatory factor analysis, path analysis, partial least squares, path modelling, and latent growth curve modelling, as exceptional cases, with the general SEM framework consisting of two components: the structural and the measurement model. This gives SEM several advantages such as allowing researchers to use “latent” variables or constructs that re then related to each other. A latent variable

is an unmeasured variable that is not directly observed but is inferred (through a statistical model) from other variables that are observed (directly measured). The measurement component consists of a confirmatory factor analysis (CFA). CFA is a particular form of factor analysis and it is employed to specify (and test) how measures of a predefined construct are consistent with a researcher's understanding of the nature of that construct or factor. This is accomplished by estimating and evaluating the factor loading of each item (e.g. observed variable) used to map on to the unobserved latent variable.

The structural part of SEM specifies the relationship between these latent variables with each other and possibly with other observed variables[146]. Before describing this when it involves latent variables (latent variable path analysis), I will outline traditional path analysis, which studies the relationships among observed (non-latent) variables. Path analysis can be thought as a particular form of multiple regression analysis that is employed to investigate and describe the directed dependencies among a set of variables. Single indicators are employed for each variable in the structural model that is going to be studies. A basic example of a path analysis model is shown below in Figure 3:

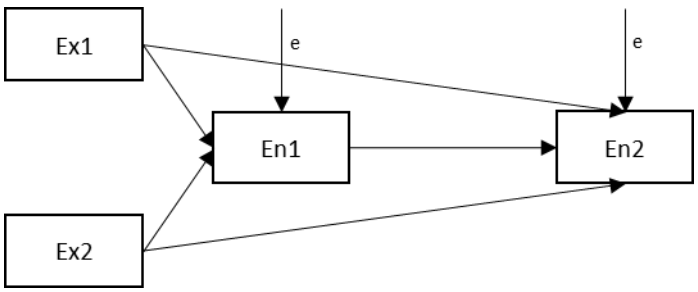


Figure 3 Example of basic path analysis model with exogenous (Ex) and endogenous (En) variables

In path analyses, single-headed arrows in Figure 3 are usually interpreted to indicate assumed causal relations. These arrows point from cause to effect. A double-headed arrow indicates a correlation, implying no assumed causality. In SEM, the independent variables are called exogenous variables (i.e. Ex1 and Ex2 in the diagram) while the dependent variables are called endogenous variables (En1 and En2 in the model). Endogenous variables can cause other endogenous variables, but not exogenous variables. Endogenous variables could also be affected by other variables not explicitly included in the diagram which are usually represented by the error term "*e*". To note, within an SEM diagram, an exogenous variable is always considered to be an independent variable while the endogenous variable can act as independent and dependent, depending on the SEM equations. A path coefficient indicates the direct effect of a variable (assumed to be a cause) on another variable. Path coefficients are often reported after standardization as this aids the comparison of the strength of effects. The standardization is obtained by multiplying the regression coefficient by the standard deviations of the corresponding explanatory variable (e.g. cause). The idea of standardization can be extended to apply to partial regression coefficients which are defined as "the expected change in the dependent variable associated with a unit change in a given predictor while controlling for the correlated effects of other predictors"[147]. Traditional path analysis using observed variables (depicted with a square or rectangle in Figure 3) assumes perfect reliability of the observed measures. Hence, path coefficients are derived based on this unrealistic assumption[148].

Latent variable path analysis addresses this main limitation and allows researchers to study the relationship between multiple and imperfectly observed measures of underlying latent factors. These latent factors are usually represented with circles or ellipses in SEM diagrams. In Figure 4a, a number of observed variables or items (i.e. ind-var1, ind-var2 and ind-var3) with measurement error associated to each of them (e8, e9 and e10) load

on to a single latent variable (i.e. L-var1). Factor loadings are usually reported on the arrows that connect the latent variable to the observed ones (i.e. ".65". ".68" and ".74").

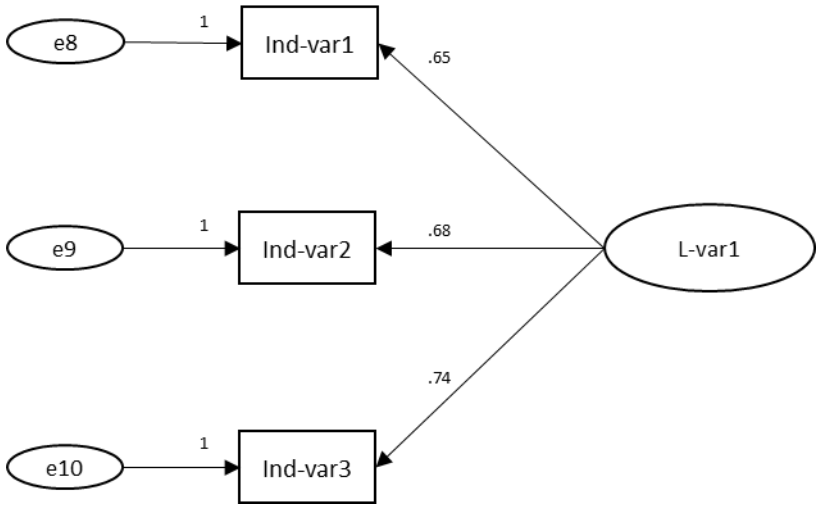


Figure 4a Observed and latent variables with factor loading and measurement error

When path analysis includes latent variables specified via CFA, we have a fully specified SEM, or in other words latent variable path analysis.

Interpreting results from latent variable path analysis is a complex procedure where several parameters should be taken in to account. Also, as for its simpler specifications (CFA and path analysis), various model fit indexes should be examined. These include the Chi-square statistics, Root Mean Square Error of Approximation (RMSEA) and increment fit indexes such as the comparative fit index (CFI) and the Tucker-Lewis index (TLI). The chi-square statistic compares the observed and model fitted variance-covariance among the observed variables: a significant statistic would indicate a poor fit. When this is found, improvements could be considered. The RMSEA should be less than 0.08 and CFI and TLI should be greater than 0.90 for the model to be considered to be satisfactory[149]. Also, when using latent variables to defined separate constructs, the correlation between them should not be too high (discriminant validity), while in general

factor loadings for any latent variable should be high (convergent validity) and path coefficients should be examined and removed to aid model parsimony if not significant[148].

When specifying SEM that involves multiple endogenous variables, as depicted for example in Figure 4a, a path coefficient indicates the direct effect of a variable on another variable. Direct effect refers to the pathway from a variable to another while controlling for a selected variable that may lie on its causal path (the mediator). The indirect effect describes the pathways from the first variable to the outcome that involves the mediator. In other words, an indirect effect occurs when the effect of one variable (either observed or latent) on a second is mediated, in whole or part, by one or more other intervening variables[150]. In practice, we may be interested in studying multiple mediators For example, if we look at Figure 4b both direct and indirect effects of 1 on 4 are assumed to be present, with the indirect effects involving two mediators: 2 and 3. Moreover, the total indirect effect of 1 on 4 is actually made up of three specific indirect effects involving compound paths running through 2 only, 3 only, and through both 2 and 3.

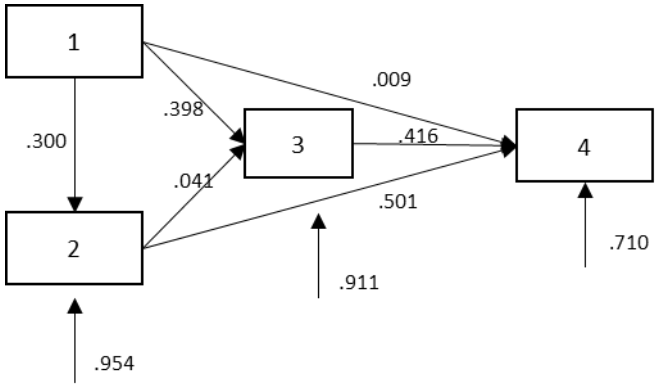


Figure 4b Direct and indirect effects in path analysis, including path coefficients and factor loadings

3.2.5 Studying the impact of conduct problems' risk factors on educational achievement

To investigate whether previously identified risk factors for CP associate longitudinally to increase the risk of poor academic achievement in adolescence and to investigate differences across trajectory groups and gender I have tested the developmental cascade model shown in Figure 5.

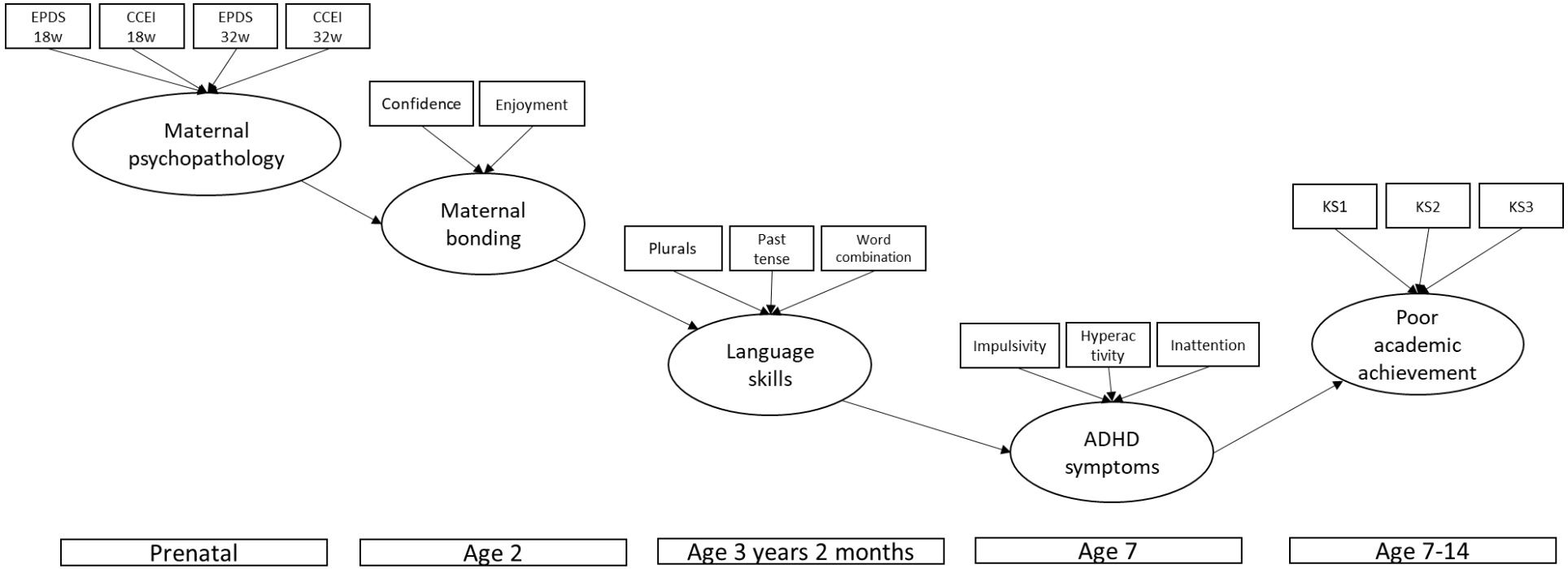


Figure 5 Hypothesised cascade model linking prenatal and postnatal risk factors and resulting in poor academic achievement in early adolescence. Latent variables are represented in circles. Observed variables are represented in rectangles

I used CFA to derive latent factors from the relevant observed variables, as specified in Figure 5, using MPlus version 8[151].

The construct “Maternal psychopathology” was derived from the scores of two scales administered at two time-points: the Crown-Crisp Experiential Index[152] and the Edinburgh Postnatal Depression Scale[153], administered at 18 and 32 weeks of gestation. The construct “Maternal bonding” at age two was obtained using by combining items belonging to the following two domains: confidence (6 items) and enjoyment of baby (5 items). The construct “Language skills” was derived using four subscales drawn from the MacArthur Toddler Communication Questionnaire[154]. This assessed vocabulary (receptive and expressive), plurals, past tense and word combination (the ability to join words together within an utterance) at age three years. “ADHD” was derived using maternal reports of three ADHD-related dimensions (impulsivity, hyperactivity and inattention) of the Development and Well-Being Assessment[155] (DAWBA) interview at age 7. “Poor academic achievement” was derived by national standardised tests. Data were used to evaluate academic progress throughout primary education. Year-on-year progress of UK children is divided into “key stages”, assessed by compulsory national tests at the end of each stage. For Key Stage 1, at the end of Year 2 (6-7 years of age), English (reading, writing) and Mathematics were examined. For Key Stage 2, at the end of Year 6 (10-11 years of age), tests of English, Science, and Mathematics were administered, while these three subjects were again assessed for Key Stage 3 at the end of Year 9 (13-14 years of age).

Once the CFA was specified, I studied the associations between thee latent variables, using their temporal order to specify the direction of effects (i.e. maternal psychopathology to maternal bonding; maternal bonding to language skills; language skills to ADHD symptoms; and ADHD symptoms to academic achievement). In

addition, I included direct associations between each of these domains and the outcome (poor academic achievement).

I fitted this model using the ALSPAC data described in Chapter 2, restricted to participants that had been classified as belonging to the EOP and the CL trajectories. The reason for this is that I am interested in looking at differences in the developmental process that may account for desistance/persistence of CP in childhood and adolescence. In addition, I will also investigate gender differences. To do this I used the multiple groups' option in Mplus. I employed nested models to compare coefficients across trajectory groups. Specifically, I compared a fully constrained model (omnibus model or reference model) to models where the paths of interest were freely estimated. Where the Chi2 statistic for a model comparison was significant between EOP and CL trajectories, I conducted follow-up analyses that tested gender differences within the trajectory groups.

3.2.6 Implementation

CP trajectories used for this particular analysis were previously created by Barker and Maughan[98] using repeated assessments of child CP at ages 4, 7, 8, 10, 12, and 13 years, using parent-administered SDQ in ALSPAC. The questionnaire assesses CP with the following five items: "often has temper tantrums or hot tempers", "generally obedient, usually does what adults request", "often fights with other children or bullies them", "often lies or cheats" and "steals from home, school or elsewhere." Binary indicators (0=not high risk; 1=high risk) were created at each age based on national norms established for 5- to 10-year-old boys and girls in England and Wales[156]. The cut-offs used in the present study are strong predictors of conduct disorder[5].

Barker and Maughan used growth mixture models[157] to estimate the trajectories in Mplus, Version 4.2[158]. A series of models were fitted beginning with a one-group trajectory model and moving to a six-group trajectory model. All models were estimated

with random starting values. Models that allowed boys and girls to vary in growth parameters of trajectory groups (variant) were compared with models for which I restricted the growth parameters of each trajectory to be the same for boys and girls (invariant).

As described above, the hypothesised cascade model was fitted in the subgroups of ALSPAC participants who had been classified by Barker and Maughan and being EOP or CL.

A sample of the syntax using the “grouping” option in Mplus is displayed below:

```
grouping is
!CP_Trajsex (1=CLm 2=CLf 3=EOPm 4=EOPf) ;
CP_Traj (3=CL 4=EOP);
!sex (1=M 2=F);

analysis:
estimator is mlr;
iter = 10000;


model:
!here I define the latent constructs
Academic by KS1* KS2 KS3 ;
Academic@1;

ADHD by impulse7* activity7 innatt7 ;
ADHD@1;

Language by Vocab* Plurals PastTense WordComb ;
Language@1;

MatBond by MatCon@1 MatEnj@1 ;

MatPsy by anx_18w* epds_18w anx_32wks epds_32w ;
```

```
MatPsy@1;

anx_18w with epds_18w;
anx_32wks with epds_32w;

! Pathways to the Academic factor
Academic on MatPsy ;
Academic on MatBond ;
Academic on Language ;
Academic on ADHD ;

! Pathways to the ADHD factor
ADHD on Language ;
ADHD on MatBond ;
ADHD on MatPsy ;

! Pathways to the Language factor
Language on MatBond ;
Language on MatPsy ;

! Pathways to the MatBond factor
MatBond on MatPsy ;

!and then indirect
model indirect:

Academic ind MatPsy ;
Academic ind MatBond ;
Academic ind Language ;
Academic ind  ADHD ;
```

Where “Academic” is the latent variable derived using KS1 KS2 KS3 scores; “ADHD” is the latent variable derived using impulse7 activity7 innatt7 which are symptoms of impulsivity, hyperactivity and inattention respectively at age 7 from the DAWBA. “Language” is the latent variable derived using Vocab Plurals PastTense WordComb

which are the scores on the vocabulary, plurals, past tense and word combination subscales of the MacArthur Toddler Communication Questionnaire. “MatBond” is the latent variable derived using MatCon@1 MatEnj@1 which are indicators of maternal connectedness to the child and maternal enjoyment of the child[159] (see section 5.1.2 for more details). “MatPsy” is the latent variable derived using anx_18w* epds_18w anx_32wks epds_32w which are the scores of maternal anxiety and depression on the Crown-Crisp Experiential Index[152] and the Edinburgh Postnatal Depression Scale[153], respectively.

3.2.7 The role of school experience in mediating the association between conduct problems trajectories and NEET status

To investigate research question number 3 (What is the role that school experience plays in mediating the effect of CP trajectories on later poor education and employment outcome (NEET)?) I have used ALSPAC data and performed mediation analysis adopting a counterfactual approach. This involved comparing the average outcomes predicted under scenarios where different values of the exposure (CP trajectories) and mediator (school experience) are assumed to be set. Natural direct and indirect effects were used to formalise these comparisons with G-computation, (implemented using the G-formula command in STATA), with standard errors derived via bootstrap procedures.

G-formula is part of the so-called “generalised methods” proposed by J Robins[160] to estimate the causal effect of time-varying exposures on outcomes in the presence of time-varying confounders which may themselves also be affected by the exposures. As mediation analysis can be viewed as a particular case of a time-varying exposure setting, this approach is also suitable to estimate direct and indirect effects[161].

To proceed, one has to specify the assumed relationships among exposure (CP trajectories), mediators (school experience), and outcome (NEET status at age 20 years), and also to identify potential confounders in their associations. I did this via a

directed acyclic graph (DAG). A DAG is a useful tool for specifying assumed causal relations between variables and developing appropriate analytical strategies[162]. I then expressed the target of estimation in terms of the average potential outcomes that one would expect under alternative scenarios for the exposure and the mediator.

3.2.8 Directed acyclic graphs

As the name suggests a DAG is a graphic representation that includes one-way arrows which indicate the direction of the assumed causal relationship between two variables. The acyclic properties of the graph imply that arrows will not go back from a variable where they have descended from. Only paths in which the entire sequence of arrows point away from the exposure towards the outcome are considered causal paths[163] (Schrier and Platt, 2008). The path constituted by: CP trajectories → School experience → NEET is one such causal path in the DAG presented in Figure 6. School experience constitutes a mediating factor through which the causal effect of CP trajectories on NEET is presumed (but not assumed) to be mediated. Backdoor paths are non-causal paths between the exposure and outcome of interest that start with by arrowheads pointing towards the exposure[164] and ending with arrows pointing towards the outcome. An example of a backdoor path in Figure 6 is: CP trajectory groups ← social class (based on maternal occupation) → NEET. When possible, all backdoor paths should be closed either via adjustment or because they include a collider (defined below). Being strategic in choosing which variables to adjust for in the analyses may pay off, since several backdoor paths might be closed by conditioning on the same variable(s), leading the selection of a minimally sufficient set of confounders to include in the analyses. As stated above, paths are also closed if they include a collider. A collider is a variable on a path where two or more arrowheads point[165]. For example, in Figure 6, KS4_IDACI is a collider on the path: CP trajectory groups ← maternal occupation → KS4_IDACI ← maternal depression → NEET. Because associations are not transmitted along a path that includes (at least) a collider, there is

no confounding arising from that path. Identifying the colliders in a path is also important because conditioning on them would open their path: in the example, conditioning on KS4_IDACI would induce a spurious association between maternal occupation and maternal depression and hence open up the path from CP trajectory groups to maternal occupation, KS4_IDACI, and maternal depression, to NEET, although it was originally closed. The software DAGitty was used to build our DAG[166]. The output from running this software includes the minimum set of variables that would control for the confounding contributing to the association between the exposure and outcome.

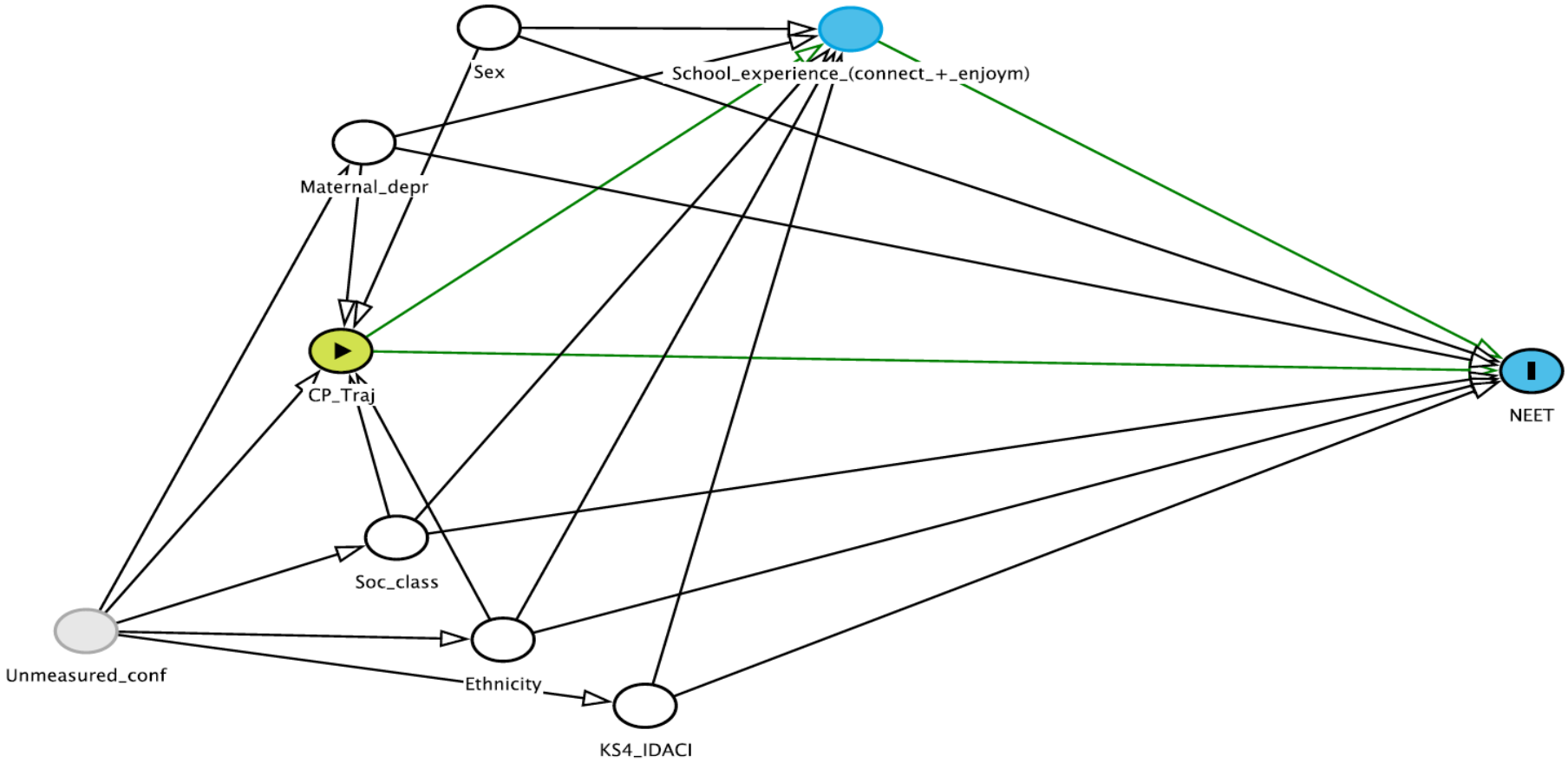


Figure 6 Directed Acyclic Graph showing (in green) the causal path of interest. In white, potential confounders.

3.2.9 Mediation effects

To investigate the extent of the mediating contribution of school experience to the causal relationship between CP trajectories and NEET, I adopted the counterfactual-based definitions of natural direct effect (NDE) and natural indirect effect (NIE) recently proposed in the literature as a generalisation of the decomposition of total effects derived from path analysis and well-known in social sciences[167]. The advantage of the new definitions is that they are not constrained to fit linear models for outcome and mediators, hence allowing for interactions and other non-linearities, as well as binary (or count) outcomes and mediators[168]. As for the direct and indirect effects derived from path analysis, the sum of NDE and NIE gives the total effect (TCE), hence allowing the derivation of the percentage contributed by a mediator to the effect of the exposure on the outcome.

For a binary exposure, taking values 0 and 1, the NDE compares what, on average, would occur to the outcome had all individuals in the population had their exposure been set to 1 or 0, while the mediator had been set to its "natural value" occurring if all were unexposed. The NIE instead compares what, on average, would occur to the outcome, had all individuals in the population had their exposure been set to 1, while the mediator had been set to its value either under exposure or not exposure. The identification of these mediation effects (as well as of those derived from path analysis) relies on assumptions of no unmeasured confounding for the relationships between exposure and mediators, mediators and outcome, and exposure and outcome. Identification of mediating effects in general also relies on the assumption of no intermediate confounding, which means that no additional mediator variable acts as a confounder for the mediator-outcome relationship.

In this application, the exposure was CP trajectories (in 4 groups, namely Low, EOP, AO, and CL), the outcome was NEET (in two groups, "NEET" and "not NEET") and the mediator, school experience, was quantified via two scores: school connectedness and

enjoyment which had been derived in previous ALSPAC publications[169] and were collapsed in a single continuous score. Five confounders were controlled for: gender, ethnicity, socioeconomic status, maternal depression and index of deprivation affecting children. An example e of the STATA syntax used to estimate the natural direct and indirect effects of CP trajectories on NEET via and not via school experience is reported below (complete-records analysis):

```
#delimit ;
                gformula y x m1a m1b m1ax2 m1ax3 m1ax4  c1 c2 c3
c4 c5,
                mediation outcome(y) exposure(x) mediator(m1a
m1b)
                base_confs(c1 c2 c2 c3 c4 c5)
                oce baseline(1) control(m1a:6,m1b:2)
                commands(y:logit, m1a:regress, m1b:regress)
                equations(

y:  i.x m1a m1b m1ax2 m1ax3 m1ax4 i.c1 i.c2 c3 i.c4 i.c5,

m1b: i.x m1a     m1ax2 m1ax3 m1ax4 i.c1 i.c2 c3 i.c4 i.c5,

m1a: i.x                          i.c1 i.c2 c3 i.c4 i.c5

)
                derived(m1ax2 m1ax3 m1ax4)
                derrules(

m1ax2 : m1a*(x==2),

m1ax3 : m1a*(x==3),

m1ax4 : m1a*(x==4),

)
minsim samples(100) moreMC simulations(150000) replace seed(79)
logRR;
#delimit cr
```

Where “y” denotes the outcome (NEET), “x” the exposure (CP trajectory group), “m1a” and “m1b” the two measures of the mediator (school connectedness and school enjoyment), “c1-c5” the confounders (gender, ethnicity, social class based on maternal occupation, maternal depression and IDACI) and “m1ax2”, “m1ax3”, and “m1ax4” the interaction terms between the first component of the mediator and the exposure.

Initial analyses of the associations between CP trajectories and NEET were restricted to the 3288 children with available exposure and outcome data. Because data on confounders and mediators were affected by missingness, only 1077 children had complete data on all relevant variables. For this reason mediation analyses were carried out on the complete records only (i.e. with N=1077) and also with single stochastics imputation by chained equations[170] (White et al., 2011), with 10 burn-in iterations. This allowed us to obtain estimates based on all the original 3,288 children, under the missing at random assumption where the available exposure, mediator, confounder and outcome variables were included in the imputation model[171] (MAR). The plausibility of this assumption was investigated by logistic regression where a binary indicator of missingness in any of the relevant variables was created for each child in the study. Note that, because standard errors were obtained using a bootstrap procedure that included the imputation step, multiple imputation was not required to obtain valid inferences. Results obtained using the complete exposure-outcome sample (N=3288) via imputation, and the complete records were then compared to assess the impact of selection bias (under MAR).

3.2.10 School-level predictors of conduct problems trajectories

To investigate question number 4 (What is the role of structural/organisational school-factors and school atmosphere in predicting different CP trajectories from early to mid-adolescence, while controlling for individual-level factors?) I have used data from the Learning Together study. I run longitudinal latent class analysis (LLCA) to identify

different trajectories of CP, and then I fitted a series of logistic regression models to investigate whether a number of school-level factors could predict class membership.

3.2.11 Longitudinal Latent Class Analysis

The analyses proceeded in two steps. First, models for the developmental trajectories were estimated for self-reported CP and antisocial behaviour (ESYTC), replicating the work by Barker and Maughan[98]. LLCA[172] was used to estimate the trajectories in Mplus. In doing this, I employed a multilevel approach (clustering at the school-level) and accounted for variation between schools.

LLCA is simpler than other approaches such as growth mixture modelling (GMM) and latent growth class analysis (LGCA) because it does not impose any parametric function of time. Given that there is a maximum of three observations in the present study, this seems the most sensible/flexible option. A series of models were fitted beginning with a one-group trajectory model and moving to a four-group trajectory model. All models were estimated with multiple random starting values to check that the maximization routine did not stop at a local maximum[173]. Models that allowed boys and girls to vary in the growth parameters used to define the trajectory groups (freely estimated) were compared with models for which I restricted the growth parameters of each individual trajectory to be the same for boys and girls (constrained). When constraining growth parameters in Mplus, the statistical indices available to establish the best fit model are the Bayesian Information Criterion or BIC and entropy[98]. The BIC is a commonly used fit index in which lower values indicate a more parsimonious (but equally good) model. Entropy is a measure of classification accuracy with values closer to 1 indexing greater precision (range=0–1)[174].

Once the best LLCA model was selected, individual-specific predicted latent classes were saved and then imported into STATA, where step 2 was conducted. These were the most likely class predicted for each individual which were treated as the new

outcome of interest. Because two classes were identified in step 1, logistic regression models were fitted in this second step, with individual-level and school-level variables included as predictors, accounting for school-clustering when estimating robust standard errors. The individual-level variables were considered always together, and school-level predictors/factors were examined one by one and then selected the most significant using forward selection with p of entry at 10% level. This was because I was interested in investigating school-level factors while controlling for individual-level factors, rather than examining individual-level factors per se.

Below is an example of the Mplus syntax use to run step 1:

```
VARIABLE:
      NAMES ARE  id age1  misb1 age2 misb2 age3 misb3
                 school single type male  fambase;
      USEV ARE misb1 misb2 misb3 school ;
      USEOBSERVATIONS male EQ 1;
      MISSING ARE .;
     IDVARIABLE= id;
      CLUSTER = school;
      CLASSES= C(3);
      WITHIN = misb1 misb2 misb3;
ANALYSIS: TYPE = MIXTURE TWOLEVEL;
    STARTS = 100 50;
    PROCESS=10(STARTS);
MODEL:
    %WITHIN%
    %OVERALL%
    %BETWEEN%
    %OVERALL%
    C#1; C#2; C#1 WITH C#2;
OUTPUT: sampstat TECH1 TECH8;
SAVEDATA: FILE IS LLCA_M_3_cl.dat;
SAVE IS fscores cprob;
FORMAT IS free;
```

where “misb1”, “misb2”, and “misb3” are the three school misbehaviour scores (ESYTC score) at the three time-points (baseline, 24 months follow-up and 36 months follow-up) and school is the level of aggregation necessary to run multilevel models analysis. Below is an example of the Stata syntax used to run the final model of step 2:

```
logistic class i.ethnicity i.lone family_af i.school_dep
i.single i.school_type i.ofsted idaci bb_total,base vce(cluster
school) nolog
```

where “class” is the binary indicator of latent trajectory, while “ethnicity”, “lone”, “family_af” are individual-level variables (namely ethnic group, whether child has both or single parent, and family affluence) and “school_dep”, “single”, “school_type”, “Ofsted”, “idaci”, “bb_total” are the school-level variables (namely school deprivation, whether school gender is single or mixed, type of school, Ofsted rating, index of deprivation affecting children, and school atmosphere).

Chapter 4

In this chapter, I will describe what I did to conduct my systematic review and meta-analysis on psychosocial outcomes of different CP trajectories. I will show the search strategy that yielded the initial set of studies and how I screened them. Results will be presented in text and graphically (forest plots) and they will be discussed in the light of previous literature. This work has been published[175] and it is available online: Bevilacqua L, Hale D, Barker ED, Viner R. Conduct problems trajectories and psychosocial outcomes: a systematic review and meta-analysis. Eur Child Adolesc Psychiatry. 2018 Oct;27(10):1239-1260.

4.1 Conduct problems trajectories and psychosocial outcomes: a systematic review and meta-analysis.

Abstract: There is increasing evidence that youth who follow the early onset persistent (EOP), adolescent-onset (AO) and childhood-limited (CL) trajectories of CP show varying patterns of health, mental health, educational, and social outcomes in adulthood. However, there has been no systematic review and meta-analysis on outcomes associated with different CP trajectories. I systematically reviewed the literature of longitudinal studies considering the outcomes of three CP trajectories: EOP, AO, and CL compared with individuals with low levels of CP (low). I performed a series of meta-analyses comparing each trajectory to the low group for eight different outcomes in early adulthood or later. Thirteen studies met our inclusion criteria. Outcomes were mental health (depression), cannabis use, alcohol use, self-reported aggression, official records of antisocial behaviour, poor general health, poor education, and poor employment. Overall, EOP individuals showed a significant higher risk of poor outcome followed by AO individuals, CL individuals, and finally participants in the low group. All CP trajectories showed a higher risk of poor psychosocial outcomes compared to the low group, but the magnitude of risk differed across

trajectories, with a general trend for the EOP to perform significantly worse, followed by the AO and CL. Early intervention is recommended across domains to maximise the likelihood of desistance from antisocial behaviour and improvement on several psychosocial outcomes.

4.1.1 Introduction

The EOP, AO and CL trajectories have been used in several longitudinal studies that seek to investigate the consequences of CP and antisocial behaviour across life[176]. EOP individuals are exposed to multiple risk factors, which may negatively impact their psychological and physical health over the years. Several studies have identified both early and adolescent risk factors associated with EOP. Early risk factors include maternal psychopathology and harsh parenting, partner cruelty to mother but also mother and child diet[177, 178]. Adolescence risk factors include peer problems, emotional difficulties and high risk of affiliating with deviant peers[97,163]. For AO individuals, parental instability, low IQ and poorly controlled temperament seem to be known early risk factors[179]. Concomitant risk factors in adolescents with CP include high-risk sexual behaviour, academic difficulties, and substance use[55, 180]. Previous research with CL individuals showed that early risk factors are similar to those seen in EOP individuals and include maltreatment, family conflict and maternal maladjustment[181, 182] but present with lower levels compared to EOP. CL individuals show relatively normal levels of CP in adolescence and some studies showed remission of peer rejection and emotional difficulties, suggesting that this group improves on a number of domains and have a typical adolescence[111]. Others however, showed negative outcomes in a number of areas such as higher rates of teenage parenthood in females and lower academic achievement compared to individuals without CP (or Low)[183].

These risk-factors and behaviours across the different developmental trajectories discussed so far may well have a direct impact on an individual's health. However, more complex processes have been hypothesised to describe how the wear and tear

of CP individuals' life-styles has an impact on multiple domains at later stages of their life: Caspi and Moffitt (1995) have suggested that the process of cumulative continuity operates such that risk factors at one time-point have an impact on later adaptation[66]. Developmental "snares" such as imprisonment, early pregnancy, or addiction to alcohol or drugs may tie individuals with CP to chronic patterns of maladaptive life-styles which may result in multiple difficulties in the transition to adulthood.

CP trajectory studies have shown that this wear and tear can result in both mental and physical health problems in early-adulthood and adulthood, especially for the EOP and AO individuals.

For example, Odgers and colleagues investigated the health burden of different CP trajectories at age 32[2]. EOP individuals were at significantly higher risk of mental health problems, engaging in violent acts, using illicit substances and having health problems (e.g. serious injuries, chronic illnesses) compared to individuals with low levels of CP. AO also showed higher risk on most domains considered, but this was generally not as high as in EOP. Although indistinguishable from EOP in terms of baseline symptoms of CP, CL individuals did not show significantly higher risk of poor outcomes on most of the measures considered in this study.

In another study, authors investigated outcomes of EOP, AO and CL individuals on a number of outcomes[101]. They found that EOP individuals were at higher risk of tobacco and substance use, criminal and risky sexual behaviour, gambling and mental health at age 18. Higher rates of risky sexual behaviour and substance use were observed in AO individuals. Although the authors did not find that CL individuals were at significantly higher risk in the adjusted results, they concluded that CL individuals may transition into young adulthood with slightly higher risk of displaying difficulties compared to Low individuals. Other studies, however, found that CL individuals showed significantly higher risk of engaging in aggressive and rule-breaking behaviours, feeling

withdrawn/depressed and having thought problems at age 17 compared to those in the Low trajectory group[102].

In summary, previous studies conducted in several countries on a range of life outcomes of different CP trajectories have generally found that EOP youth have the highest risk of poor outcomes in early adulthood and adulthood[184]. However, results seem to be less clear for the AO and CL groups. Literature reviews on developmental trajectories of antisocial behaviour and their outcomes have been conducted, but did not include a quantitative analysis and only included females[185]. In this section, the literature regarding a range of health, mental health, educational and social outcomes associated with CP trajectories will be systematically reviewed. A systematic review and meta-analysis represents a powerful tool to summarise data in this field. The work conducted in this section will clarify EOP individuals' outcomes and shed light on the outcomes of AO and CL individuals, which are less well understood. To our knowledge, this is the first systematic review and meta-analysis to investigate health, mental health, educational and social outcomes of different CP trajectories.

4.1.2 Methods

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[186]. Initial searches were conducted on 26th May, 2015 with a follow-up search conducted on 26th August 2016. Searches were undertaken using PubMed (Medline) and PsycINFO as these were considered most relevant given the research question. Figure 7 shows the PRISMA flowchart, with details of included and excluded papers with reason. Details of the searches performed in Medline and PsycINFO can be found in chapter 3.

Study inclusion and exclusion criteria:

I screened studies based on the following inclusion and exclusion criteria:

Inclusion criteria:

- Longitudinal studies that compared subtypes of conduct disorder/CP based on age of onset (e.g. childhood vs adolescent-onset as defined by the DSM-IV which sets a cut off at age 10) OR
- Studies where growth models were employed in order to compare outcomes different trajectory groups of conduct disorder/CP individuals
- Studies where exposures (child and adolescent assessments) include formal clinical diagnoses of CD or validated epidemiological measures of significant behavioural problems associated with CD but without a formal diagnosis being present (aggressive, destructive, disruptive, deceitful behaviour and violation of rules) from child, parent or teacher report
- Studies where outcomes were assessed ≥17 years. This cut-off was considered appropriate given our interest not only in health and social but also educational outcomes.

Exclusion criteria:

- Cross-sectional studies in adulthood with retrospective recall of earlier behaviour problems (due to known problems with reporter bias and recall in these types of studies[137]
- Intervention studies
- Non-longitudinal studies
- Studies with outcomes assessed at age <17
- Studies where age of onset of conduct disorder/CP is not specified or only one time-point of assessment is included
- Studies not reported in English

Study Selection:

After removing all duplicates, all abstracts were screened. The full-text was retrieved for studies not excluded based on the abstract. EPPI Reviewer was used to screen all the studies identified by the searches[137]. For all studies identified which met our inclusion criteria, I searched the reference list and all articles which cited the target paper for further studies relevant for our work. When necessary, contact was made with study authors to request full-text or details regarding the paper. Two authors (LB and DH) contributed to the screening of the studies. Some discrepancies/uncertainties emerged and were related mainly to understanding whether the study in question included data before and after age ten, as well as outcomes assessed at age 17 or later. These discrepancies/uncertainties were resolved by discussion.

Data extraction and collection:

I developed a data extraction template which I applied across all included studies. This included: title and year of publication, assessment measurements, covariates, the outcome measures, number of individuals in each trajectory, effect size and country of provenance. This is available in the full-text (https://link.springer.com/article/10.1007/s00787-017-1053-4).

Summary measures:

I used Odds Ratios (ORs) as my main summary statistics to perform the meta-analyses. Where ORs were not available in the paper, they were calculated from available information (i.e. mean and standard deviation or mean and standard error) using the Campbell Collaboration Effect Size calculator[141]. Where non-significant differences were reported but information was insufficient to calculate ORs, I set ORs as equal to one, assuming total equivalence between CP trajectories and the Low group.

Where multiple papers were drawn from the same sample, I included only one study in the meta-analyses opting for the study with the largest number of outcomes considered.

Synthesis of results:

To perform the meta-analyses, I mapped studies to type of outcome considered. The majority of the outcomes reported in the included studies mapped to eight domains: mental health (depression or depressive mood), cannabis use, alcohol use, self-reported aggression, criminal/antisocial behaviour (official records), poor general health, poor education and poor employment outcome. Meta-analyses were performed for each of these outcome categories where at least three analyses were available. The number of studies included for each meta-analysis differed due to outcome variables considered in each study.

Data were analysed using STATA 13[142]. I used random-effects meta-analyses to compute pooled effect sizes and confidence intervals. Past research suggests that the random-effects model is a more conservative test and is preferable over fixed-effects models where there is significant heterogeneity and allows for calculation of measures of heterogeneity across studies (I-square) for each meta-analysis[46,140]. To test for significant differences in effect sizes across trajectories, I observed whether the confidence intervals for effect sizes overlapped; non-overlap was interpreted as a significant difference between effect sizes. This is a conservative estimate of significant differences which is appropriate given the multiple comparisons being made[187].

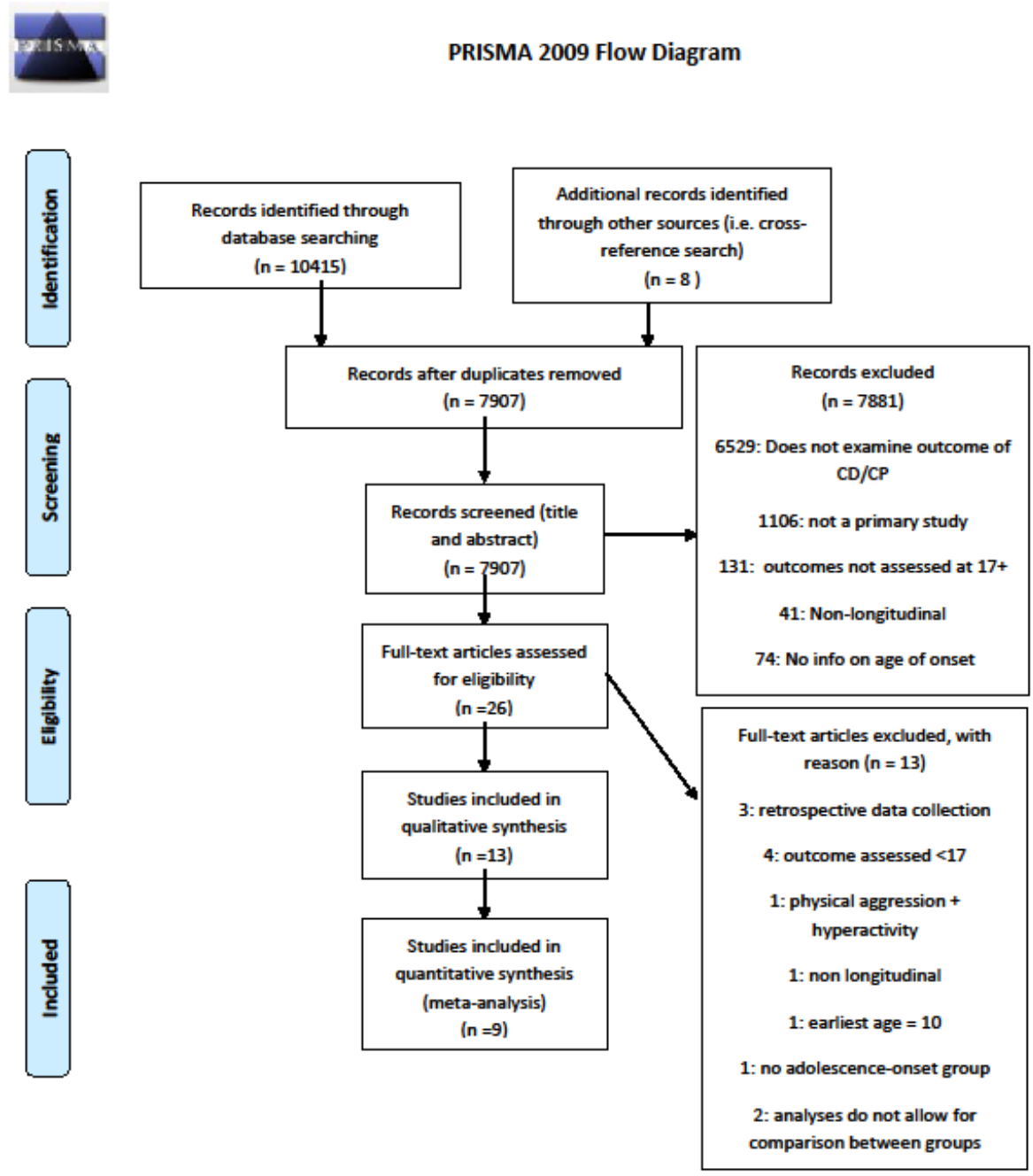


Figure 7 Flow chart with details of excluded and included articles

4.1.3 Results

I identified 13 studies which met my inclusion criteria with a total of 10,663 individuals. All studies made use of three comparable trajectory groups of CP onset and

persistence/desistance: Early-Onset Persistent or Life-course persistent (EOP); Adolescent-onset or Adolescent-limited or Increasing (AO); Childhood-Limited or Childhood-Desisting (CL); a fourth trajectory, the Low CP (Low) was used as the reference category. Only one study did not include the CL trajectory[188].

Table 1 describes each study included in the review, including a quality assessment based on a modified version of the Newcastle-Ottawa Scale. At the first data collection point, age across the studies ranged from four to nine with an unweighted mean across all studies of 5.53 years old. The age at which outcomes were assessed ranged across studies from 17 to 32 years old, with an unweighted mean age of 22.5 years old. Three of the 13 studies selected were conducted in the US, three in Australia, four in New Zealand, two in the UK, one in Belgium. Three studies included a male-only sample while all the others included a mixed-gender sample. In general, the quality of the studies was moderate (average of four out of six stars). More specifically, I observed good study quality in terms of the representativeness of the study population and ascertainment of exposure. This last aspect in particular is important to determine the overall reliability of a study. Attrition was high in a number of cases. This was somewhat expected due to the large time interval that characterised most of our studies.

Table 1 Study characteristics and quality assessment

Author	Age at exposure	T2, T3…	Age at outcome	Country	Gender	Selection	Comparability	Attrition	Total
Alink & Egeland, 2013	5	6, 7, 8, 11	28	US	Mixed	★★★	☆☆	☆	★★★
Bor et al., 2010	5	14	21	Australia	Mixed	★★★	☆☆	☆	★★★
Kretschmer et al., 2014	4	6 assessments from 4 to 13	17yrs 9mts	UK (ALSPAC)	Mixed	★★★	★★	☆	★★★★★
Moffitt et al., 2002	5	5, 7, 9, 11, 13, 15, 18, 21	26	NZ (Dunedin)	Males	★★★	☆☆	★	★★★★
Moffitt et al., 1996	5	5, 7, 9, 11, 13, 15	18	NZ (Dunedin)	Males	★★★	☆☆	★	★★★★
Odgers et al., 2008	7	9, 11, 13, 15, 18, 21 and 26	32	NZ (Dunedin)	Mixed	★★★	★☆	★	★★★★★
Odgers et al., 2007	7	9, 11, 13, 15, 18, 21 and 26	32	NZ (Dunedin)	Males	★★★	★☆	★	★★★★★
Roisman et al., 2004	grade 1	grades 2, 3, 6 and age 16	23	US	Mixed	★★★	☆☆	★	★★★★
Xie et al., 2011	grade 4	annual evaluations from grade 4 to grade 12	grade 12	US	Mixed	★★★	★☆	★	★★★★★

Hayatbakhsh M et al., 2008	5	14	21	Australia	Mixed	★★★	★☆	★	★★★★★
Stringaris A, Lewis G, Maughan B, 2014	4	7, 8, 10, 12, 13	18	UK (ALSPAC)	Mixed	★★☆	★★	☆	★★★
McGee et al., 2011	5	14	21	Australia	Mixed	★★★	★☆	☆	★★★★
Sentse et al., 2016	between 5 and 8	6-9, 9-12, 12-15, 14-17	17-20	Belgium	Mixed	★★★	☆☆	☆	★★★

The measures used in each study to assess CP in childhood and adolescence and measures of adult outcomes are shown in Appendix, with Table 13 showing health and substance use outcomes and Table 14 showing conduct, educational and social outcomes.

The results of the meta-analyses are shown in Figures 8 and 9. Figure 8 shows forest plots of individual and overall (pooled) ORs and l-square for each trajectory (relative to the reference group, Low) for health and substance use outcomes, with Figure 9 showing the same for conduct, educational and social outcomes. A summary table of data from these meta-analyses can be found in the Appendix (Table 15).

Seven studies examined mental health outcomes, including but not limited to depressive feelings and clinical diagnosis of depression. The largest effect size was found for the EOP trajectory (pooled OR= 2.24, 95% CI= 1.67–3.01). The AO trajectory was also associated with significantly higher odds of depression/depressive mood in young adulthood (pooled OR= 1.58, 95% CI= 1.19-2.08). The CL trajectory was also associated with higher odds but this finding was not significant (pooled OR= 1.29, 95% CI= 1.00-1.66).

Seven studies examined cannabis use. The largest effect size was observed for the AO trajectory (pooled OR= 3.78, 95% CI= 2.54-5.63). EOP individuals were also at higher odds of using cannabis in young adulthood (pooled OR= 3.34, 95% CI= 2.53-4.41). The CL trajectory was not significantly associated with higher odds of cannabis use (pooled OR= 1.14, 95% CI= 0.89-1.47).

Five studies examined alcohol use. Here, the largest effect size was observed for the EOP trajectory (pooled OR= 1.85, 95% CI= 1.04-3.28). AO participants were also at significantly higher odds of drinking excessive amounts of alcohol in young adulthood (pooled OR= 1.72, 95% CI= 1.23-2.41). CL individuals were not at higher odds of

drinking excessive amount of alcohol in young adulthood (pooled OR= 1.14, 95% CI= 0.80-1.63.

Seven studies examined self-reported aggression. The largest effect size was observed for the EOP trajectory (pooled OR= 5.40, 95% CI= 2.80-10.43). AO individuals were also at significantly higher odds of self-reporting high levels of aggression in young adulthood (pooled OR= 3.55, 95% CI= 2.07-6.08). CL individuals were also at significantly higher odds of self-reporting high levels of aggression in young adulthood (pooled OR= 1.75, 95% CI= 1.21-2.53).

Six studies included official records of criminal behaviour. The largest effect size was observed for the EOP trajectory (pooled OR= 3.18, 95% CI= 1.73-5.85). AO individuals were also found to be at significantly higher odds of having an official record of involvement in criminal activity (pooled OR= 2.29, 95% CI= 1.43-3.67). For CL individuals, I observed a trend towards being more likely to have an official record of involvement in criminal activity, but this did not reach statistical significance (pooled OR= 1.28, 95% CI= 0.99-1.66).

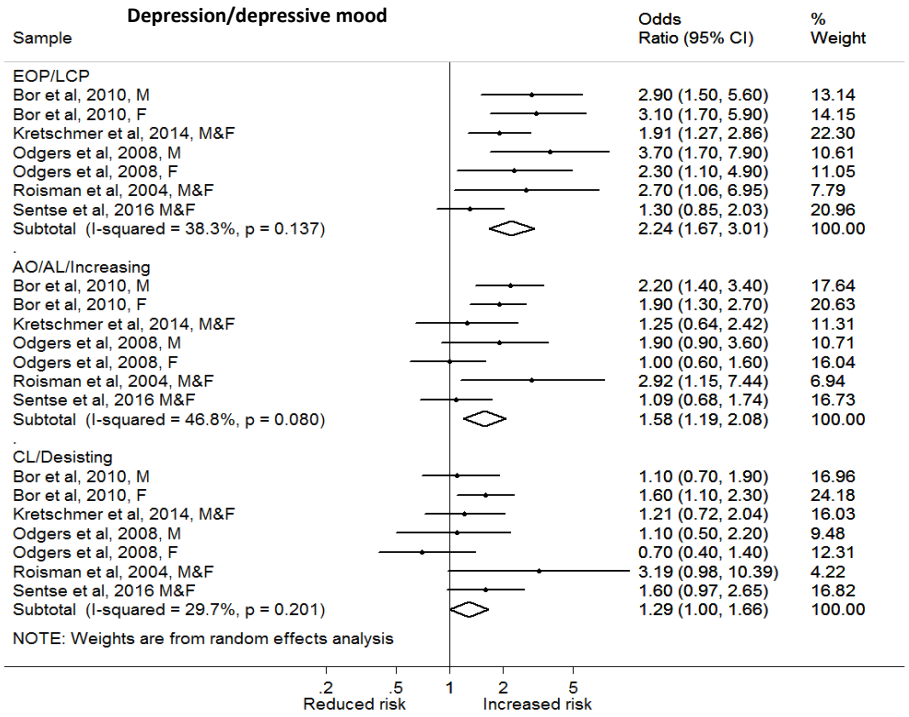
Four studies examined general health outcomes. Here, the largest effect size was observed for the AO trajectory (pooled OR= 2.38, 95% CI= 1.25-4.53). Similarly EOP individuals were found to be at significantly higher odds to report general health problems in young adulthood (pooled OR= 2.35, 95% CI= 1.48-3.73). CL individuals were not found to be at higher odds of reporting general health problems in young adulthood (pooled OR= 1.36, 95% CI= 0.89-2.10).

Six studies examined education outcome (poor education). I observed the largest effect size for the EOP trajectory (pooled OR= 4.14, 95% CI= 1.95-8.82). Also AO and CL individuals were found to be at significantly higher odds of having poor education outcome in young adulthood (pooled OR= 2.35, 95% CI= 1.44-3.82 and 1.83, 95% CI= 1.26-2.65 respectively).

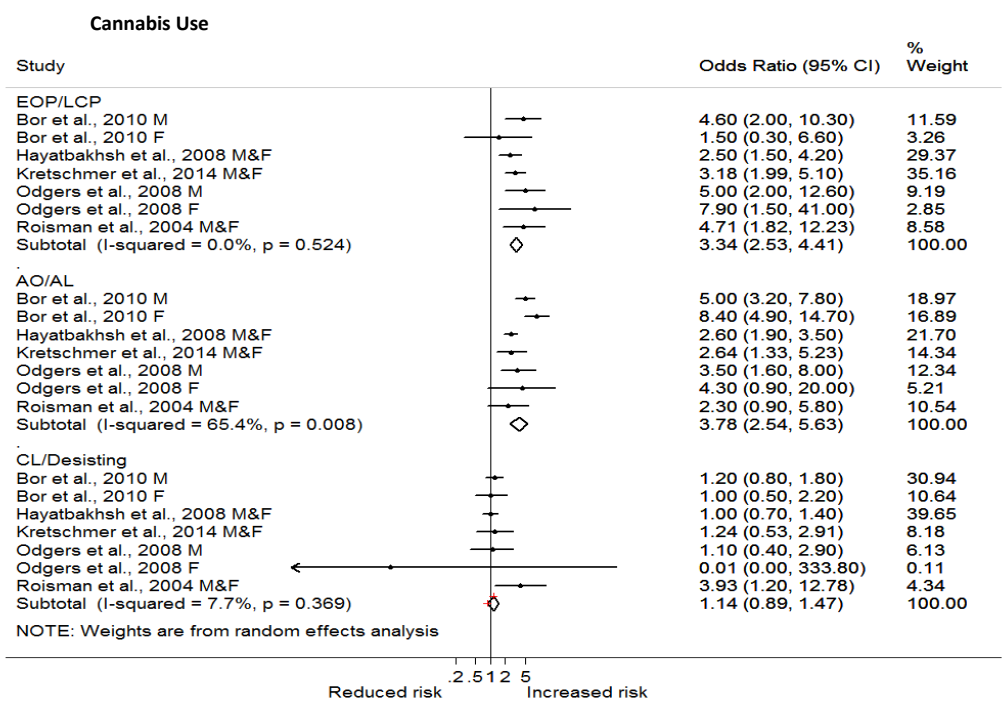
Five studies examined poor occupational outcome (or poor employment outcome). Here, the largest effect size was observed for the EOP trajectory (pooled OR= 2.00, 95% CI= 1.43-2.79). AO and CL showed a trend towards having a poorer employment outcome but I did not observe statistical significance (pooled OR= 1.22, 95%, CI= 0.95-1.55 and 1.14, 95% CI= 0.90-1.45 respectively).

Across all meta-analyses, I observed a poorer outcome in individuals belonging to EOP and AO trajectory than in individuals in the Low trajectory, with EOP individuals usually showing the highest odds (apart from cannabis use and general health, where the risk was slightly lower compared to AO individuals); for these two trajectories, all pooled ORs were statistically significant, with the only exception being for poor employment outcome for the AO group. CL individuals showed a trend towards being at higher odds of poor psychosocial outcomes compared to those in the Low group. However, statistical significance was reached only in self-reported aggression and poor education.

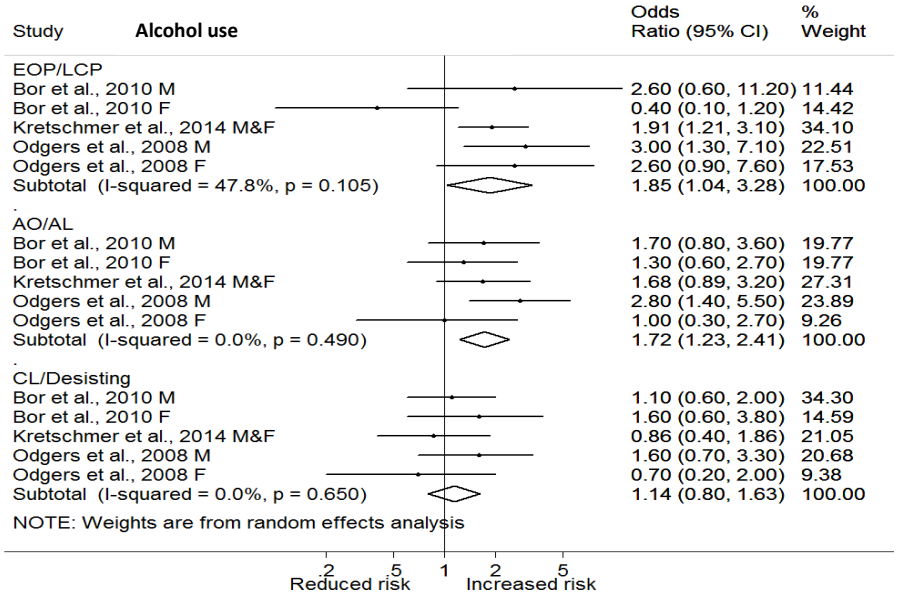
When comparing CP trajectories, the EOP was not found to be at significantly increased odds compared to the AO on any of the outcomes considered. However, EOP individuals showed significantly higher odds than CL on mental health, cannabis use, self-reported aggression, official records of criminal behaviour and poor employment outcome. The AO conferred significant increased odds compared to the CL only for cannabis use in early adulthood.


Depression/depressive mood
Sample
Odds Ratio (95% CI)
% Weight
EOP/LCP
Bor et al, 2010, M 2.90 (1.50, 5.60) 13.14
Bor et al, 2010, F 3.10 (1.70, 5.90) 14.15
Kretschmer et al, 2014, M&F 1.91 (1.27, 2.86) 22.30
Odgers et al, 2008, M 3.70 (1.70, 7.90) 10.61
Odgers et al, 2008, F 2.30 (1.10, 4.90) 11.05
Roisman et al, 2004, M&F 2.70 (1.06, 6.95) 7.79
Sentse et al, 2016 M&F 1.30 (0.85, 2.03) 20.96
Subtotal (I-squared = 38.3%, p = 0.137) 2.24 (1.67, 3.01) 100.00
AO/AL/Increasing
Bor et al, 2010, M 2.20 (1.40, 3.40) 17.64
Bor et al, 2010, F 1.90 (1.30, 2.70) 20.63
Kretschmer et al, 2014, M&F 1.25 (0.64, 2.42) 11.31
Odgers et al, 2008, M 1.90 (0.90, 3.60) 10.71
Odgers et al, 2008, F 1.00 (0.60, 1.60) 16.04
Roisman et al, 2004, M&F 2.92 (1.15, 7.44) 6.94
Sentse et al, 2016 M&F 1.09 (0.68, 1.74) 16.73
Subtotal (I-squared = 46.8%, p = 0.080) 1.58 (1.19, 2.08) 100.00
CL/Desisting
Bor et al, 2010, M 1.10 (0.70, 1.90) 16.96
Bor et al, 2010, F 1.60 (1.10, 2.30) 24.18
Kretschmer et al, 2014, M&F 1.21 (0.72, 2.04) 16.03
Odgers et al, 2008, M 1.10 (0.50, 2.20) 9.48
Odgers et al, 2008, F 0.70 (0.40, 1.40) 12.31
Roisman et al, 2004, M&F 3.19 (0.98, 10.39) 4.22
Sentse et al, 2016 M&F 1.60 (0.97, 2.65) 16.82
Subtotal (I-squared = 29.7%, p = 0.201) 1.29 (1.00, 1.66) 100.00
NOTE: Weights are from random effects analysis
.2 .5 1 2 5
Reduced risk
Increased risk

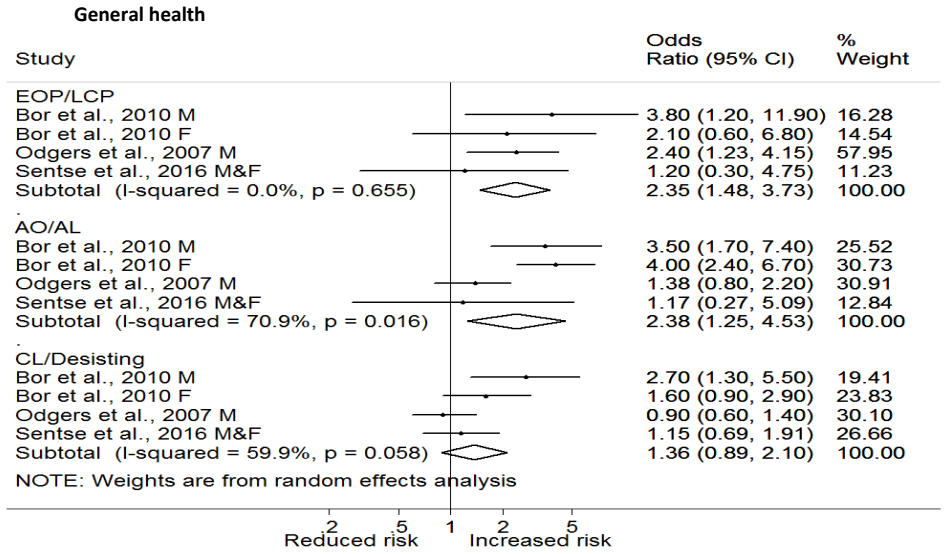
a)


Cannabis Use
Study
Odds Ratio (95% CI)
% Weight
EOP/LCP
Bor et al., 2010 M 4.60 (2.00, 10.30) 11.59
Bor et al., 2010 F 1.50 (0.30, 6.60) 3.26
Hayatbakhsh et al., 2008 M&F 2.50 (1.50, 4.20) 29.37
Kretschmer et al., 2014 M&F 3.18 (1.99, 5.10) 35.16
Odgers et al., 2008 M 5.00 (2.00, 12.60) 9.19
Odgers et al., 2008 F 7.90 (1.50, 41.00) 2.85
Roisman et al., 2004 M&F 4.71 (1.82, 12.23) 8.58
Subtotal (I-squared = 0.0%, p = 0.524) 3.34 (2.53, 4.41) 100.00
AO/AL
Bor et al., 2010 M 5.00 (3.20, 7.80) 18.97
Bor et al., 2010 F 8.40 (4.90, 14.70) 16.89
Hayatbakhsh et al., 2008 M&F 2.60 (1.90, 3.50) 21.70
Kretschmer et al., 2014 M&F 2.64 (1.33, 5.23) 14.34
Odgers et al., 2008 M 3.50 (1.60, 8.00) 12.34
Odgers et al., 2008 F 4.30 (0.90, 20.00) 5.21
Roisman et al., 2004 M&F 2.30 (0.90, 5.80) 10.54
Subtotal (I-squared = 65.4%, p = 0.008) 3.78 (2.54, 5.63) 100.00
CL/Desisting
Bor et al., 2010 M 1.20 (0.80, 1.80) 30.94
Bor et al., 2010 F 1.00 (0.50, 2.20) 10.64
Hayatbakhsh et al., 2008 M&F 1.00 (0.70, 1.40) 39.65
Kretschmer et al., 2014 M&F 1.24 (0.53, 2.91) 8.18
Odgers et al., 2008 M 1.10 (0.40, 2.90) 6.13
Odgers et al., 2008 F 0.01 (0.00, 333.80) 0.11
Roisman et al., 2004 M&F 3.93 (1.20, 12.78) 4.34
Subtotal (I-squared = 7.7%, p = 0.369) 1.14 (0.89, 1.47) 100.00
NOTE: Weights are from random effects analysis
.2 .5 1 2 5
Reduced risk
Increased risk

b)

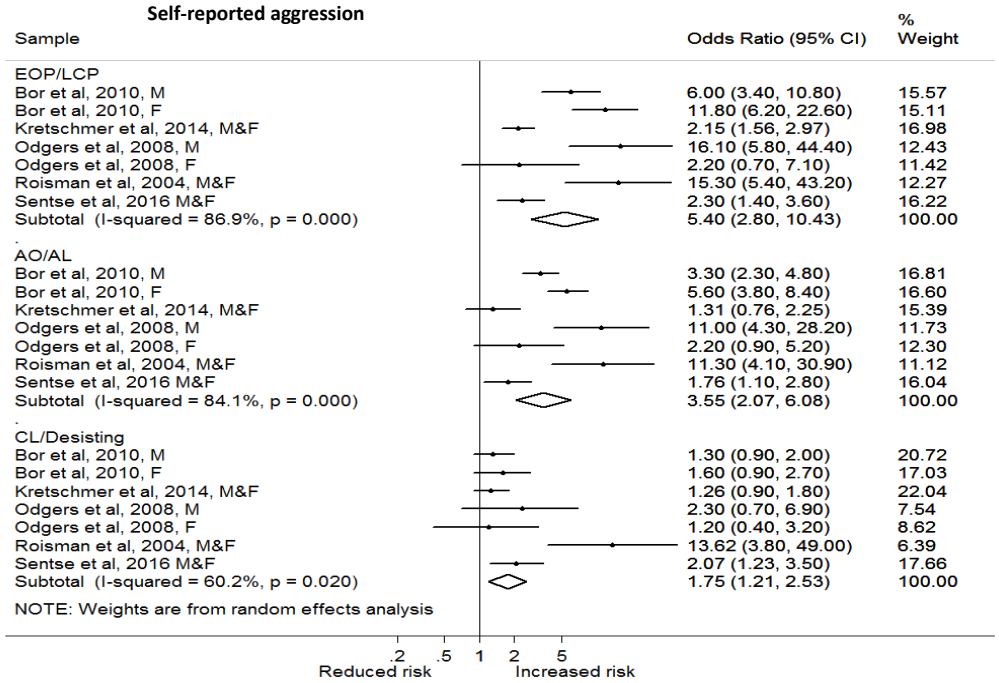


c)

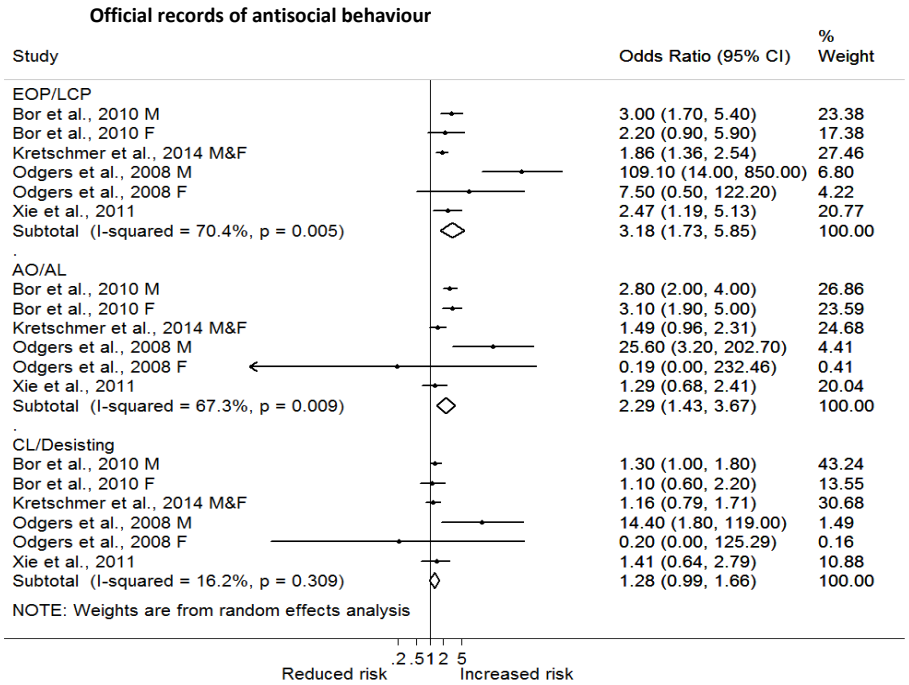


d)

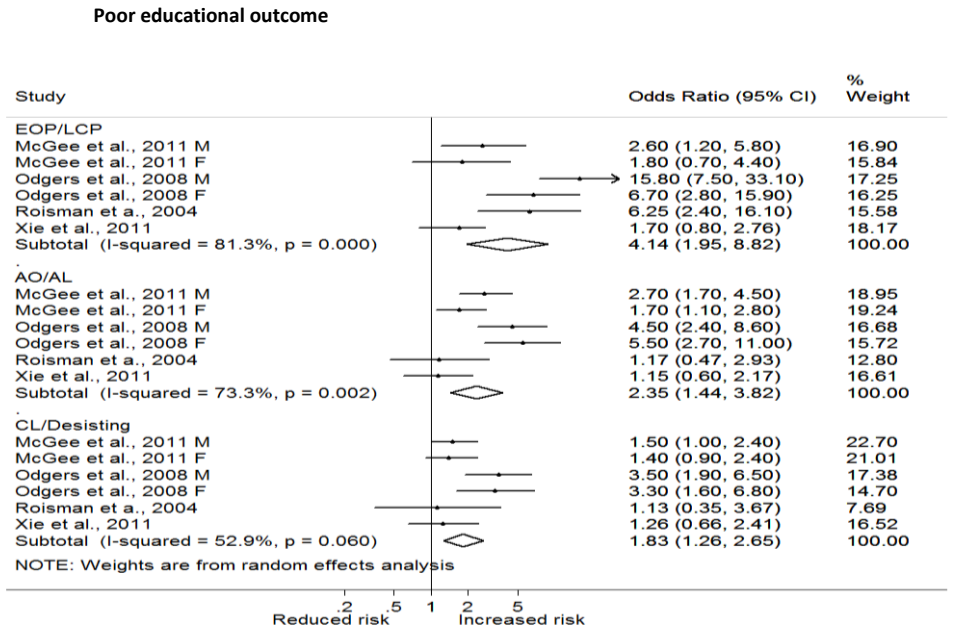
Figure 8. Forest plots showing odds ratios for poor a) mental health (depression or depressive mood), b) cannabis use, c) alcohol use and d) general health in young adulthood for the three CP trajectories compared to the reference category "low" (not shown in figures)


Self-reported aggression
Sample
Odds Ratio (95% CI)
% Weight
EOP/LCP
Bor et al, 2010, M 6.00 (3.40, 10.80) 15.57
Bor et al, 2010, F 11.80 (6.20, 22.60) 15.11
Kretschmer et al, 2014, M&F 2.15 (1.56, 2.97) 16.98
Odgers et al, 2008, M 16.10 (5.80, 44.40) 12.43
Odgers et al, 2008, F 2.20 (0.70, 7.10) 11.42
Roisman et al, 2004, M&F 15.30 (5.40, 43.20) 12.27
Sentse et al, 2016 M&F 2.30 (1.40, 3.60) 16.22
Subtotal (I-squared = 86.9%, p = 0.000) 5.40 (2.80, 10.43) 100.00
AO/AL
Bor et al, 2010, M 3.30 (2.30, 4.80) 16.81
Bor et al, 2010, F 5.60 (3.80, 8.40) 16.60
Kretschmer et al, 2014, M&F 1.31 (0.76, 2.25) 15.39
Odgers et al, 2008, M 11.00 (4.30, 28.20) 11.73
Odgers et al, 2008, F 2.20 (0.90, 5.20) 12.30
Roisman et al, 2004, M&F 11.30 (4.10, 30.90) 11.12
Sentse et al, 2016 M&F 1.76 (1.10, 2.80) 16.04
Subtotal (I-squared = 84.1%, p = 0.000) 3.55 (2.07, 6.08) 100.00
CL/Desisting
Bor et al, 2010, M 1.30 (0.90, 2.00) 20.72
Bor et al, 2010, F 1.60 (0.90, 2.70) 17.03
Kretschmer et al, 2014, M&F 1.26 (0.90, 1.80) 22.04
Odgers et al, 2008, M 2.30 (0.70, 6.90) 7.54
Odgers et al, 2008, F 1.20 (0.40, 3.20) 8.62
Roisman et al, 2004, M&F 13.62 (3.80, 49.00) 6.39
Sentse et al, 2016 M&F 2.07 (1.23, 3.50) 17.66
Subtotal (I-squared = 60.2%, p = 0.020) 1.75 (1.21, 2.53) 100.00
NOTE: Weights are from random effects analysis
.2 .5 1 2 5
Reduced risk
Increased risk

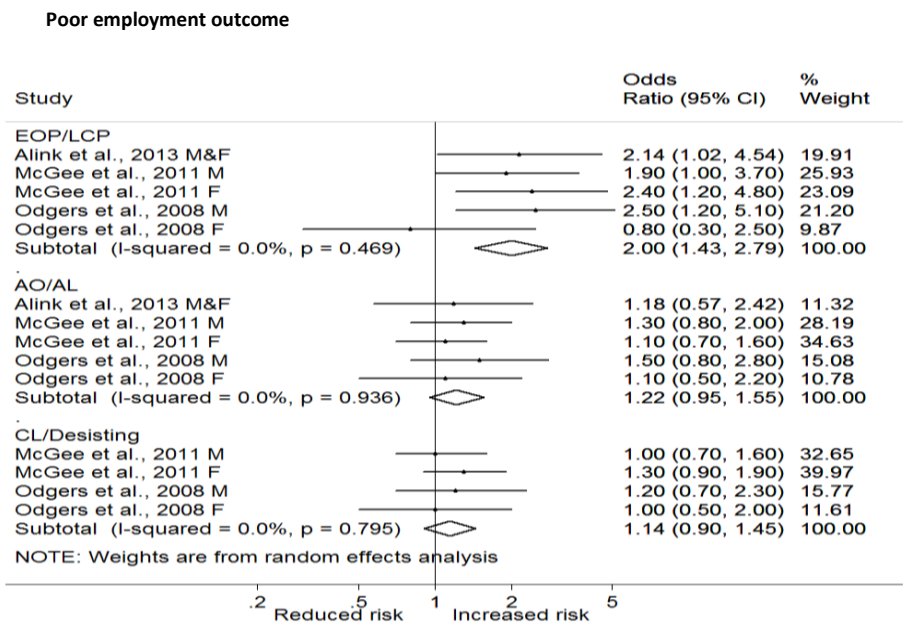
a)


Official records of antisocial behaviour
Study
Odds Ratio (95% CI)
% Weight
EOP/LCP
Bor et al., 2010 M 3.00 (1.70, 5.40) 23.38
Bor et al., 2010 F 2.20 (0.90, 5.90) 17.38
Kretschmer et al., 2014 M&F 1.86 (1.36, 2.54) 27.46
Odgers et al., 2008 M 109.10 (14.00, 850.00) 6.80
Odgers et al., 2008 F 7.50 (0.50, 122.20) 4.22
Xie et al., 2011 2.47 (1.19, 5.13) 20.77
Subtotal (I-squared = 70.4%, p = 0.005) 3.18 (1.73, 5.85) 100.00
AO/AL
Bor et al., 2010 M 2.80 (2.00, 4.00) 26.86
Bor et al., 2010 F 3.10 (1.90, 5.00) 23.59
Kretschmer et al., 2014 M&F 1.49 (0.96, 2.31) 24.68
Odgers et al., 2008 M 25.60 (3.20, 202.70) 4.41
Odgers et al., 2008 F 0.19 (0.00, 232.46) 0.41
Xie et al., 2011 1.29 (0.68, 2.41) 20.04
Subtotal (I-squared = 67.3%, p = 0.009) 2.29 (1.43, 3.67) 100.00
CL/Desisting
Bor et al., 2010 M 1.30 (1.00, 1.80) 43.24
Bor et al., 2010 F 1.10 (0.60, 2.20) 13.55
Kretschmer et al., 2014 M&F 1.16 (0.79, 1.71) 30.68
Odgers et al., 2008 M 14.40 (1.80, 119.00) 1.49
Odgers et al., 2008 F 0.20 (0.00, 125.29) 0.16
Xie et al., 2011 1.41 (0.64, 2.79) 10.88
Subtotal (I-squared = 16.2%, p = 0.309) 1.28 (0.99, 1.66) 100.00
NOTE: Weights are from random effects analysis
.2 .5 1 2 5
Reduced risk
Increased risk

b)



c)



d)

Figure 9 Forest plots showing odds ratios for poor a) self-reported aggression, b) official records of criminal or antisocial behaviour c) poor educational outcome and d) poor employment outcome in young adulthood for the three CP trajectories compared to the reference category "low" (not shown in figures)

4.1.4 Discussion

The aim of the present work was to conduct a systematic review and meta-analysis on psychosocial outcomes of different developmental trajectories of CP. Results from longitudinal studies of health, mental health, educational and employment outcomes associated with CP trajectories suggests that EOP, AO and CL were associated with poorer outcomes compared to the Low trajectory. Yet I identified a consistent "hierarchy of risk" amongst the trajectories. I found that the trajectory at highest risk of poor outcomes in adulthood is the EOP trajectory, with the highest or equal highest ORs across nearly all outcomes studied. For poor employment outcomes, the EOP was the only trajectory to have significantly higher risk than the Low. The AO trajectory had an intermediate risk across most outcomes, with a significantly higher risk of poor outcome compared to the Low trajectory across seven of eight outcomes (poor employment outcome being the exception). The CL trajectory had the lowest ORs across all outcomes compared to the EOP and AO trajectories. CL individuals were at significantly higher risk of poor outcome compared to those in the Low trajectory on self-reported aggression and poor educational outcomes. Highest ORs across trajectories were observed for self-reported aggression and poor educational outcomes. Given the interconnectedness of the outcomes considered, it is not surprising to see a trend across domains. Our findings suggest that age of onset of CP alone is not a strong predictor of outcomes, given that the highest and lowest risk trajectories are both childhood-onset. Instead, I suggest that the course of CP across childhood and adolescence is most predictive of later outcomes.

The finding that the EOP trajectory had the highest risk of poor early adult outcomes is consistent with previous reports. It has been posited that EOP individuals differ from AO individuals in terms of negative predisposing genetic factors and early neurocognitive characteristics[180]. More recent studies have also shown that these individuals present with increased levels of environmental risk factors in prenatal

stages[178] and early age[189]. A potential explanation for the EOP's negative outcomes across several domains is that genetic and environmental factors (which are likely to increase vulnerability for long-term psychiatry/physical morbidity independently) interact to maximise likelihood of developmental snares occurring across several stages of life – particularly adolescence. These developmental snares decrease the likelihood for these individuals to "recover" and shift to a more healthy and adaptive course of development. I speculate that the interaction between predisposing genetic factors and negative environment is particularly relevant for explaining not only the continuity of violent and antisocial acts, but also the variety of difficulties observed across several domains examined here (e.g. health).

In contrast, the finding that AO individuals were at higher risk of poor outcomes compared to those in the Low trajectory conflicts with reports that problem behaviour in adolescence is a transient and relatively normative phenomenon[95]. In this group I also observed higher risk of self-reported aggressive behaviour and official records of antisocial behaviour. This finding contrasts the notion that AO individuals tend to be on the non-aggressive spectrum. They, however, showed lower risk on these outcomes compared to EOP, in line with previous research[107]. Given the lack of data regarding long-term outcomes of AO individuals, I suggest that the interchangeable use of "Adolescent-Limited" and "Adolescent-Onset" may require careful consideration.

I found the CL trajectory to have the least negative outcomes compared to the EOP and AO trajectories, although those in this group had significantly poorer educational outcomes and problems with aggression in early adult life compared to those in the Low trajectory. I note that ORs for other outcomes were in the same direction and of a similar order to other CP trajectories, although they did not reach significance. These findings support the suggestion that full recovery from CP rarely occurs and contradict the idea that CL individuals should be indistinguishable from typical individuals in adulthood[95, 111]. Some have suggested that the decrease in problem behaviours in CL

youth may occur in parallel with the development of “off-putting” personality characteristics, such as social awkwardness and social anxiety[190]. The present results do not support this hypothesis in that CL individuals were not at higher risk of internalising problems compared to the EOP or AO trajectories examined in the present work. Instead, these findings may be partially explained by the suggestion that CL youth have lower levels of environmental difficulties (e.g. family adversity, receiving adequate school support etc.) and, more importantly, higher levels of effortful control. The interaction between these factors may decrease internalising problems (perhaps via good levels of peer support)[111, 178]. I have not tested this hypothesis directly but given the importance of understanding causal factors underlying changes in aggressive behaviour, I advocate further investigation.

While I did include conduct disorder as a search term, all studies identified were non-clinical observational studies that relied on reports of conduct problem behaviours. Although the measures that these studies used, including the CBCL and SDQ are predictive of CD and other clinical diagnoses[93], the CP trajectories themselves are not clinical. That said, research has nonetheless been able to show that CP trajectories associate with real life outcomes, especially for EOP youth. In fact, it has been suggested that early, sustained and assiduous intervention should be warranted for those who display behavioural problems in early age[191-193]. By doing so, I could prevent these individuals from persisting and perhaps limit them to stay within a CL trajectory, with consequent adult outcome improvement.

In the present study I have shown that the impact of behavioural problems in childhood and adolescence can be seen in early adulthood/adulthood across several interconnected domains of life. This highlights the urgency for intervention in CP children and adolescents. Combined with data coming from research on predisposing factors of developmental course of CP that suggest that risk factors may be found at

multiple levels, I speculate that multi-systemic (e.g. school and family) interventions may be most effective[194, 195].

Strengths and limitations:

To my knowledge, this is the first systematic review investigating the adult outcomes of CP trajectories. I considered a wide range of health, social and educational outcomes and found consistency in categorisation of CP trajectories across all studies. Several limitations apply to this review. Though trajectories were comparable across studies, I acknowledge that the methods used to derive these trajectories differed, with some studies using two time points and others applying general growth mixture models. Also, I acknowledge that growth mixture models have limitations, which include over-fitting the number of trajectories which can lead to biased estimates of covariate effects (i.e. outcomes of trajectories)[173, 196]. Furthermore, the measures used to construct these trajectories differed across studies (e.g. different versions of the SDQ or CBCL, or other teacher-reported measures) resulting in some degree of measurement inconsistency. I accept that the most reliable source of data should include multiple informants, and this was not often available in the studies identified for inclusion.

Similarly, outcome measurement slightly differed across studies within each meta-analysis, and this might be the reason for high heterogeneity in a number of cases. Due to small number of studies included in our meta-analyses, I decided not to run a sensitivity analysis to explore heterogeneity as suggested by Cochrane Handbook for Systematic Reviews of Interventions[197]. It should be noted however, that I-squared fell well within the acceptable limits i.e. ≤ 60% in the majority of meta-analyses[198]. In addition, a 95% confidence interval for the I-squared was not available for those studies where heterogeneity was high: this prevents us from concluding that heterogeneity was in effect falling outside acceptable limits[199].

I also acknowledge that the age of outcome in the studies I identified was quite low (mean age 22.5). It could be argued that this may have resulted in outcomes being particularly negative for AO individuals, due to the relatively short gap between onset of behavioural problems and outcome measurement However, ORs for AO individuals did not decrease in size when I conducted the meta-analyses without those studies with very early age at outcome (i.e. age 17 or 18), but slightly increased (results available in supplemental information). Our review has examined relatively early outcomes/correlates: future research should focus on long-term outcomes associated with different CP trajectories, beyond early adulthood.

I included data on both sexes as our original question did not seek to investigate this by gender. There were a large number of mixed sex samples and repeating analyses by sex would have led to small numbers in each analysis.

Although the majority of studies adjusted for factors such as socioeconomic status, gender, and other variables that usually associated with mental health, a minority did not provide adjusted summary statistics requiring the use of unadjusted effect sizes.

Conclusions and future directions:

To conclude, all trajectories of CP were associated with poorer outcomes in several psychosocial domains when compared to individuals without CP, particularly those belonging to the EOP trajectory. AO individuals were at intermediate risk and CL individuals at least risk. When compared to CL, EOP individuals were still showing higher risk on poor mental health, cannabis use, self-reported aggression, official records of criminal behaviour and poor employment. To investigate whether the same pattern of results is observed later on in life, future research should make use of longitudinal datasets with a wider age span. In addition, future work should focus on integrating multiple CP subtype categories (presence/absence of callous-unemotional traits and physical aggression vs rule-breaking) in order to better understand and

predict the development and outcome of young people with CP, given that age of onset is only one way of classifying CP[200]. Being able to identify those at higher risk of poor psychosocial outcome will help guide and allocate prevention and intervention programs more effectively.

Chapter 5

In this chapter, I will describe the theoretical background and methods to test a developmental cascade model of poor academic achievement in two trajectories of early-onset CP youth: EOP and CL. I will present results in text and graphically and discuss findings mainly in the light of potential clinical implications.

5.1 Developmental pathways towards poor academic achievement in early-onset conduct problems trajectories

Abstract: Early-onset CP trajectories (namely EOP and CL) differ in terms of their early risk factors. However, for those who follow early-onset trajectories, it remains unclear how these risks inter-relate at discrete developmental points and whether they form a developmental cascade which leads to low academic achievement in adolescence, itself a robust risk for long-term outcomes. Using longitudinal birth cohort data, this study sought to 1) examine differences in risk factors across trajectories and gender; 2) investigate longitudinal inter-relations between these risk factors and 3) test a developmental cascade model where prenatal maternal psychopathology led to low academic achievement via maternal bonding, language skills and ADHD symptoms. EOP males generally showed the highest risk and CL females the lowest on most domains considered. Each risk factor could predict the next one down the chronological line. However, the overall cascade effect was not significant. Multi-group analyses revealed differences in the association between ADHD and academic achievement, whereby CL females showed the highest magnitude of association. Results suggest targets for in-depth inquiry and intervention in specific groups of individuals with CP.

5.1.1 Introduction

Research has shown that EOP and CL individuals can be difficult to distinguish in terms of their behavioural manifestation in childhood, but they may also differ in terms

of prenatal and postnatal risks[98]. EOP youth have been shown to have predisposing familial risks, genetic and neuropsychological defects and temperamental hyperactivity, which could interact with environmental factors to potentiate more severe and persistent behavioural problems[101]. On the other hand, previous work has revealed similar prenatal and postnatal risk domains for CL youth as EOP children, such as prenatal maternal psychopathology, postnatal maternal bonding, and neuropsychological functioning; however, these risk factors are present at higher levels in EOP compared to CL. For example, mothers of EOP individuals have higher levels of anxiety during the prenatal period and lower levels of enjoyment of the child in the postnatal period compared to CL[98]. These differences at sensitive developmental periods may partially differentiate the divergent developmental trajectories of EOP and CL, and also account for different educational and social outcomes in adolescence and adulthood[111].

Interaction and transactions within and between multiple prenatal and postnatal risk domains may also have a cumulative impact on development, through what is known as a "developmental cascade"[201]. For example, developmental cascade models have been proposed by Dodge et al. (2009) to conceptualise the onset of illicit substance use; here, it was proposed that difficult child temperament could lead to parenting problems, which would, later on, be associated with behaviour and peer problems, which would eventually maximise the likelihood of substance use in adolescence[202]. Although research has identified a number of risk factors that are elevated in both CL and EOP trajectories, these have not been studied within the context of a cascade model.

The current study had two aims. First, I sought to explore whether established prenatal and postnatal risk exposures for CP differed across EOP and CL trajectory groups and across gender at discrete time-points during childhood. Second, I sought to examine longitudinal inter-relations between these risk factors using an integrated

developmental cascade model. Specifically, I tested the cumulative effect of prenatal maternal psychopathology, maternal bonding at age 2, language skills at age 3 and childhood symptoms of Attention Deficit Hyperactivity Disorder (ADHD) at age 7 on academic achievement at age 7-14. I focused on academic achievement as our outcome because this is a crucial factor for predicting future life success. In the United Kingdom, for example, without achieving a "Pass" (A*–C grade) in mathematics and English exams at the end of compulsory education, students are generally not considered for higher education, thus lowering chances of employability[203].

Differences between EOP and CL CP trajectories, and between males and females will be tested within this developmental model. With the present study, I hope to shed light on whether risk factors for different CP trajectory and gender groups may differ, but also inter-relate developmentally, from the prenatal period to adolescence, to increase risk of poor academic achievement, a domain that predicts several adult outcomes (e.g. mental health and employment). This may lead to a better understanding of what areas and time-windows should be targeted for intervention across different CP groups and gender.

CP risk factors as predictors of poor academic achievement

Research has demonstrated the predictive utility of a number of risk factors for CP that are also associated with poor academic achievement. These include: prenatal maternal psychopathology, maternal bonding, child's language skills and child's ADHD symptoms. This evidence will now be outlined individually for each risk factor. It should be noted that there may be other risk factors not considered in the present study that contribute to low academic achievement in adolescence in EOP and CL groups.

Prenatal maternal psychopathology and academic achievement

Previous work suggests that maternal psychopathology in the prenatal/perinatal period can have long-lasting effects on child cognitive ability and, subsequently, their

academic performance. Van der Bergh et al. (2004) found that high perinatal maternal anxiety was associated with lower Wechsler Intelligence Scale for Children (WISC) scores in mid-adolescence (more specifically, vocabulary and block design)[204]. In their review, Mennes, Stiers, Lagae, & Van den Bergh (2006) reported that children of prenatally anxious mothers performed selectively worse in tasks involving a higher load on cognitive control[205]. Barker et al.[206] (2011) found that antenatal depression was associated with lower IQ at age 8 in a large UK sample, while Niederhofer & Reiter[207] (2004) found that prenatal maternal stress was associated with significantly lower school marks when children were aged 5. Others have suggested that such associations are mediated by the effect of maternal stress and psychopathology on foetal brain development, which can underlie not only cognitive but also emotional and behavioural deficits at later stages of life[208]. Animal studies have offered evidence in support of this hypothesis and have suggested that maternal stress can selectively alter neuronal density in the cerebellum, an area that underlies cognitive and language functions[209, 210].

Maternal bonding and academic achievement

Past research has highlighted the association between positive maternal bonding and secure mother-child attachment and child social[211] and cognitive skills[212]. A relatively under-investigated area, however, is the impact of maternal bonding on later child academic skills. Kim, Boldt & Kochanska (2015) found that a positive mother-child relationship at age 8 predicted greater school competence (including school engagement) at age 10[213]. Among mothers of premature babies, Boyce, Cook, Simonsmeier & Hendershot[214] (2015) found that perceived hassle at the time of delivery (e.g. child is difficult to soothe or unusual care demands) predicted poorer child's vocabulary at age 6-8. Also, the authors also reported that mutual enjoyment in mother-child interactions was associated with better vocabulary skills, listening comprehension and applied problems.

Language skills and academic achievement

Early language skills have been consistently shown to associate with later academic achievement. For example, Young et al. (2002) found that young adults aged 19 who were previously identified as having language impairments at age 5 lagged significantly behind controls in all areas of academic achievement, even after controlling for intelligence[215]. Walker, Greenwood, Hart and Carta (1994) found that SES-related differences in child language prior to school were predictive of subsequent academic achievement assessed on standardised tests in kindergarten through grade 3[216]. Hohm, Jennen-Steinmetz, Schmidt & Laucht (2007) investigated whether language development at 10 months was predictive of scholastic achievement at age 10. Both expressive and receptive language performance at 10 months were significantly associated with cognitive and educational outcomes 10 years later[217].

ADHD symptoms and academic achievement

Attention-deficit/hyperactivity disorder (ADHD) is characterised by pervasive behavioural symptoms of hyperactivity, impulsivity and inattention, beginning in childhood[218]. Children and young people with ADHD-like symptoms lack the ability to control their attention, emotion and behaviour. This has important implications for mastering self-regulation strategies which are crucial to perform well academically[219]. Graziano, Reavis, Keane & Calkins (2007) showed that emotion regulation was not only significantly associated with teacher reports of children's academic success and productivity, but also with standardised literacy and math achievement scores[220]. A potential mechanism for this association is that ADHD has an impact on a number of cognitive domains (e.g. executive functions) which are necessary for academic success.

A dynamic cascade model of development

Given that these risk domains have been shown to associate with poor academic achievement, it is possible that interactions between these risks may engender a cumulative effect on the development of academic skills. To describe this developmental process, I proposed the dynamic cascade model presented in Figure 10 and 11. This is only one potential cascade model, and I recognise that several alternative cascade models may provide equally plausible explanations for these data. In addition, the chronological association of the variables taken in to account is based not only on previous literature but also on the data available at specific time-points in ALSPAC.

Specifically, I hypothesised that prenatal maternal psychopathology would predict poor maternal bonding to the child. It is plausible that depression and anxiety will have a negative impact on the development of the mother-child relationship, as evidenced in previous studies. For example, a depressed mother, low in mood and energy levels, may perceive the baby as a burden and may not enjoy caring for the child as much as a non-depressed mother would[221].

Poor bonding could be predictive of subsequent poor language skills; for example, poor verbal interactions between mother and child may impact on the child's capacity to develop appropriate language skills at later stages of life[222].

We hypothesised that child's language skills would be associated with child's ADHD symptoms. Language is a complex process that requires several cognitive skills, which are often impaired in ADHD. ADHD and language impairment may arise from shared neuropsychological deficits, but some researchers have suggested that linguistic ability may be important for subsequent development of attention and behaviour regulation[223, 224]. Others have posited that language may be important to effectively communicate needs and thus trigger effective parenting, reducing the child's levels of frustration that may otherwise manifest as abrupt or impulsive behaviour[225]. Please refer to previous section for the link between ADHD and academic achievement.

The present study has three main aims: first, I will investigate whether risk exposures for CP differed across EOP and CL trajectory groups and across gender at discrete time-points during childhood. Second, I will look at the longitudinal inter-relations of these risk factors and I will test for group and gender differences using nested model comparisons; third, I will use a developmental cascade model to test the indirect effect of prenatal maternal psychopathology, maternal bonding, language skills and childhood symptoms of ADHD on academic achievement in late childhood/early adolescence.

To our knowledge, this is the first study to test longitudinal associations between well-established (e.g. maternal psychopathology) and less studied (e.g. poor language skills) risk factors for early-onset CP subtypes and later academic achievement.

5.1.2 Methods

Participants

The Avon Longitudinal Study of Parents and Children (ALSPAC) is an ongoing UK epidemiological study established to understand how genetic and environmental characteristics influence health and development in parents and children. All pregnant women resident in the former Avon Health Authority of south-west England with expected delivery dates between April 1, 1991 and December 31, 1992 were eligible for recruitment. The resulting cohort included 14,541 pregnancies, of which 13,988 were alive at 12 months of age. ALSPAC is broadly representative of the UK population as a whole compared to 1991 National Census Data[123]. The ethnic composition of the initial sample, though consistent with the Avon area at the time of recruitment, was primarily White (96.09%). Ethical approval was obtained from the ALSPAC Law and Ethics Committee, as well as local Research Ethics Committees. More information is available on the study website: http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/.

Measures

-Conduct problem (CP) trajectories: Trajectories of CP development have previously been derived within the ALSPAC sample[98]. Latent class growth analysis (LCGA) was carried out by these authors using mother reports of CP at six time-points (ages 4, 7, 8, 10, 12, and 13). CP was measured using the "conduct problem" subscale of the Strengths and Difficulties Questionnaire[5]. The summed score at each age-point was dichotomised at the threshold of scores of ≥4, yielding six binary indicators for the latent growth classes[226]. Although this procedure may cause losing some information, established binary risk scores are better indicated for investigating chronic risk for outcomes [226]. The four resulting trajectories were described as low (70.1%), childhood-limited (CL; 12.1%), adolescent-onset (AO; 8.5%) and early-onset persistent (EOP; 9.2%). The total sample size was 7,218 (boys= 51%). Only participants classified as EOP and CL were included in the present analyses

-Prenatal maternal psychopathology: Maternal anxiety and depression was assessed by the Crown-Crisp Experiential Index (CCEI) and the Edinburgh Postnatal Depression Scale (EPDS, respectively[152, 153]. The anxiety subscale of the CCEI comprises eight self-report items, measuring the frequency with which anxiety-related feelings and behaviours are experienced along a four-point scale ("never" to "very often"). The EPDS is a 10-item self-report questionnaire of depressive symptoms experienced in the last seven days. Assessments were conducted at 18 and 32 weeks of gestation. These dimensions were used to identify a latent construct of prenatal maternal psychopathology.

-Maternal bonding: A measure of maternal bonding was obtained at age 2 years by combining items belonging to the following two domains: confidence (6 items) and enjoyment of baby (5 items). Example "confidence" items included "I feel unsure I am doing the right thing for the child" and "I feel it was the wrong time to have a child" (both reverse coded). "Enjoyment" items included "I enjoy seeing the child develop", and "I feel fulfilled by the child". Mothers rated these items from 0 (never feel) to 3 (exact

feeling). Summing these two subscales produced an overall maternal bonding score, with higher scores indicating greater bonding[159]. These dimensions were used to identify a latent construct of maternal bonding.

-Language skills: A measure of linguistic ability was derived using four subscales drawn from the MacArthur Toddler Communication Questionnaire[154]. These assessed vocabulary (receptive and expressive), plurals, past tense and word combination (the ability to join words together within an utterance) at age 3 years. These scores are based on parents' observations of their child's language skills on a day-to-day basis in the child's natural environment. These dimensions were used to identify a latent construct of language skills.

-Child's ADHD symptoms: ADHD was measured using maternal reports of three ADHD-related dimensions (impulsivity, hyperactivity and inattention) of the Development and Well-Being Assessment (DAWBA; interview at age 7[155]. The DAWBA was administered via computer-based package of questionnaires, interviews, and rating techniques used to assess adolescent psychopathology based on DSM–IV criteria. These dimensions were used to identify a latent construct of the child's ADHD symptoms.

-Child's academic performance: National standardised tests data were used to evaluate academic progress throughout primary education. Year-on-year progress of UK children is divided into "key stages", assessed by compulsory national tests at the end of each stage. For Key Stage 1, at the end of Year 2 (6-7 years of age), English (reading, writing) and Mathematics were examined. For Key Stage 2, at the end of Year 6 (10-11 years of age), tests of English, Science, and Mathematics were administered, while these three subjects were again assessed for Key Stage 3 at the end of Year 9 (13-14 years of age). Total scores for Key Stages 1, 2, and 3 were derived by summing the national curriculum level scores (Levels 1-8) achieved for each subject. This was taken to represent the latent academic score.

Statistical analyses

Step 1 – mean differences in the risk factors identified by the cascade model were calculated across CP groups and gender: differences in the distribution of observed measures of the relevant risk factors at each time-point were examined between EOP and CL groups and between males and females, using independent sample t-tests.

Step 2 – longitudinal associations between CFA-specified latent risk factors (plus group and gender differences): I estimated associations between each of the temporally-ordered risk factors and the next one down in chronological order (i.e. maternal psychopathology→maternal bonding; maternal bonding→language skills; language skills→ADHD symptoms; and ADHD symptoms→ academic achievement). I also estimated the associations between each predictor domain and the outcome. The domains were defined via latent factors derived by combining observed data, collected at different time-points (i.e. for maternal psychopathology data were collected at 18 and 32 weeks of gestation, but ADHD symptoms were available at age 7 only) using a Confirmatory Factor Analysis (CFA) framework. I employed nested models to compare coefficients across trajectory groups. Specifically, I compared a fully constrained model (omnibus model or reference model) to models where the paths of interest were freely estimated. Where the $\chi 2$ statistic for a model comparison was significant between EOP and CL trajectories, I conducted follow-up analyses that tested gender differences within the trajectory groups.

Step 3 – Grand cascade indirect effect and smaller indirect effects: I then tested an overall indirect effect or "grand developmental cascade", defined as the product term of each individual pathway in the cascade (i.e. maternal psychopathology→maternal bonding →language skills→ADHD symptoms→academic achievement). As standard errors of indirect effects derived analytically are known to be biased, they were calculated using bootstrap techniques with 10,000 replicates leading to bias corrected 95% confidence intervals[227].

Model fit was determined through the Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI; acceptable fit for both >0.90) and root mean square error of approximation (RMSEA; acceptable fit ≤0.08)[228, 229]. Maximum likelihood estimation was used to estimate the model parameters. Missing data were handled through full information maximum likelihood under the assumption that missingness was at random, given the variables included in the model[230]. All analyses were conducted using Mplus Version 8 for Windows[158].

5.1.3 Results

Step 1 – mean differences across groups and gender: Descriptive statistics for the manifest variables, from which latent factors were derived, are described in Tables 2 and 3. Nested models showed that the correlation coefficients varied significantly across groups ($\chi2(10)= 9.549$, $p= 0.002$) and also across gender within groups (CLm VS CLf: $\chi2(20)= 17.471$, $p< 0.000$; EOPm VS EOPf: $\chi2(20)= 26.053$, $p< 0.000$).

From independent-samples t-tests, youth following the EOP trajectory reported higher levels of prenatal maternal psychopathology and ADHD symptoms, and lower levels of maternal bonding and academic achievement, compared to their CL counterparts. EOP and CL youth did not significantly differ on their language skills. With regard to gender differences, within the CL trajectory, females had significantly higher scores on the "vocabulary", "plurals" and "word combination" language subtests than males. A similar trend was observed within the EOP trajectory, with females scoring higher on all four language components (vocabulary, plurals, past tense and word combination). For the three ADHD sub-components (impulsivity, hyperactivity and inattention), females performed better than males in both the CL and EOP trajectories. Regarding academic achievement, females in both the EOP and CL trajectory groups showed higher KS1 (age 6-7) test performance than their male counterparts. In the EOP group, females also performed better than males at the KS3 (age 13-14) examination point (Table 3).

Table 2 Mean, standard deviations, and t-test comparison between CL and EOP on observed variables scores.

Concept – var name	**CL (N=875)**				**EOP (N=666)**				
	N present(missing%)	Mean	Std dev.	95% CI (min max)	N present(missing%)	Mean	Std dev.	95% CI (min max)	p-value
1) Maternal psychopathology (prenatal)	.	.	.	.		.	.	.	**.**
Anxiety (18 wks) - anx_18w	87(9.82%)	5.14	3.58	(4.89, 5.39)	596(10.51%)	5.79	3.55	(5.50, 6.07)	**0.001**
Depression (18 wks) - epds_18w	77(8.8%)	7.23	4.76	(6.91, 7.57)	59(8.86%)	7.97	4.77	(7.59, 8.35)	**0.004**
Anxiety (32 wks) - anx_32wks	56(6.4)	5.45	3.61	(5.21, 5.69)	51(7.66%)	6.35	3.75	(6.05, 6.65)	**< 0.001**
Depression (32 wks) - epds_32w	45(5.14)	7.23	5.12	(6.88, 7.58)	39(5.86%)	8.59	5.21	(8.18, 9.01)	**< 0.001**
3) Maternal bonding	.	.	.	.		.	.	.	**.**
Maternal confidence – matcon	57(6.51%)	13.92	2.36	(13.76, 14.08)	54(8.11%)	13.41	2.36	(13.21, 13.59)	**< 0.001**
Maternal enjoyment - matenj	61(6.97%)	12.43	2.56	(12.25, 12.60)	54(8.11%)	11.93	2.68	(11.7, 12.14)	**< 0.001**
4) Language	.	.	.	.		.	.	.	**.**
Word combination - wordcomb	27(30.08%)	21.96	4.85	(21.63, 22.29)	30(4.51%)	21.54	5.28	(21.1, 21.95)	0.125
Past tense - pasttense	33(3.77%)	33.18	10.02	(32.51, 33.86)	35(5.25%)	32.47	11.11	(31.61, 33.34)	0.115
Plurals - plurals	38(4.34%)	9.99	2.23	(9.83, 10.14)	40(6.01%)	10	2.29	(9.82, 10.17)	0.877
Vocabulary - vocab	43(4.91%)	226.68	32.98	(224.46, 228.90)	46(6.91%)	223.26	36.06	(220.45, 226.06)	0.053

5) ADHD	.	.	.	.		.	.	.		**.**
Impulsivity (7yrs) impulse7		1.88	2.06	(1.73,	2.02)	3	2.45	(2.80,	3.20)	**< 0.001**
Activity (7yrs) activity 7		1.87	2.55	(1.69,	2.04)	3.51	3.22	(3.25,	3.77)	**< 0.001**
Inattention (7yrs) inatt 7		3.4	4.1	(3.11,	3.68)	5.88	4.98	(5.48,	6.29)	**< 0.001**
6) Academic achievement	.	.	.	.		.	.	.		**.**
KS1 – ks1	141(16.11%)	9.66	3.67	(9.40,	9.93)	107(16.06%)	8.94	3.61	(8.64, 9.24)	**< 0.001**
KS2 – ks2	116(13.25%)	12.81	1.91	(12.67, 12.94)		90(13.51%)	12.31	2.13	(12.13, 12.4)	**< 0.001**
KS3 – ks3	210(24%)	16.37	3.75	(16.08, 16.65)		146(21.92%)	15.32	3.81	(14.9, 15.6)	**< 0.001**

	CL Males (N=474)		CL Females (N=401)				EOP Males (N=379)		EOP Females (N=287)			
	Mean	Std dev.	Mean	Std dev.	*t*	p-value	Mean	Std dev.	Mean	Std dev.	*t*	p-value
1) Maternal psychopathology (prenatal)	.	.	.	.	.		.	.	.	.	.	
Anxiety (18 wks) - anx_18w	5.12	3.51	5.19	3.67	-0.28	0.782	5.81	3.55	5.76	3.55	0.15	0.874
Depression (18 wks) - epds_18w	7.12	4.62	7.37	4.91	-0.73	0.461	8.18	4.86	7.69	4.63	1.24	0.214
Anxiety (32 wks) - anx_32wks	5.39	3.54	5.53	3.71	-0.56	0.575	6.48	3.84	6.17	3.64	1.02	0.304
Depression (32 wks) - epds_32w	7.09	4.89	7.4	5.38	-0.86	0.385	8.81	5.52	8.31	4.78	1.19	0.23
3) Maternal bonding	.	.	.	.	.		.	.	.	.	.	
Maternal confidence – matcon	13.98	2.38	13.85	2.33	0.75	0.451	13.3	2.4	13.54	2.29	-1.29	0.195
Maternal enjoyment - matenj	12.46	2.54	12.39	2.6	0.37	0.71	11.76	2.82	12.15	2.46	-1.79	0.072
4) Language	.	.	.	.	.		.	.	.	.	.	

Table 3 Mean, standard deviations, and t-test comparison between males and females within the EOP and CL trajectories on observed variables scores.

Vocabulary - vocab	222.37	39.1	231.84	22.66	**-4.2**	< 0.001	218.87	39.13	229.05	30.66	**-3.55**	< 0.001
Plurals - plurals	9.81	2.43	10.2	1.96	**-2.53**	0.011	9.78	2.47	10.28	2.01	**-2.7**	0.006
Past tense - pasttense	32.57	10.94	33.91	8.77	-1.92	0.054	31.15	12.03	34.19	9.52	**-3.42**	< 0.001
Word combination - wordcomb	21.56	5.26	22.42	4.28	**-2.56**	0.01	20.84	5.72	22.44	4.49	**-3.76**	< 0.001
5) ADHD	.	.	.	.	.		.	.	.	.	.	
Impulsivity (7yrs) impulse7	2.04	2.17	1.69	1.9	**2.39**	0.017	3.31	2.51	2.59	2.31	**3.6**	< 0.001
Activity (7yrs) activity 7	2.23	2.72	1.45	2.27	**4.34**	< 0.001	4.41	3.27	2.31	2.72	**8.32**	< 0.001
Inattention (7yrs) inatt 7	4.06	4.46	2.62	3.49	**5.001**	< 0.001	6.9	5.1	4.55	4.5	**5.87**	< 0.001
6) Academic achievement	.	.	.	.	.		.	.	.	.	.	
KS1 – ks1	9.34	3.68	10.03	3.62	**-2.55**	0.01	8.48	3.58	9.51	3.56	**-3.38**	< 0.001
KS2 – ks2	12.8	1.93	12.81	1.86	-0.09	0.927	12.22	2.04	12.41	2.23	-1.07	0.285
KS3 – ks3	16.37	3.73	16.36	3.77	0.04	0.967	14.98	3.98	15.73	3.56	**-2.22**	0.026

Step 2 – longitudinal associations between CFA-specified latent risk factors (plus group and gender differences): the correlation matrix (Table 4) shows the correlations between all latent variables. The model presented in Figure 10 and 11, offered an adequate fit for the data: $\chi2(480)= 10083.853$, $p<.0001$; CFI= 0.963, TLI= 0.957; RMSEA= 0.047 (90% CI= 0.042 – 0.053). As hypothesised, prenatal maternal psychopathology predicted lower levels of maternal bonding, which in turn predicted poorer language skills (although the coefficient in the CL group was borderline significant), itself predicting worse ADHD symptoms, which in turn predicted lower levels of academic achievement. In terms of the associations between each predictor domain and academic achievement, I found that maternal psychopathology negatively predicted academic achievement in EOP only (although the coefficient was only marginally significant). Against our expectations, I found that maternal bonding negatively predicted academic achievement in both groups. Language skills positively predicted academic achievement in both groups.

We tested differences in path coefficients across trajectories using nested model comparisons (Table 16 in the Appendix). I first tested an omnibus null model, constraining the four paths that formed the “grand cascade” to be invariant for CL and EOP groups against a model where these four parameters were allowed to be freely estimated and found a significant difference ($\chi2 (4)= 4.485$, $p= 0.034$). Upon further investigation, I found that the only path coefficient that significantly differed across the two trajectory groups was the path from ADHD to academic achievement ($\chi2 (1)= 3.986$, $p= 0.046$) where CL showed a higher coefficient compared to EOP (CL: b= -0.359, SE= 0.044, p= <0.001; EOP: b= -0.213, SE= 0.050, p= <0.001). When I conducted nested model comparisons between gender-split trajectories, CL females showed a significantly higher association between ADHD and academic achievement (b= 0.407, SE= 0.063, p= <0.001) compared to the other groups (CLm: b= -0.324, SE= 0.062, p= <0.001; EOPm: b= -0.199, SE= 0.065, p= 0.002; EOPf: b= -0.233, SE=

0.076, p= <0.003). Other paths did not significantly differ across trajectories or gender. These findings held when ADHD was sub-divided into its three components (i.e. impulsivity, hyperactivity and inattention; see Table 17 in the Appendix).

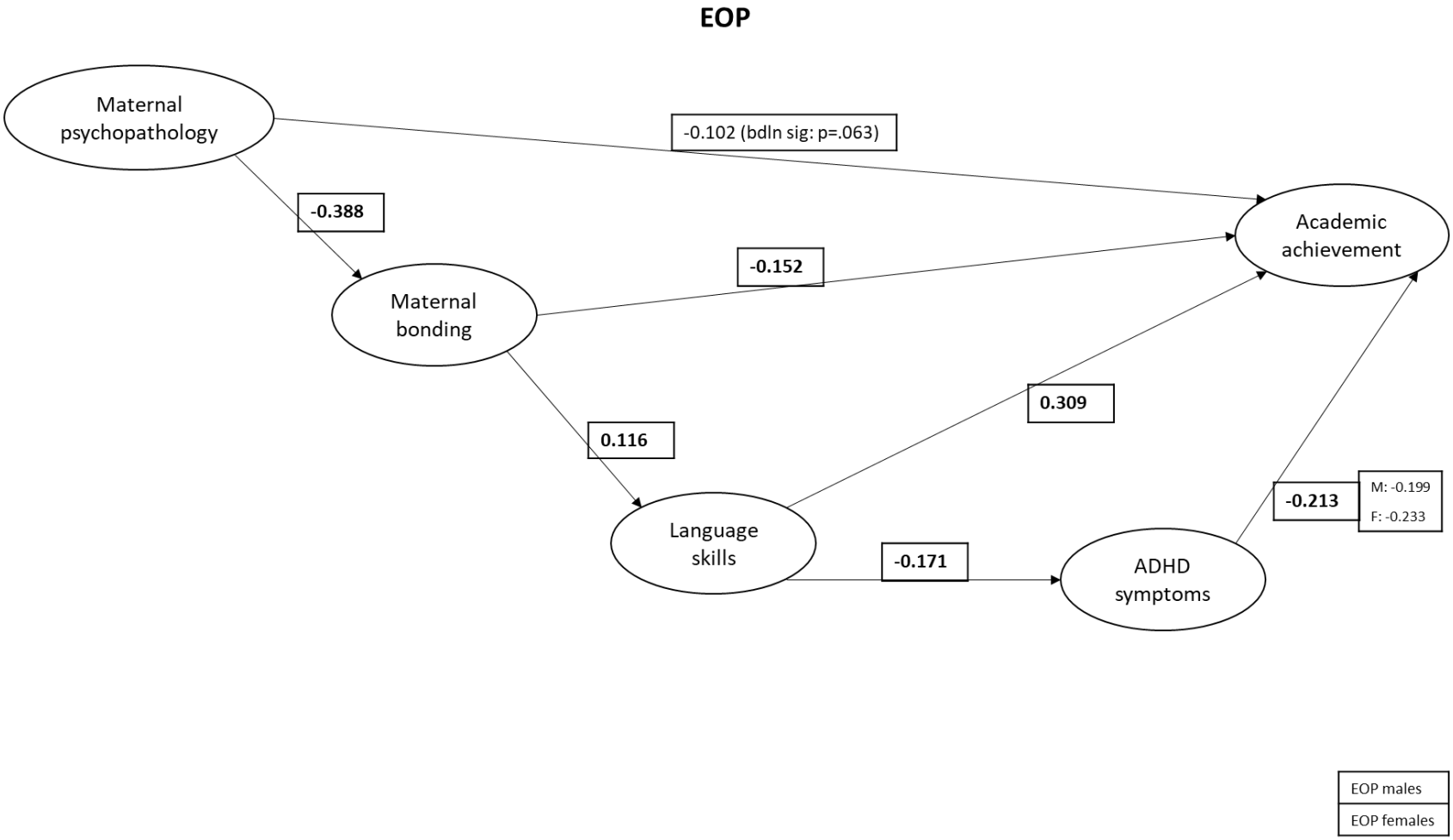


Figure 10 Dynamic cascade model in EOP showing within-group sex differences (when present).

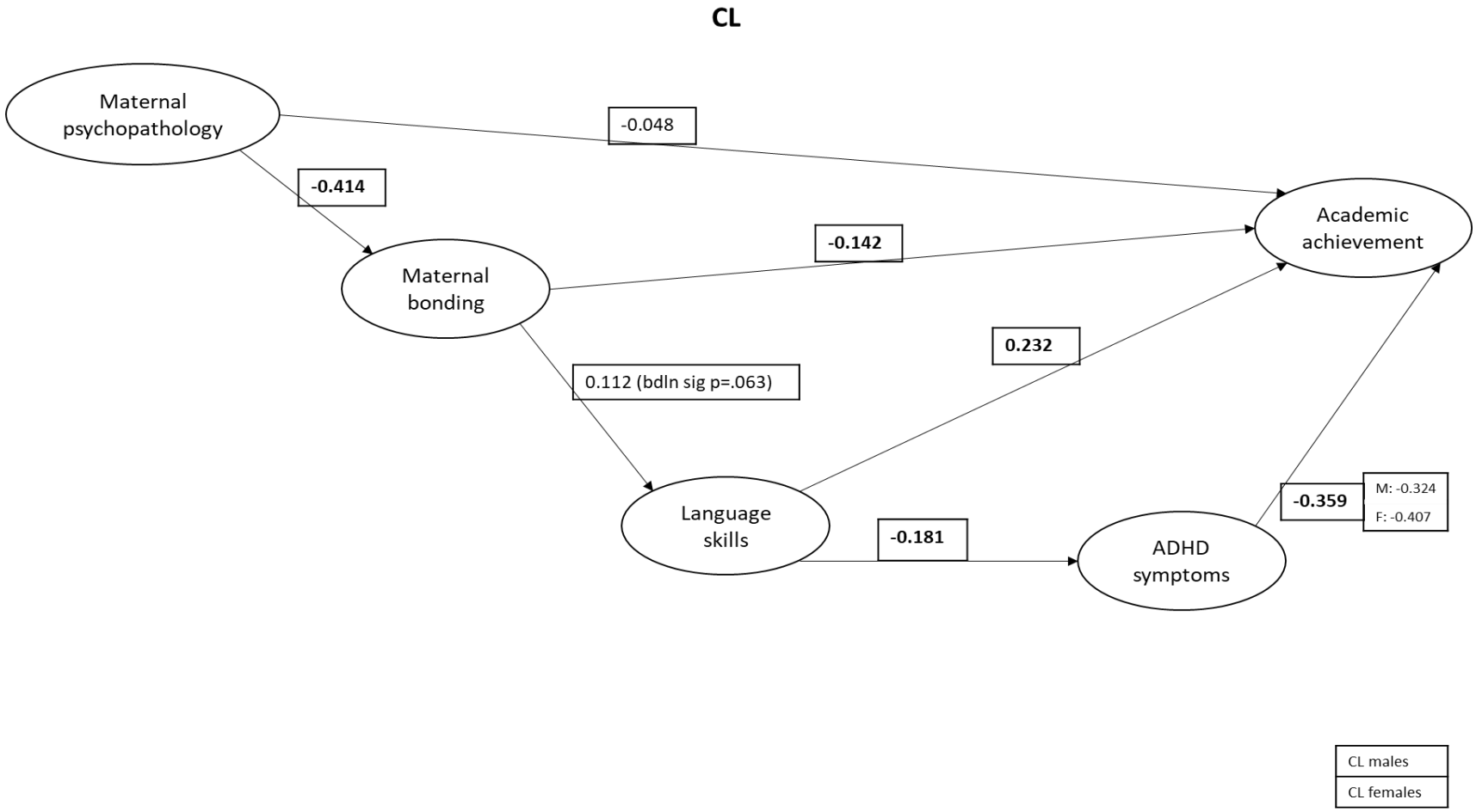


Figure 11 Dynamic cascade model in CL showing within-group sex differences (when present).

Table 4 Correlation matrix between all latent factors. Males are shown in the bottom left and females in the top right of the diagonals

CL	Academic	ADHD	Language	MatBond	MatPsy
Academic	.	-0.413***	0.286***	-0.032	**-0.118***
ADHD	-0.354***	.	**-0.114**	-0.211**	0.177**
Language	0.291***	**-0.218*****	.	-0.218	**-0.115**
MatBond	-0.029	-0.181**	0.122	.	-0.453***
MatPsy	**0.049**	0.023	**-0.004**	-0.376***	.
EOP	Academic	ADHD	Language	MatBond	MatPsy
Academic	.	-0.273***	**0.235****	0.077	-0.070
ADHD	-0.204**	.	-0.195*	-0.122	0.149*
Language	**0.398*****	-0.147**	.	0.175*	**-0.056**
MatBond	-0.111	-0.199*	0.134*	.	-0.332***
MatPsy	-0.126*bdln	0.021	**-0.213****	-0.423***	.

***= *p*= <0.000; **= *p*= <0.001; *= *p*= <0.05. Bold coefficients indicate a significant difference between males and females.

Step 3 – “Grand cascade” indirect effect and smaller indirect effects: I did not find a strong evidence for a significant “grand cascade” indirect effect for either the two-group (i.e. CL and EOP) or the four-group analyses (i.e. CLm, CLf, EOPm and EOPf), as the upper 95% confidence intervals was “0” for all bootstrapped estimates (see Table 5). All estimates of indirect effects were negative, indicating their harmful effect on academic achievement. In other words, results point to a small borderline significant negative effect of maternal psychopathology, with one SD increase in the latent maternal psychopathology dimension having a negative indirect effect (cascading via mat bonding, language develop and ADHD) of 0.003/0.002 units in academic achievement. I estimated three additional (smaller) indirect effects. These were 1) the indirect effect from maternal psychopathology carried via maternal bonding to academic achievement, 2) the indirect effect from maternal bonding carried via language to academic achievement and 3) the indirect effect from language carried via ADHD to academic achievement. Not surprisingly 2) and 3) were all positive, indicating the positive effect of maternal bonding and language development. The fact that the estimate indirect effect of maternal psychopathology that involves maternal bonding was also positive requires further exploration. 1) and 3) were significant in both EOP and CL and 3) had a higher coefficient in CL than EOP (although non-significantly as 95% bootstrapped confidence interval on the difference between the two did cross zero).

Table 5 “Grand cascade” indirect effects from maternal psychopathology to academic achievement plus three smaller indirect effects

	Prenatal	Age 2	Age 3	Age 7	Age 7-14			
Grand cascade						**Estimate**	**95%CI (lower)**	**95%CI (upper)**
CL	MatPsy→	MatBond→	Language→	ADHD→	Academic	-0.003	-0.010	0.000
EOP	MatPsy→	MatBond→	Language→	ADHD→	Academic	-0.002	-0.007	0.000
						Estimate	95%CI (lower)	95%CI (upper)
CLm	MatPsy→	MatBond→	Language→	ADHD→	Academic	-0.004	-0.012	0.000
CLf	MatPsy→	MatBond→	Language→	ADHD→	Academic	-0.001	-0.008	0.001
EOPm	MatPsy→	MatBond→	Language→	ADHD→	Academic	-0.001	-0.005	0.001
EOPf	MatPsy→	MatBond→	Language→	ADHD→	Academic	-0.003	-0.018	0.000
Smaller ind. effects						**Estimate**	**95%CI (lower)**	**95%CI (upper)**
CL	MatPsy→	MatBond→			Academic	0.059	0.019	0.105
EOP	MatPsy→	MatBond→			Academic	0.059	0.016	0.114
CL		MatBond→	Language→		Academic	0.026	0.000	0.069
EOP		MatBond→	Language→		Academic	0.036	0.003	0.074
CL			Language→	ADHD→	Academic	0.065	0.026	0.106
EOP			Language→	ADHD→	Academic	0.036	0.012	0.067

5.1.4 Discussion

In the present work, I first aimed to explore whether risk exposures for CP differed across EOP and CL trajectory groups and gender at discrete time-points during childhood. Second, I sought to investigate a developmental cascade model here longitudinal inter-relations between these risk factors and I tested for trajectory group and gender differences in path coefficients. Third, I tested the indirect effects underlying this cascade model. Specifically, I tested if prenatal maternal psychopathology on academic achievement in late childhood/early adolescence (age 7-14) via the intervening variables of maternal bonding at age 2, language skills at age 3 and childhood symptoms of ADHD at age 7.

First, regarding exposure differences between the two (EOP and CL) groups, these findings supported previous studies[98] that EOP youth reported significantly higher risk exposure compared to CL individuals on all domains, except for language skills at age 3. As stated, this finding is in line with previous literature showing greater risk exposure across several prenatal and postnatal domains among EOP individuals. The presence of higher levels of risk may make it more difficult for EOP individuals to be exposed to opportunities for change (e.g. poor maternal bonding may form the basis for difficulties in socialising, which in turn may increase risk for social exclusion and victimisation, which will increase risk of antisocial behaviour). Of particular relevance is the fact that the EOP group showed significantly higher risk for poor academic achievement compared to CL youth. This may lead to more persisting patterns of antisocial behaviour through various mechanisms (e.g. poor academic achievement, school failure, association with deviant peers, engagement in serious antisocial activities, imprisonment, difficulty to find a job, persisting criminal and illegal activities etc.). Alone, this finding may indicate that intervention efforts to improve academic achievement should target primarily individuals with a persistent pattern of CP.

With regard to discrete gender differences, I observed lower levels of risk in females. Girls in the CL group performed significantly better than males on vocabulary, plurals and word combination. In the EOP, females performed significantly better than males on the tests concerning past tense also. This reflects previous findings from a large European study by Erikkson et al. (2011), who found that girls were slightly ahead of boys in terms of early communicative gestures, in productive vocabulary, and in combining words[231]. Better language skills in females may be the result of more efficient neural mechanisms underlying the processing of linguistic stimuli compared to males. This biological advantage may act as a protective factor against both the development of CP and academic underachievement. Females also showed, as expected, an advantage (lower symptoms) compared to males on ADHD symptoms.

In terms of academic achievement, females showed better standardised test results over males in both trajectories. This was most evident at Key Stage 1 (e.g. age 6-7). Again, this may stem from a general advantage in females over males in terms of cognitive skills such as executive functions, which are necessary to perform well at school. It is interesting to note that our finding that females in both trajectories had lower levels of ADHD symptoms is in contrast with the paradoxical gender effects described by Loeber and Keenan[232] who observed in their review that although girls show a much lower prevalence in Conduct Disorder than males, where they do they are at higher risk of other comorbid conditions (e.g. hyperactivity) compared to males. It could be argued that this effect is only seen in clinical populations and therefore it is not observed in our study (which may include only a minority of individuals who meet the threshold for medical diagnosis of a Conduct Disorder).

Second, this is the first study where previously identified risk factors for CP are shown to be longitudinally associated to one another from prenatal period to adolescence. In the cascade, each predictor domain associated with the next in both EOP and CL groups. However, the path from maternal bonding to language skills was of borderline

significance in the CL group. A significant difference across groups in terms of magnitude of coefficient was found in the path from ADHD to poor academic achievement. Here, CL showed a significantly higher coefficient than EOP. In general, ADHD presents with less severity in the CL group compared to the EOP group. However, it seems that these lower ADHD symptoms in CL are more strongly predictive of future academic problems compared to EOP: targeting ADHD symptoms in children with CP may drastically reduce risk of poor academic achievement in adolescence, especially in those that are on a desisting trajectory. Future research should try to identify in early age those individuals who are more likely to be on a persisting vs desisting trajectory.

Upon further investigation, I found that females showed a higher coefficient compared to males within both trajectories on this specific path. That is, although females in both CP groups have significantly less severe ADHD symptoms compared to males, these are significantly more strongly associated with future academic problems. It may be argued that gender potentiates the effect of ADHD symptoms in predicting future academic problems. The present finding suggests that prevention efforts in CP should target ADHD symptoms particularly in females, as these strongly predict higher risk of poor academic achievement in adolescence in both early-onset subtypes of CP.

In addition, the distal paths in the EOP group (e.g. maternal psychopathology to academic achievement) had a slightly higher coefficients than CL. However, a formal difference across groups was not found when formal statistical tests (i.e. nested model comparison) was carried out. In line with the Developmental Origins of Health and Disease theory[233] I speculate that higher levels of maternal psychopathology in EOP compared to CL may account for foetal neurodevelopmental abnormalities, which have a long lasting impact and can be seen at the level of cognition and behaviour at later stages of life[234]. In this sense, intervention targeting pregnant women with high levels of

depressive symptoms may be important in reducing risk of poor language skills and later academic achievement in offspring, independent of postnatal processes.

Although the paths from maternal psychopathology to academic achievement, and from language to academic achievement were in the expected direction (negative for the former and positive for the latter), the specific effect from maternal bonding to academic achievement estimated by our model was negative. The finding held when maternal bonding was broken down in to its two components (maternal confidence and maternal enjoyment of the child). It could be that individuals with lower maternal bonding turn to more external sources of satisfaction and security, such as school achievement. Or, it could be that higher bonding correlates with nurturance, a factor that may impede the development of independent and achievement behaviours.

Third, against our expectations, the results of this study did not seem to support the proposed developmental cascade. The indirect effect carried through maternal bonding, language skills and ADHD was found to be non-significant. However, I tested for and found smaller indirect effects. For example, higher maternal psychopathology associated with lower academic achievement via lower maternal bonding and the one from language to academic achievement via ADHD. It is of particular interest to note that the latter was higher (although non-significantly) in CL compared to EOP (CL: b= 0.065, CI= 0.026 – 0.106; EOP: b= 0.036, CI= 0.012 – 0.067). This strengthens the hypothesis that ADHD plays an important role in the development of academic problems in youth with CP, particularly in the CL trajectory.

Strengths and limitations:

Several limitations should be borne in mind when interpreting the results of the present study. First, as in all pathway models, I highlight that I have tested one of many potential cascades. Factors that form this specific cascade can be potentially re-organised and other variables can be included to form different models. Second, I

acknowledge that there are differences in how the constructs used for this model were measured: while academic achievement was measured through official school records and takes into account three time points (KS1, KS2 and KS3), others (such as maternal bonding and language skills) were measured at one time point and using only one informant, thus making the measurement not particularly solid. Also, we recognise that the trajectories we employed were made using dichotomised scores from SDQ: this is likely to have caused loss of information.

Although ALSPAC features a broad and representative sample of individuals from different socioeconomic backgrounds, the entire cohort features relatively low rates of ethnic minorities. In addition, we did not control for family SES in this particular model. Future research should address this by employing a more ethnically-diverse sample and by controlling for family SES. In addition, ALSPAC presents with high rates of attrition over time, with children of younger and poorer mothers being more likely to be lost in follow-ups. However, although attrition affected prevalence rates of depression in the mother and the externalising behaviours in the children, previous studies have suggested that the associations between risks and outcomes remained intact, although conservative estimates, of the likely true effects[235].

Another limitation of this work is the absence of genetics data in the model. Individuals with CP (particularly those with high levels of callous-unemotional traits, which, according to previous literature are more likely to belong to the EOP group) may show a genetic vulnerability. In this sense, the association between risk factors may be explained, at least in part, by to underlying (unmeasured) genetic factors[236].

Conclusions and future directions:

The present study investigated potential differences in several prenatal and postnatal risk factors across two early-onset CP groups, namely CL and EOP, and across gender. In addition, I assessed whether these risk factors were associated

longitudinally and I tested for differences in these relationships across these two developmental groups and across gender. Furthermore, through a developmental cascade model, I examined whether an effect was being carried from prenatal maternal psychopathology through postnatal maternal bonding at age 2, language skills at age 3, ADHD symptoms at age 7 to academic achievement at age 7-14.

We found that EOP individuals were generally exposed to higher levels of risk across most domains compared to CL, and in general, higher levels of risk were seen in males across the two trajectories examined. I did not find a strong evidence for an indirect effect being carried through the grand cascade, starting with prenatal maternal psychopathology and ending with academic achievement. However, these risk domains could predict the following one down in the chronological line. In particular, I found that ADHD predicted poor academic achievement (and significantly more so for CL females). In addition, I found that ADHD partially explained the association between language skills and academic achievement more so in CL than EOP. This may highlight the importance of targeting CL individuals for intervention programs in order to decrease the impact that ADHD symptoms will have on later academic achievement. Future research should focus on what factors associated with females in the CL group may explain why ADHD in this specific group is more strongly predictive of later academic problems.

Chapter 6

In this chapter, I will explore the potential role that school experience in adolescence has in mediating the association between CP trajectories and later NEET status. To do this I will adopt methods from modern mediation analysis that invoke the concept of potential outcomes, e.g. outcomes that would be observed under different hypothetical interventions. Results will be discussed in the light of practical implications for schools.

6.1 The role of school experience in mediating the association between conduct problems trajectories and NEET status

Abstract: Previous research has shown that children and adolescents on different CP trajectories are exposed to a higher risk of being not in education employment or training (NEET) in young adulthood/adulthood. However, there has not been much research on factors that may mediate the association between CP trajectories and NEET status at age 20. In the present study, I investigated the role of school experience at age 14 years in mediating the association between CP trajectory group defined from age 4 to 13, namely Early-Onset Persistent (EOP), Adolescent-Onset (AO) and Childhood-Limited (CL), and Low (L) and NEET status at age 20. Using G-computation, I estimated the natural direct and indirect effects of CP trajectory group on NEET using data from ALSPAC. I found that school experience mediates the relationship between EOP trajectory and NEET status at age 20. The impact of attrition on these results was also investigated via imputation of missing values under the assumption of missing at random. These findings highlight the role of schools in potentially minimising the risk of becoming NEET in high-risk youth.

6.1.1 Introduction

As reported in previous chapters, research has identified three developmental trajectories for CP across childhood and adolescence, in addition to a “normal”

trajectory group of individuals (or Low) who do not develop CP. EOP youths show early childhood-onset CP, with these behaviours persisting and often increasing in frequency and severity into adolescence[95, 181]. CL youths also show childhood-onset CP, but these behaviours decrease to low levels in adolescence, while AO individuals show no childhood symptomatology, with behavioural problems beginning in early-adolescence/adolescence.

Research has shown that these three trajectory groups differ in relation to risk of poor psychosocial outcomes in early adulthood/adulthood, such as poor health and mental health, antisocial behaviour, and “Not being in Education, Employment, or Training” (NEET)[2, 55]. The latter outcome is particularly important given its costs to society. Previous studies (Coles et al., 2010) estimated that in 2009 there were 208,000 individuals aged 16-18 reported as NEET in the UK, resulting in a financial cost of up to £32 billion and a resource cost of £76 billion[237]. A more recent report, shows that in 2017 about 790,000 people (13.3% of the UK population aged 16-24) were NEET[238]. As such, it is important to identify the factors that explain, at least in part, why children and adolescents on different CP trajectories are at risk of later negative outcomes such as being NEET.

Investigations into childhood and adolescent factors that could mediate the association between CP and poor psychosocial outcomes (such as antisocial behaviours and being NEET) have suggested that in children displaying CP, concentration problems and ADHD symptoms could promote persistent antisocial behaviour in both adolescence and adulthood[239]. ADHD symptoms may lead to more frequent coercive behaviour management from parents and teachers and, in turn, sustained levels of aggressive/disruptive behaviour over the developmental course. Peer rejection has also been associated with aggressive behaviour in adolescence, and later stages of life[240, 241]. Peer rejection may serve to hasten the disruptive child's drift into a deviant peer group in late childhood and early adolescence. In these deviant peer groups,

delinquent behaviour is easily reinforced, paving the way towards later antisocial behaviour and general maladjustment.

Finally, school factors have been related to CP outcomes. For example, poor academic achievement has been found to be strongly predictive of poor employment outcomes and delinquent behaviour in youth displaying CP[112]. Furthermore, previous studies with non-CP youth suggest that other, more subjective factors such as school connectedness promote positive youth development, and that poor school connectedness in year 8 at age 12 is associated with mental health difficulties and substance use in year 10 at age 14[113]. School enjoyment may also impact these outcomes; for example in a UK study authors found that school enjoyment at age 7 was associated with better school engagement at age 10 and 13, which was in turn predictive of greater academic progression from Key Stage 3 to Key Stage 4 (between age 11 and 14)[109]. However, these studies have investigated typically developing individuals and it is not clear whether aspects of school experience impact the development of youths with CP as well. More specifically, it is not clear whether school connectedness and enjoyment can mediate the association between CP and more distal outcomes such as poor educational and social outcomes (i.e. being NEET) in young adulthood.

The primary aim of the present study was to investigate the role of school connectedness and enjoyment as potential mediators of the association between CP class membership and risk of being NEET in young adulthood (age 20). Specifically, I tested for mediation in each CP trajectory group, namely EOP, AO and CL. Our main hypothesis is that school experience would play a protective role against being NEET in early adulthood to a different extent depending on the developmental trajectory considered. Understanding whether school experience in different groups of CP youths may impact the course of development toward adverse psychosocial outcomes can inform targeted prevention and intervention efforts, particularly at the level of schools.

6.1.2 Methods

Participants

The Avon Longitudinal Study of Parents and Children (ALSPAC) is an ongoing UK epidemiological study established to understand how genetic and environmental characteristics influence health and development in parents and children. All pregnant women resident in the former Avon Health Authority of south-west England with expected delivery dates between April 1, 1991 and December 31, 1992 were eligible for recruitment. The resulting cohort included 14,541 pregnancies, of which 13,988 were alive at 12 months of age. ALSPAC is broadly representative of the UK population as a whole compared to 1991 National Census Data[123]. The ethnic composition of the initial sample, though consistent with the Avon area at the time of recruitment, was primarily white British (96.09%). Ethical approval was obtained from the ALSPAC Law and Ethics Committee, as well as local Research Ethics Committees. More information are available on the study website: http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/

Measures

-Conduct problems trajectories: CP trajectories have previously been described within the in ALSPAC sample (see Barker & Maughan, 2009) and these variables were used in this study. Unlike the data in Chapter 5, here I used data on all participants for which CP class was available. Trajectories were defined by Barker and Maughan using latent class growth analysis (LCGA) models applied to six assessments (at ages 4, 7, 8, 10, 12, and 13) of mother-reported CP, measured using the “conduct problem” subscale of the Strengths and Difficulties Questionnaire (SDQ, Goodman, 2001). The four resulting trajectories were described as low (L= 70.1 %), childhood-limited (CL= 12.1 %), adolescent-onset (AO= 8.5 %) and early-onset persistent (EOP= 9.2 %). Sample size was 7,218 (boys= 51%)[98].

-School experience: ten questions about school experience were asked to study participants. Seven were about school connectedness such as “School is a place where other pupils are friendly” or “School is a place where other pupils accept me” and three about school enjoyment such as “School is a place where I get excited about the work I do” or “School is a place where I enjoy what I do in class”. The questions were in the form of statements with a choice of response boxes to tick ranging from strongly agree to strongly disagree. Two total sum scores (one for connectedness and one for enjoyment) were generated for the present analyses. Data were collected when participants were 14.

-NEET: respondents had to choose between answering “yes” or “no” to the question “Are you currently in education, employment or training”. This question was asked when respondents were 20 years old.

Potential confounders for our analysis were identified based on evidence from the literature regarding risk factors for NEET that may be related to the exposure and mediators. The following variables were considered as potential confounders:

-Gender: male or female.

-Ethnicity: white or non-white.

-Social class based on maternal occupation: unskilled, partly skilled, skilled manual, skilled non-manual, managerial and technical, professional. Responses were collapsed as follows to generate a binary variable: unskilled, partly skilled, skilled manual= “Medium low/low social class” and skilled non-manual, managerial and technical, professional= “Medium high/high social class”. This information was collected when mother was pregnant.

-Maternal depression: Edinburgh Postnatal Depression Scale (EPDS). This is a 10-item self-report questionnaire measuring depressive symptoms over the past 7 days (e.g. “I have been so unhappy that I have had difficulty sleeping”, “I have felt sad or

miserable"). Each item is scored on a four-point Likert scale (0-3), with a total score ranging from 0-30. A cut-point of ≥10 was used as the threshold for a possible depression. In primary care settings this is often the threshold used to indicate a risk that depression may be present and a woman should receive further evaluation[153]. Despite the name this measure can also be used during gestational period and I used data collected at 18-20 week gestation[242].

-Income Deprivation Affecting Children Index (IDACI) score: IDACI is an index of poverty in the neighbourhood where children and young people live. It measures the proportion of children and young people in a local area under the age of 16 that live in a low-income household, where higher scores correspond to more impoverished areas[134]. This data were collected when participants were in Key Stage 4.

Ethical approval to collect the outcome data and undertake the analysis was obtained from ALSPAC's Law and Ethics Committee, a registered Institutional Review Board.

Analyses

Identification of confounders: to explicitly specify the assumed relationships among exposure (CP trajectories), mediators (school connectedness and enjoyment treated as a two dimensional factor: school experience), and outcome (NEET status at age 20 years), and also to identify potential confounders in their associations, a directed acyclic graph (DAG) was created. A DAG is a theoretical tool for specifying causal relations between variables and developing appropriate analytical strategies[162]. The justification of the assumptions comes from external sources, but the transparency of the graphical display of the assumptions in the DAG makes them explicit and open for criticism[164]. Our assumed web of causation surrounding the association between CP trajectories and NEET is shown in Figure 12.

As the name suggests a DAG only includes one-way arrows which indicate the direction of the assumed causal relationship. The path constituted by: dysfunctional CP

trajectories → School experience → NEET is the only indirect causal path in the DAG presented in Figure 6.1 (another causal path is the direct path from CP trajectories to NEET). School experience constitutes a mediating factor through which the causal effect of CP trajectories on NEET is presumed (but not assumed) to be mediated. Backdoor paths are non-causal paths between the exposure and outcome of interest characterised by arrowheads pointing towards the exposure[164] and ending with arrows pointing towards the outcome. An example of a backdoor path in Figure 12 is: CP trajectory groups ← social class (based on maternal occupation) → NEET. When possible, all backdoor paths should be closed either via adjustment or because they include a collider (defined below). Being strategic in choosing which variables to adjust for in the analyses may pay off, since several backdoor paths might be closed by conditioning on the same variable(s), leading the selection of a minimally sufficient set of confounders to include in the analyses. As stated above, paths are also closed if they include a collider. A collider is a variable on a path where two or more arrowheads point[165]. For example, in Figure 1, KS4_IDACI is a collider on the path: CP trajectory groups ← maternal occupation → KS4_IDACI ← maternal depression → NEET. Because associations are not transmitted along a path that includes (at least) a collider, there is no confounding arising from that path. Identifying the colliders in a path is also important because conditioning on them would open their path: in the example, conditioning on KS4_IDACI would induce a spurious association between maternal occupation and maternal depression and hence open up the path from CP trajectory groups, to maternal occupation, KS4_IDACI, and Maternal depression, to NEET, although it was originally closed. Software DAGitty was used to build our DAG. This software indicates the minimum number of confounders to account for in order to close all backdoor pathways and avoid biased estimates[166].

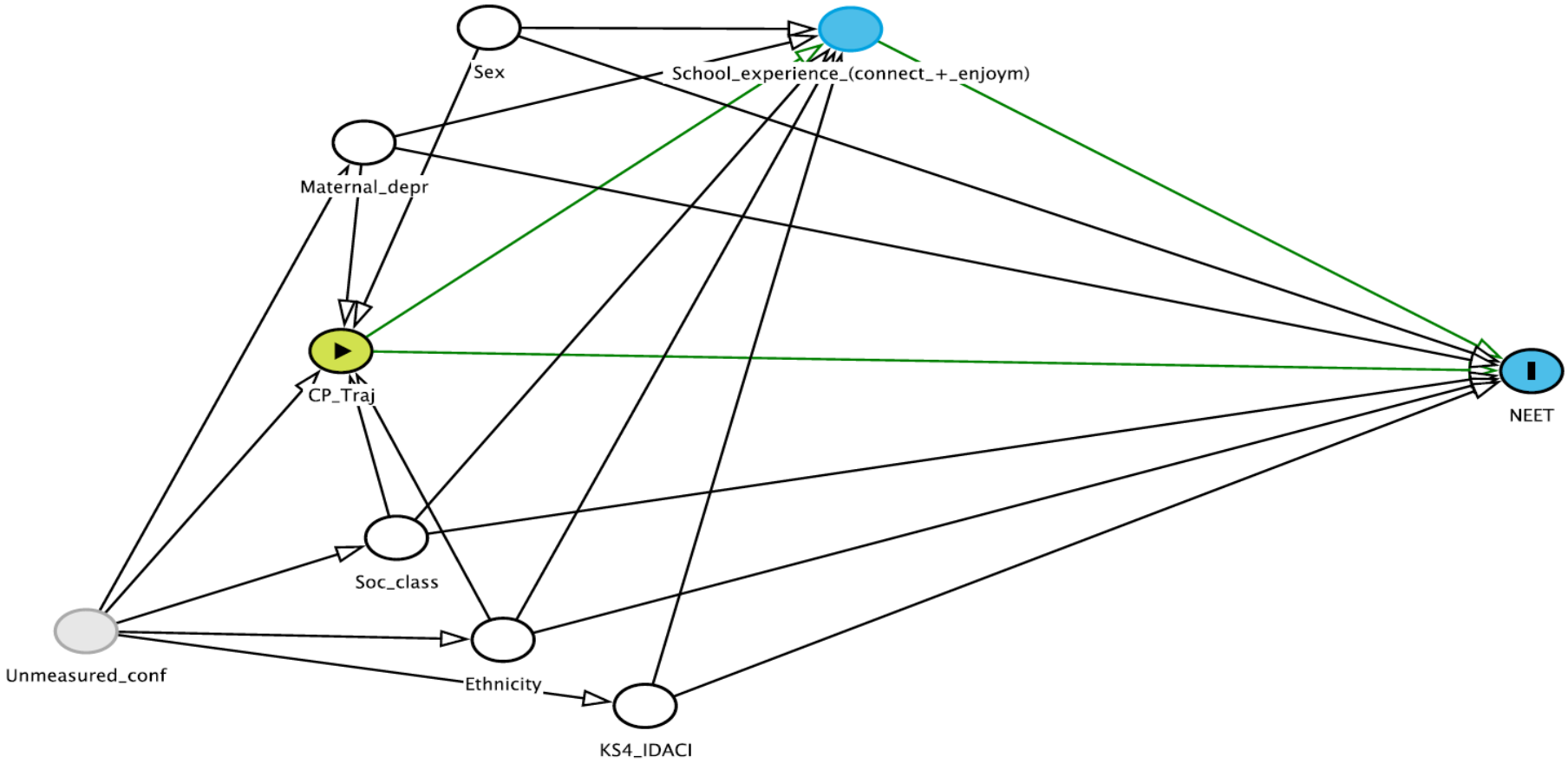


Figure 52 Directed Acyclic Graph. In green, the mediation path I will investigate.

Statistical analyses:

To investigate the extent of the mediating contribution of school experience (with school connectedness and enjoyment considered jointly) to the causal relationship between CP trajectories and NEET, I adopted the counterfactual-based definitions of natural direct effect (NDE) and natural indirect effect (NIE) recently proposed in the literature as a generalisation of the decomposition of total effects derived from path analysis and well-known in social sciences[167]. The advantage of the new definitions is that they are not constrained to linear models for outcome and mediators, hence allowing for interactions and other non-linearities, as well as binary (or count) outcomes and mediators[168]. As for the direct and indirect effects derived from path analysis, the sum of NDE and NIE gives the total causal effect (TCE), hence allowing the derivation of the percentage contributed by a mediator to the effect of the exposure on the outcome.

For a binary exposure, taking values 0 and 1, the NDE compares what, on average, would occur to the outcome had all individuals in the population had their exposure been set to 1 or 0, while the mediator had been set to its "natural value" occurring if all were unexposed. The NIE instead compares what, on average, would occur to the outcome, had all individuals in the population had their exposure been set to 1, while the mediator had been set to its value either under exposure or not exposure. The identification of these mediation effects (as well as of those derived from path analysis) relies on assumptions of no unmeasured confounding for the relationships between exposure and mediators, mediators and outcome, and exposure and outcome. When outcome and mediator models are non-linear, identification of natural effects also rely on the assumption of no intermediate confounding, which means that no additional mediator variable acts as a confounder for the mediators-outcome relationship.

The NDE and NIE were estimated using g-computation via Monte Carlo simulation[160] and implemented in STATA via the gformula command on a 200,000-fold expanded

dataset[243]. Effects were expressed as risk ratios: I compared risks of being NEET under different combinations of exposure and mediators values. Standard errors (SEs) were estimated using the non-parametric bootstrap (with 100 bootstrap samples). There is evidence that numbers of samples greater than 100 lead to negligible improvements in the estimation of standard errors[244].

The analyses were restricted to the 3288 children with available exposure and outcome data. Because data on confounders and mediators were affected by missingness, leading to 1077 children with complete data on all relevant variables, I also used single stochastics imputation by chained equations[170] with 10 burn-in iterations to obtain estimates based on all the original 3,288 children, under the missing at random assumption (MAR)[171]. The plausibility of this assumption was investigated by logistic regression where a binary indicator of missingness in any of the relevant variable was created for each child in the study. Note that, because standard errors were obtained using a bootstrap procedure that included the imputation step, multiple imputation was not required to obtain valid estimates. Results obtained using the complete exposure-outcome sample (N=3288) via imputation, and the complete records were then compared to assess the impact of selection bias (under MAR). Models were initially run without including truancy as a confounder, and repeated including truancy as an intermediate confounder.

6.1.3 Results

Trajectories were previously derived (see Barker and Maughan 2009) from the 7216 ALSPAC participants with at least four mother-reports of CP between age 4 and 13 years old (full sample). Of these, only 3288 (45.5%) had data available on NEET at age 20 (complete outcome sample) and, among them, only 1077(14.9%) had complete data on all confounders and mediators (complete cases sample). Comparing these three samples allowed us to investigate the potential impact of selection bias. Figure 13 shows that the percentage distribution of both EOP and CL is the same in the complete

outcome and the complete cases samples. This does not seem to be the case for the AO group, which contributes to 7.3% of participants in the complete exposure-outcome sample and only 5.5% in the complete records sample. Predictors of missingness (at the level outcome, confounders, and mediators) were examined by logistic regression and indicated that belonging to the AO trajectory group, coming from a low social class, having mother that suffered from depressive symptoms during pregnancy, having high deprivation scores at age 15-16 (KS4) and low score on school enjoyment were the strongest predictors of missingness (see Appendix Table 18).

Figure 13 Missing data across trajectory groups and across samples

The main participants' characteristics (overall for the complete outcome sample and separately by trajectory groups) are shown in Table 6. To note is that a higher proportion of being NEET was found in the EOP group compared to the other groups. Also, I observed little heterogeneity across trajectories in the school connectedness scale but slightly more in the school enjoyment scale (with EOP showing lower scores). The AO group seem to be less balanced than others in terms of male-to-female ratio. In general, I observed relatively high levels of missing data, especially at the level of the mediators.

Table 7 reports the TCE and the NDE and NIE of CP trajectories on NEET via school experience estimated using the complete exposure-outcome sample. Effects are expressed as risk ratios (RRs) of NEET for each CP trajectory (EOP, AO and CL) relative to the "normative" trajectory (L), which was used as our reference category. The results show that the total risk of NEET increases from AO and CL (which showed a similar magnitude of risk) to EOP relative to L (CL: RR= 1.61; 95% CI= 1.07, 2.43; AO: RR= 1.57; 95% CI= 0.99, 2.49; EOP: RR= 2.55; 95% CI= 1.80, 3.62). When these effects were partitioned into the components mediated and not mediated via school experience I found that, for AO and CL there was very small mediated effect (estimated NIE for AO= 0.98; 95% CI= 0.88, 1.08; and for CL= 1.04; 95% CI= 0.91, 1.18). There was however evidence of mediation via school experience for the EOP trajectory (EOP= 1.22; 95% CI= 1.04, 1.43), explaining about 21.1% of the total effect.

Results were stronger but in the same direction when I analysed the data in the complete case analyses (where I had 1077 individuals with data complete at the level of all confounders and mediators too): the increase in estimated RRs is indicative of the impact of selection bias affecting the subset of 1,077 participants with complete records (see Table 19 in the Appendix).

Finally, I repeated these analyses also including truancy as an intermediate confounder. Truancy is known to be highly predictive of future NEET[245, 246]. However,

this model did not differ from the one without truancy (additional information available in Table 20 in the Appendix). To note that truancy was not only very uncommon but also highly correlated with KS4/IDACI.

Table 6 Participants' characteristics (complete outcome sample)

	Overall N= 3288	**1 Low N= 2445 (74.4%)**	**2 AO N= 241 (7.3%)**	**3 CL N= 369 (11.2%)**	**4 EOP N= 233 (7.1%)**
OUTCOME					
NEET					
No N (%)	3055 (92.91)	2308 (94.40)	218 (90.46)	332 (89.97)	197 (84.55)
Yes N (%)	233 (7.09)	137 (5.6)	23 (9.5)	37 (10)	36 (15.5)
Missing N (%)	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
MEDIATORS					
School connectedness Median (25 percentile, 75 percentile)	21 (20, 24)	21.5 (21, 24)	21 (20, 23)	21 (20, 23)	21 (19, 23)
Missing N (%)	*1471 (44.7)*	*1053 (43.1)*	*132 (54.7)*	*166 (44.9)*	*120 (51.5)*
School Enjoyment Median (25 percentile, 75 percentile)	8 (7, 9)	8 (7, 9)	8 (6, 9)	8 (7, 9)	8 (6, 8)
Missing N (%)	*1104 (33.5)*	*796 (32.5)*	*90 (37.3)*	*128 (34.6)*	*90 (38.6)*
CONFOUNDERS					
Sex					
M N (%)	1323 (40.24)	975 (39.88)	86 (35.68)	157 (42.55)	105 (45.06)
F N (%)	1965 (59.76)	1470 (60.12)	155 (64.32)	212 (57.45)	128 (54.94)
Missing N (%)	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Ethnicity					
White N (%)	3102 (96.76)	2,316 (97.07)	226 (97)	341 (95.52)	219 (95.22)

Non-White N (%)	104 (3.24)	70 (2.93)	7 (3)	16 (4.48)	11 (4.78)
Missing N (%)	*82 (2.4)*	*59 (2.4)*	*8 (3.3)*	*12 (3.2)*	*3 (1.2)*
Deprivation					
IDACI KS4 Median (25th, 27th percentile)	.08 (.04, .15)	.08 (.04, .15)	.085 (.045, .185)	.08 (.05, .18)	.1 (.05, .195)
Missing N (%)	*522 (15.8)*	*392 (16)*	*41 (17)*	*56 (15.1)*	*33 (14.1)*
Soc class based on Mother occupation					
Professional, Managerial, Skilled non-manual (1,2,3=0)	2426 (83.22)	1829 (84.29)	169 (80.86)	259 (79.45)	169 (80.48)
Skilled manual, partly skilled, unskilled (4,5,6=1)	486 (16.78)	341 (15.71)	40 (19.14)	67 (20.55)	41 (19.52)
Missing N (%)	*373 (11.3)*	*275 (11.2)*	*32 (13.2)*	*43 (11.6)*	*23 (9.8)*
Maternal depression					
EPDS (no depression)	2144 (75.76)	1643 (78.57)	133 (64.88)	224 (69.35)	144 (68.25)
EPDS (possible depression)	686 (24.24)	448 (21.43)	72 (35.12)	99 (30.65)	67 (31.75)
Missing N (%)	*458 (13.9)*	*354 (14.4)*	*36 (14.9)*	*46 (12.4)*	*22 (9.4)*

Table 7 Estimated total, direct and indirect effects expressed as risk ratios (RR) of CP trajectory group on NEET at age 20 year relative to the reference group (Low) (N=3288)

Adolescent–onset vs Low	**G-comp est. (RR) 3288**	**P-value**	**L 95% CI**	**U 95% CI**
Total Causal Effect	1.570	0.056	0.989	2.491
Natural Direct Effect	1.606	0.048	1.004	2.576
Natural Indirect Effect	0.977	0.655	0.879	1.084
Percentage Mediated	-0.052	0.931	-1.256	1.151
Childhood-Limited vs Low				
Total Causal Effect	1.614	0.022	1.072	2.435
Natural Direct Effect	1.556	0.045	1.010	2.396
Natural Indirect Effect	1.038	0.576	0.910	1.185
Percentage Mediated	0.078	0.759	-0.424	0.580
Early-Onset Persistent vs Low				
Total Causal Effect	2.552	<0.001	1.799	3.620
Natural Direct Effect	2.092	<0.001	1.492	2.934
Natural Indirect Effect	1.219	0.015	1.039	1.432
Percentage Mediated	0.211	0.025	0.026	0.398

6.1.4 Discussion

The present study represents the first investigation on the role of school connectedness and enjoyment as potential mediators of the association between CP trajectories and risk of being NEET in young adulthood (age 20 years). I identified the protective effects of school connection and school enjoyment on the risk of being NEET in the most adverse CP trajectory group, e.g. that with an early onset and persisting pattern of CP. In this group, school connectedness and enjoyment mediated up to 21.1% of the risk of NEET compared to the normative trajectory. This finding held when I further adjusted for truancy. I did not identify a protective role for school experience in the CL or AOP trajectory groups.

Our findings are consistent with a much broader literature on the role of school connectedness and enjoyment in protecting young people from a range of health harms (i.e. Resnick 1997), “acting out” behaviours, including risk for delinquency and CP and academic achievement[247]. Also, they are in line with previous research showing that school connectedness may decrease the likelihood of poor adjustment at later stages of life[113]. The findings presented here extend previous research in that they add that school connectedness partially decreases risk of poor outcomes not only in typical but also in high-risk youth, such as individuals with persisting patterns of CP. In addition, they add that school enjoyment, a factor that has not been widely studied in the past, plays an important role in decreasing risk of poor outcomes in CP youth. The fact that school connectedness and enjoyment in mid-adolescence still have the potential to improve outcomes in high-risk youth, where CP emerge early in life, is somehow comforting and suggests that adolescence may be a time where high-risk individuals are responsive to environmental changes.

In terms of potential mechanisms, it could be that enjoying school promotes curiosity towards certain subjects which may become the field of study/work of individuals when they exit school and enter University/work. Also, it could be that a sense of enjoyment

and connectedness to school facilitates and promotes commitment to academic values and encourages students to perform well academically. In line with this hypothesis, Won et al. (2018) found that sense of belonging to school functioned as significant predictor of metacognitive and academic time-management strategies[248]. This may improve academic achievement and it may follow that a better school performance will increase chances of attending University and/or find employment. At the basis of this association there may be a virtuous cycle where achievement and enjoyment form a circular dependency: school enjoyment leads to higher achievement and achievement leads to more school enjoyment. The investigation of potential mechanisms is beyond the scope of this work, but future research efforts should be directed at understanding these processes in order to provide valuable information that may help guide intervention programs.

We did not observe a significant mediating effect for school connection/ enjoyment on NEET in either the CL or the AO group, relative to L. For CL, this is perhaps not surprising, as CP in this group had essentially resolved by the time the school connection mediator was measured and this group had the lowest risk of NEET outcome. For AO, our finding of no significant mediation was contrary to our expectations. I believe that this finding may reflect a high proportion of missing data particularly at the level of mediators and confounders in this group. This may have resulted in lack of power to detect a significant effect, or unaccounted selection bias affecting this group more than the others. These possible explanations are supported by the fact that AO individuals had a particularly high level of missing data at the level of the mediator, compared to EOP and CL individuals. Alternatively, it could be that, in effect, in this group and at this particular stage of their life, school experience does not have the potential to trigger virtuous processes that minimise risk of being NEET later on.

I adopted the counterfactual-based definitions of natural direct effect (NDE) and natural indirect effect (NIE) a generalisation of the decomposition of total effects derived from path analysis and carried out the estimations using g-computation. Compared to similar investigations[249] (i.e. Petras et al. 2004), this study employed a larger sample size and included both females and males. In addition, the outcome I am considering in the present study is associated with many others domains (e.g. health, mental health, substance use, imprisonment) and as such represent a powerful indicator of general adjustment.

Strengths and limitations:

To my knowledge, this is the first time that subjective aspects of school such as students' feelings of school connectedness and enjoyment are studied as potential mediators of the association between CP trajectories and risk of NEET. I benefitted from a large sample size, and employed a powerful statistical technique (g-formula), which have an advantage over traditional SEM in that it allows more precise estimation of the coefficients in the presence of binary outcomes.

Our findings should be considered within the context of a number of limitations. First, ALSPAC is a large birth cohort but it is not ethnically diverse, with vast majority (over 95%) of White British participants. Second, like most large longitudinal cohorts, ALSPAC shows attrition over time, with children of younger and more socially disadvantaged mothers more likely to be lost in follow-up.

Drawing and interrogating DAGs are useful steps for identifying confounders while avoiding conditioning on colliders and hence inducing bias in the estimation of causal effects. I acknowledge that the DAG presented in Figure 12 may miss some potential confounding variables. However, it does constitute our best guess of how the variables included are causally related based on the evidence provided in the literature, as well as explicating our structural assumptions.

Researchers interested in this area should look at more distal outcomes: being NEET at age 20 may carry a certain risk of not being successful at later stages of life but this would need to be formally investigated: it may be that people who are not NEET at age 20 may be NEET at later stages of life. Also, I assessed outcome at only one time point: this may have a negative impact on the consistency of the construct studied (i.e. NEET).

Conclusions and future directions:

We highlight that these findings are important from a policy perspective: they suggest that school experience have the potential to decrease risk of becoming NEET in high risk youth such as EOP individuals. Schools should focus not only on promoting academic achievement but also the overall school experience of their students. More specifically, they should focus on promoting a sense of connectedness and belonging to the school amongst their students by, for example, fostering identification process with school ethos and values. Schools should also try to make the whole experience of going to school more enjoyable for their students, for example by proposing activities that are in line with students' interests and inclinations.

Future research should make use of larger sample sizes and include more AO individuals (and ideally with a lower attrition rate). Although this group's pattern of behaviour is less worrying than that of EOP, it represents a much larger portion of young people with CP. Future studies should focus on AO individuals and investigate whether school connectedness and enjoyment, as well as other factors related to school, have the power to decrease likelihood of being NEET later in this specific group of CP youth. For example, it has been argued that deviant group affiliation is a mechanisms that may better explain antisocial activities in AO rather than EOP (who are more likely to act antisocially on their own compared to AO)[181]. Schools should focus on this particular aspect of socialisation to potentially improve future outcomes in AO youth.

Chapter 7

In this chapter, I will investigate whether and what school-level factors influence the course of CP in early-mid adolescence. To do this, I will first employ longitudinal latent class analysis to define the CP trajectories for males and females. Then, I will run a series of regression models to investigate predictors of class membership, controlling for individual and family-level factors.

7.1 School-level predictors of conduct problems trajectories

Abstract: CP can differ in terms of continuity/desistence across different stages of life such as childhood and adolescence. Although there have been a number of research efforts to investigate individual-level factors associated with continuity/desistence of CP in adolescence, less is known about school factors that may potentially underlie continuity/desistence of CP such as school-level factors. I run longitudinal latent class analysis (LLCA) to identify trajectories of CP across adolescence using the Learning Together study dataset. I then investigated the role of a number of school-level factors in predicting class membership using multinomial logistic regression. I identified two classes of CP: a stable low and a moderate-high class across males and females. A number of school-level factors predicted persistent patterns of CP in males and females separately. Positive school atmosphere was found to be strongly associated with lower risk of persistent CP across males and females. Student-teachers' relationships, sense of belonging to the school and participation in school activities are important aspects that researchers and schools should consider when implementing prevention and intervention programs for youth with CP and antisocial behaviour.

7.1.1 Introduction

Children with CP differ in terms of age of onset and persistence/desistence of such behavioural difficulties. As I have shown previously, three main groups of CP

individuals based on the age of onset and developmental course have been identified by researchers in this field. These are EOP, AO and CL. Research has investigated not only early factors associated with course of development of CP, but some have also focussed on late adolescence/early adulthood factors that may influence the course of CP and antisocial behaviour. Farrington and West (1995) observed that although offenders were not less likely to get married compared to non-offenders, getting married led to a decrease in risk of committing crimes compared to non-married individuals with previous history of antisocial behaviour[250]. In addition, they observed that marriage worked as a protective factor only if men resided with their spouse. Married men who then divorced had higher rates of offending compared to those living with their partners/wives. Warr (1998) proposes several explanations for this, including that the protective effect of marriage is operated through a decrease in time spent with potentially delinquent friends after marriage[251]. More recently, Alink and Egeland (2013) showed the effects of adaptive tasks such as doing well at work and in romantic relationships on the course of antisocial behaviour[189]. Authors observed that the relation between adaptation in emerging adulthood and later antisocial behaviour was dependant on previous antisocial course. In fact, only AO individuals who had a permanent job showed lower levels of later antisocial behaviour, but this was not the case for EOP, who seemed to be "resistant" to the effect of adaptive tasks such as being involved in a romantic relationship or having a stable job. Roisman (2004), however, found the opposite pattern. In this study[252], authors found that being successful on developmental tasks such as work and romantic relationships at age 23 was associated with desistence of antisocial behaviour in EOP only and not in AO, as predicted by Moffitt and colleagues (2002)[105].

Research in adolescence factors that may be associated with persistence/desistence in CP have also yielded interesting results. Underwood et al. (2009) found that membership to a joint trajectory of increasing levels of both social and physical

aggression was predicted by male gender, unmarried parents, African American ethnicity, and maternal authoritarian and permissive parenting, in a sample of 9-13 year old individuals[253]. Other authors found that desistence in a male sample of individuals with antisocial behaviour aged 13-25 were low physical punishment by parents in early adolescence and being employed or in school in early adulthood[254]. The following risk factors were associated with persistence in the transition to adulthood: serious delinquency during late adolescence, hard drug use, gang membership, and positive perception of problem behaviour in early adulthood. Others observed that desisting youth had more effortful control, perceived less overprotection, had lower levels of family vulnerability to externalising problems and more often lived with the same parent throughout their lives compared to youth with stable high pattern of CP[183]. A study from Petras et al. (2004) found a number of adolescent factors that were associated with the course of development of aggressive behaviour in different youth groups[249]. Authors found that in middle-school, lower levels of neighbourhood deviant behaviour were associated with lower risk of criminal arrest among boys with stable-high levels of aggression and increasing levels of aggression. Parental monitoring at age 11-12 was found to be associated with reduction of risk in terms of arrest and receiving a diagnosis of Antisocial Personality Disorder in the increasing trajectory group. Authors also investigated the role of academic performance and found that reading achievement in first grade decreased risk of arrest in the increasing trajectory group but did not find a protective effect for sixth-grade academic performance for either of the high-risk classes in terms of arrest or Antisocial Personality Disorder diagnosis.

Some researchers have attempted to propose potential mechanisms underlying decrease in CP in CL individuals: Moffitt and colleagues (2008) suggest that CL children may develop “off-putting” personality characteristics (e.g. social awkwardness and anxiety, schizotypal personality traits), such that they become increasingly socially isolated[182]. A second explanation, in contrast with the previous one, is that CL youth

become integrated within the school context, thereby actually showing a decrease in internalising as well as externalising problems, and an improvement in academic performance and peer relations. This was proposed by Veenstra et al, who investigated potential factors underlying desistence/persistence in 11-13.5 years-old CP youth[183].

According to the theory of human functioning and school organisation[114] pedagogic practice but also structural and organisational aspects of school (e.g. quality of relationship between students and teachers, weaker relationship between academic learning and broader student development) may contribute to produce students more likely to engage in health risk behaviours and violence. Research using cross-sectional samples shows that structural aspects of schools (e.g. leadership and management, school overall quality and school gender) are associated with problem behaviours such as bullying and cyberbullying[115]. Tobler et al. (2011) found that value-added education was associated with lower incidence of violent behaviours, after adjustment for individual- and school-level covariates[116]. In a review published by Sellstrom and Bremberg (2006), a number of school-level factors were associated with students' behaviour and well-being. For example, authors found that schools with low average SES had higher rates of pupil victimisation and more pupils carried weapons[255]. Mooji (1998) found that coming across fewer teachers with positive teaching behaviour, and attending a lower type of secondary school, help explain why someone is a perpetrator of disruptive/aggressive behaviour[256].

However, it is unclear whether these and other school factors can predict the developmental course of CP, which is a more precise indicator of later outcomes compared to a single-time point indicator. Using a longitudinal, UK sample of secondary school pupils age 12-14, I aim to systematically investigate the role school-level factors in predicting different trajectories of CP using a multilevel approach, while accounting for a number of individual and family-level factors. This could help us understand what the role of school is in promoting desistence of CP. In turn, this may

help guiding intervention and prevention programs that target high-risk schools and pupils with CP.

7.1.2 Methods

Participants

Data come from the control arm of the Learning Together study, a multi-centre cluster randomised controlled trial of an intervention aimed at reducing bullying and aggressive behaviours in 11 to 16 year old students in secondary schools. Data were collected in 40 participating secondary schools within the state education system across south-east England. Full details of the sampling methodology are available in the study protocol and the main outcomes paper[124]. Data were collected through questionnaires completed in school in confidential sessions supervised by the research team. Here, I will use data only from the control arm (i.e. students in schools that received no intervention but were followed for 3 years). This sample was made of 3347 at baseline, 3195 students at 24 months and 3606 students at 36 months.

Measures

CP were measured using the Edinburgh Study of Youth Transition to Crime (ESYTC)[257] a 13-item scale measuring self-reported aggression towards students and teachers (e.g. “Fight in or outside the classroom”, “Be cheeky to a teacher”, “Threaten a teacher”, and “Cheat doing homework or tests”). Each item was coded from hardly ever or never; less than once a week; at least once a week; to most days. Items are summed to provide a total score and high scores indicate greater aggressive behaviour.

The school-level factors that I investigated as potential predictors of class membership were all measured at baseline (wave 1) and were:

-School-level deprivation: proportions of students eligible for free school meal (FSM): a widely used proxy measure for economic deprivation in the UK[258]. In England and

Wales, local education authority-maintained schools must provide a free meal to students if they or their parents receive specific benefits. I used the percentage of students eligible for FSM at any time during the past six years, obtained from publicly accessible data from Department of Education school performance Tables[133].

-The Income Deprivation Affecting Children Index (IDACI) score of the schools' postal address: the IDACI scores deprivation that measures the proportion of children in a small area under the age of 16 who live in low income households[134].

- School type: our sample includes of five different types of schools: "community" (n=5), where premises and funding are provided by local authorities; "foundation" (n=6), where the school owns the premises but funding comes from the local authority; "voluntary-aided" (n=4), where the premises are owned by a charity but funding is at least partly from the local authority (note that in our sample these were religious schools); "sponsor-led academy" (n=6) which are usually created from an underperforming school which obtained an independent business or charitable sponsor and where funding comes directly from central government; and "converter academy mainstream" (n=18), which are successful schools which have opted to gain more autonomy and have funding directly from central government[135]. .

-Sex composition: mixed or single sex[133].

-School quality most recent overall Ofsted rating: Schools were classified as 1= "Outstanding", 2= "Good", 3= "Requires improvement" or 4= "Inadequate" based on the quality of teaching, leadership and management, achievement of students, and behaviour and safety of students at the school. Our sample did not include schools with a rating of "Inadequate."[133]

-Beyond Blue scale: Adolescents' perceptions of school atmosphere was assessed using a 20-item scale which assessed the extent to which adolescents perceived teacher relationships to be supportive (e.g. "In this school, teachers treat students with

respect", "In this school, teachers believe all students can learn", "The teachers at this school are fair in dealing with students"), their sense of school belonging (e.g. "I can really be myself at this school", "Most other students accept me as I am", "I feel I belong at this school"), and their level of participation in school activities (e.g. "I try hard in school", "Doing well in school is important to me", Continuing or completing my education is important to me"). Scores on the scale range from 20 to 81, with higher scores indicating a more positive school atmosphere[259].

The individual-level factors that I included as potential confounders were:

-Gender: students could classify themselves as males or females.

-Ethnicity: students could classify themselves as White British, White Other, Asian/Asian British, Black/Black British, Chinese, Chinese British, Mixed ethnicity or Other.

-Family composition: this was assessed based on student reports of who lived in their house with them. To create a dichotomous variable (two parents vs lone parent), students were classified as having two parents if they reported living with any two of the following: mother, father, step-mother, step-father, foster mother, and foster father. Students were classified as having a lone parent if they reported living with only one of these parents. In our sample, 73.91% of students reported living with two parents.

-Socioeconomic status: this was assessed using the Family Affluence Scale (FAS), developed specifically for reporting of socioeconomic status by young adolescents[214]. Four questions assess car ownership, children having their own bedroom, the number of computers at home, and the number of holidays taken in the past 12 months. A composite FAS score is calculated for each student based on his or her responses to these four items.

Analyses

Data analyses proceeded in two steps: in step 1, longitudinal latent class analysis (LLCA) was used to model the CP trajectories based on the ESYTC score at the three available time-points and examine whether there was evidence for more than one such trajectory. Clustering at the school-level was accounted for in the analyses. Mplus software[158] was used to estimate trajectories for each set number of classes. The usual approach to number of class selection was adopted (i.e. comparison of BIC, Adjusted-BIC and entropy). Models were fitted separately for boys and girls (sex-variant model) and also jointly (sex-invariant model). For each pre-specified number of classes, a likelihood ratio test was used to assess whether the joint model for boys and girls gave a better fit than the stratified one (see details in Chapter 3).

In step 2 the most likely class predicted for each individual by the best fitting model from step 1 was used as the new outcome of interest to be related to school-level predictors using logistic regression accounting for clustering at the school-level in the estimation of robust standard errors. This second step was conducted in Stata[142]. Because the aim of the analyses was the study of school-level predictors/factors, these were examined one by one, while the individual-level variables were forced into the models together (these were: ethnicity, family structure and family income). As such, these were treated as a priori confounders. The selection of the most important school-level predictors was carried out using forward selection with *p* of entry at 10% level.

7.1.3 Results

A total of 3901 pupils (1977 females, 50.7%) were available for analysis after excluding duplicates and those participants with missing data at the level of outcome. Table 8 contains the fit indices for the sex variant and sex invariant models. Overall, the sex variant models fit better than the sex invariant models. In both sexes, the two-class model appeared to have the best fit in terms of lowest Bayesian Information Criterion and highest entropy values. In both sexes, there was one class in which mean CP was low persistently across the 3 waves (named the “stable low” class) and one with mean

CP moderate to high persistently across the waves (named the "moderate/high" class). Trajectory groups are shown in Figure 14. Table 22 in the Appendix shows pattern of missing data across males and females.

Table 8 Fit indices for sex variant and sex invariant trajectory models.

	Sex variant: M (N=1924)			Sex variant: F (N=1977)			Sex invariant (N=3901)		
Trajectory number	**BIC**	**Adjust. BIC**	**Entropy**	**BIC**	**Adjust. BIC**	**Entropy**	**BIC**	**Adjust. BIC**	**Entropy**
One-group	28427.536	28408.474	100%	26940.293	26921.231	100%	55691.052	55671.987	100.00%
Two-group	**27295.163**	**27260.216**	**93.60%**	**25553.654**	**25518.706**	**93.50%**	53117.378	**53082.425**	92.50%
Three-group	26693.692	26639.683	92.80%	25046.027	24992.018	91.90%	51945.46	51891.441	91.30%

BIC= Bayesian Information Criterion (with and without sample size correction)

Table 9 shows the number and percentage (or percentiles) of Girls and Boys respectively in the Stable Low vs the Moderate/High CP trajectory groups, and unadjusted Odds Ratios.

Conduct problems trajectories (Girls)

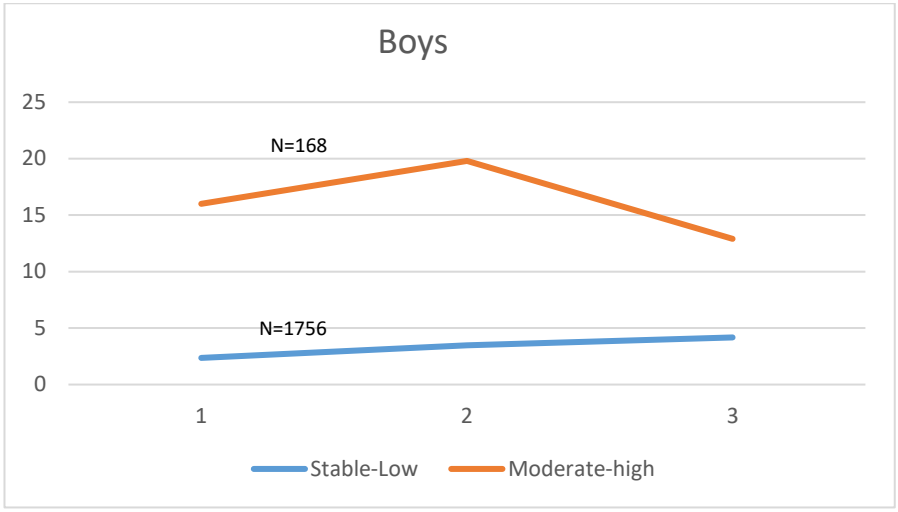
	Stable Low		**Moderate/High**		**OR**	
School-level variables						
Free School Meal						
FSM value (< 23%)	637	35.45	46	25.56	base	
FSM value (>= 23%)	1,160	64.55	134	74.44	**1.59**	**1.07-2.38**
School type						
Converter - Academy Mainstream	804	44.74	62	34.44	base	
Academy Sponsor Led	183	10.18	28	15.56	**1.98**	**1.16-3.38**
Community School	405	22.54	44	24.44	1.40	0.92-2.14
Foundation School	405	22.54	46	25.56	1.47	0.94-2.29
Total	1,797	100	180	100	.	.
IDACI					1.89	0.77-4.60
IDACI score (50th percentile)		0.21		0.29		
IDACI score (25th percentile)		0.04		0.14		
IDACI score (75th percentile)		0.38		0.48		
Ofsted						
Good	1,152	64.11	106	58.89	base	
Outstanding	495	27.55	60	33.33	1.31	0.87-1.98
Requires Improvement	150	8.35	14	7.78	1.01	0.73-1.40
Total	1,797	100	180	100		
School gender						
Only Girls	532	29.6	57	31.67	base	
Mixed	1,265	70.4	123	68.33	0.90	0.62-1.31
Total	1,797	100	180	100		
School atmosphere					**0.31**	**0.22-0.44**
Beyond Blue score (50th percentile)		3.17		2.85		
Beyond Blue score (25th percentile)		2.85		2.60		
Beyond Blue score (75th percentile)		3.5		3.214		
Individual-level variables	**N**	**%**	**N**	**%**	**Coeff.**	**95% CIs**
Family Structure						
Two parents	1,251	69.62	85	47.22	base	

Lone parent	546	30.38	95	52.78	**2.56**	**1.71-3.81**
Total	1,797	100	180	100		
Child Family Affluence					1.01	0.92-1.09
High Family Affluence (50th percentile)		6		6		
Medium Family Affluence (25th percentile)		5		5		
Low Family Affluence (75th percentile)		7		7.5		
Ethnicity						
White British	754	42.05	66	36.87	base	
White Other	193	10.76	17	9.5	1.01	0.66-1.52
Asian/Asian British	383	21.36	25	13.97	0.74	0.40-1.37
Black British	215	11.99	44	24.58	**2.33**	**1.38-3.94**
Chinese/Chinese British	6	0.33	0	0	Empty	
Mixed	135	7.53	18	10.06	1.52	0.81-2.83
Other	107	5.97	9	5.03	0.96	0.06-0.11
Total	1,793	100	179	100	.	.

Table 10 shows the number and percentage (or percentiles) of Girls and Boys respectively in the Stable Low vs the Moderate/High CP trajectory groups, and unadjusted Odds Ratios.

	Conduct problems trajectories (Boys)					
	Stable Low		**Moderate/High**		**OR**	
School-level variables						
Free School Meal						
FSM value (< 23%)	679	38.67	39	23.21	Base	
FSM value (>= 23%)	1,077	61.33	129	76.79	**2.08**	**1.22-3.54**
School type						
Converter - Academy Mainstream	744	42.37	82	48.81	base	
Academy Sponsor Led	219	12.47	32	19.05	1.32	0.60-2.89
Community School	176	10.02	12	7.14	0.61	0.30-1.24
Foundation School	437	24.89	35	20.83	0.72	0.34-1.54
Voluntary Aided School	180	10.25	7	4.17	**0.35**	**0.18-0.67**
Total	1,756	100	168	100		
IDACI					1.36	0.54-3.42
IDACI score (50th percentile)		0.23		0.23		
IDACI score (25th percentile)		0.14		0.17		
IDACI score (75th percentile)		0.38		0.38		
Ofsted						
Good	1,117	63.61	74	44.05	base	
Outstanding	476	27.11	78	46.43	**2.47**	**1.29-4.71**
Requires Improvement	163	9.28	16	9.52	**1.48**	**1.08-2.02**
Total	1,756	100	168	100		
School gender						
Only Boys	311	17.71	45	26.79	Base	
Mixed	1,445	82.29	123	73.21	0.58	0.17-2.02
Total	1,756	100	168	100		
School atmosphere					**0.25**	**0.16-0.38**
Beyond Blue score (50th percentile)		3.17		2.85		
Beyond Blue score (25th percentile)		2.89		2.42		
Beyond Blue score (75th percentile)		3.5		3.28		
Individual-level variables	**N**	**%**	**N**	**%**	**Coeff.**	**95% CIs**
Family Structure						
Two parents	1,251	69.62	85	47.22	base	

Lone parent	546	30.38	95	52.78	**2.56**	**1.71-3.81**
Total	1,797	100	180	100		
Child Family Affluence					1.01	0.92-1.09
High Family Affluence (50th percentile)		6		6		
Medium Family Affluence (25th percentile)		5		5		
Low Family Affluence (75th percentile)		7		7.5		
Ethnicity						
White British	754	42.05	66	36.87	base	
White Other	193	10.76	17	9.5	1.01	0.66-1.52
Asian/Asian British	383	21.36	25	13.97	0.74	0.40-1.37
Black British	215	11.99	44	24.58	**2.33**	**1.38-3.94**
Chinese/Chinese British	6	0.33	0	0	Empty	
Mixed	135	7.53	18	10.06	1.52	0.81-2.83
Other	107	5.97	9	5.03	0.96	0.06-0.11
Total	1,793	100	179	100	.	.



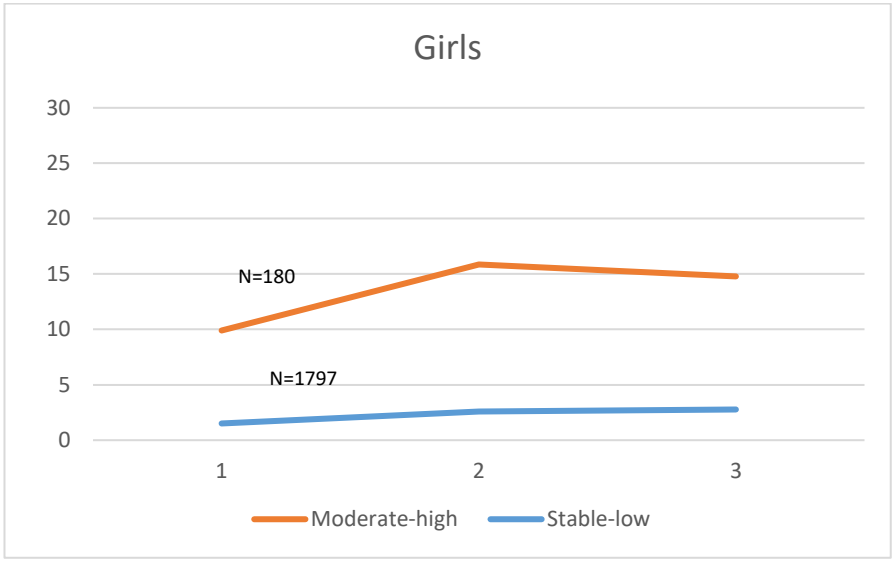


Figure 14 Predicted trajectories by latent group derived from fitting LLCA models to longitudinal ESYTC scores (mean reported on the x axis) for males and females across the three data collection points (baseline=1, 24 months=2, and 36 months=3). 9.1% of the whole females sample belonged to the Moderate-high group. 8.7% of the whole male sample belonged to the Moderate-high group.

When predicted latent trajectory class was treated as the outcome variable, and related to predictors via logistic regression, separately in males and females (Tables 11 and 12) I found a number of significant school-level variables

In the fully adjusted females' model, conditionally on the other variables included, higher percentage of FSM (OR= 1.706, CI= 1.138-2.560) and attending a school with an Ofsted rating of Outstanding (OR= 1.789, CI= 1.186-2.701) predicted higher risk of belonging to the Moderate/High trajectory compared to the Stable Low. Higher family affluence (OR= 1.094, CI= 1.014-1.181) predicted higher risk of belonging to the Moderate/High trajectory compared to the Stable Low, but this effect was very small. Better school atmosphere (OR= 0.365, CI= 0.253-0.527) predicted lower risk of belonging to the Moderate/High trajectory compared to the Stable Low.

In the fully adjusted males' model, conditionally on the other variables included, lone parenthood (OR= 1.680, CI= 1.176-2.401) predicted higher risk of belonging to the Moderate/High trajectory compared to the Stable Low. Attending a Voluntary aided school (OR= 0.208, CI= 0.117-0.368), better school atmosphere (OR= 0.257, CI= 0.165-0.402) and attending a mixed gender school (OR= 0.290, CI= 0.186-0.451) decreased risk of belonging to the Moderate/High trajectory group compared to the Stable Low. This effect may not be present in females because there are not voluntary aided schools for females in our sample.

The only factor that operated similarly across males and females was school climate (Beyond Blue scale). A better school climate at baseline was strongly protective against being in the moderate/high class in both females (OR= 0.365, CI= 0.253-0.527) and males (OR= 0.290, CI= 0.186-0.451).

Deprivation at the schoo-level, as indicated by FSM, and Ofsted rating seemed to be associated with higher risk of belonging to the High/moderate trajectory compared to the Stable Low in females only. Boys-only schools seem to predict higher risk of

persistent patterns of self-reported antisocial behaviour compared to mixed gender schools, but the effect of school gender was not observed in girls.

Table 11 Estimated odds ratios (OR) and 95% confidence intervals (CI) obtained from the final multivariable logistic regression model for assignment to the high—moderate class versus the Low class (girls only).

GIRLS model

Class	Coef.	p-value	95% CI low	95% CI up
Stable_low	base			
High_moderate vs stable				
Ethnicity				
White British	base			
White other	0.888	0.551	0.602	1.310
Asian/Asian British	0.764	0.402	0.408	1.432
Black/Black British	1.332	0.336	0.742	2.389
Chinese/Chinese British	.	.	.	.
Mixed ethnicity	1.0172	0.958	0.526	1.966
Other	0.701	0.426	0.292	1.680
Family structure				
Two parents	base			
Lone parent	**2.223**	**<0.001**	**1.480**	**3.341**
Child family affluence	**1.094**	**0.02**	**1.014**	**1.181**
School type				
Academy - Conv. Mains.	base			
Academy Sponsor Led	.	.	.	.
Community School	.	.	.	.
Foundation School	.	.	.	.
Voluntary aided	empty	.	.	.
Free School Meal				
%FSM<23%	base			
%FSM>=23%	**1.706**	**0.01**	**1.138**	**2.560**
Ofsted				

Good	base			
Outstanding	**1.789**	**0.006**	**1.186**	**2.701**
Requires Improvement	1.117	0.234	0.741	1.685
School atmosphere				
bb_total_base	**0.365**	**<0.001**	**0.253**	**0.527**
School gender				
Girls only	base			
Mixed	.	.	.	.
Deprivation				
IDACI	.	.	.	.

Table 12 Estimated odds ratios (OR) and 95% confidence intervals (CI) obtained from the final multivariable logistic regression model for assignment to the high—moderate class versus the Low class (boys only).

BOYS model				
Class	Coef.	p-value	95% CI low	95% CI up
Stable_low	base			
High_moderate vs stable				
Ethnicity				
White British	base			
White other	0.697	0.411	0.295	1.645
Asian/Asian British	1.101	0.769	0.579	2.091
Black/Black British	1.457	0.225	0.792	2.681
Chinese/Chinese British	3.899	0.124	0.688	22.087
Mixed ethnicity	0.740	0.376	0.380	1.440
Other	0.897	0.851	0.294	2.736
Family structure				
Two parents	base			
Lone parent	**1.680**	**0.004**	**1.176**	**2.401**
Child family affluence	1.059	0.356	0.936	1.199174
School type				
Academy - Conv. Mains.	base			
Academy Sponsor Led	1.233	0.400	0.757	2.006
Community School	0.743	0.224	0.459	1.199
Foundation School	0.746	0.314	0.421	1.319
Voluntary aided	**0.208**	**<0.001**	**0.117**	**0.368**
Free School Meal				
%FSM<23%	base			
%FSM>=23%	.	.	.	.

Ofsted				
Good	base			
Outstanding	1.392	0.119	0.918	2.110
Requires Improvement	1.609	0.101	0.912	2.835
School atmosphere				
bb_total_base	**0.257**	**<0.001**	**0.165**	**0.402**
School gender				
Boys only	base			
Mixed	**0.290**	**<0.001**	**0.186**	**0.451**
Deprivation				
IDACI	3.006	0.089	0.845	10.696

7.1.4 Discussion

The aim of the present study was to investigate what school-level factors are mostly associated with class membership of CP (accounting for differences in individual-level factors). To do this, I used data from the Learning Together study and run longitudinal latent class analysis and then logistic regression, accounting for clustering at the school-level. Models were run separately for males and females after evidence was found of differential relations across gender.

In our final multivariable regression model for the odds of assignment to the high-moderate class, I found that higher percentages of FSM were associated with a higher risk of persistent CP in girls only. This finding is in contrast with previous studies suggesting that family SES may be a stronger predictor of behavioural problems compared to school SES[260]. However, it is in line with many studies, conducted in several countries, which have observed an association between deprivation and behavioural problems in the school[261]. It is interesting that this effect was only present in females. Although CP are more often seen in males than females, it could be that females are more sensitive to the effect of deprived environments such as their families compared to males, and this effect may be potentiated by the proximity with other disadvantaged peers. This, however, has not been observed often in the past and some researchers have instead suggested that boys that are more sensitive to negative family influences[108]. Future research should address risk and resilience of developing CP in deprived children and young people across males and females.

In contrast to my expectations, I found that an Ofsted rating of “Outstanding” was associated with a higher risk of belonging to a persistent pattern of CP, compared to an Ofsted Rating of “Good”, in girls only. A potential explanation of this is that girls may see themselves as “naughty” in an environment that tolerates CP less. Girls may impose different standards on themselves and others in terms of behaviour and this

may be more pronounced in only-girls schools. In turn, this may result in scores on our self-reported questionnaires being higher compared to girls in mixed-sex schools.

Boys on a persistent trajectory of CP seem to be more often found in boys-only schools vs mixed gender schools. It could be that the absence of girls in boys-only schools may play a role in this. Pupils in boys-only schools may be less likely to engage in romantic relationships, a factor that has been shown to play a role in promoting desistence from antisocial behaviours in adults[250]. Also, it could be that antisocial activities are more easily spread, given that those who perform them may be seen as role-model by other males, who are in turn encouraged to behave similarly. In schools where girls are present, the ethos and values may be less gender-stereotyped, and this may represent a barrier to the development of antisocial behaviours. This remains speculative as I did not test whether pupils in boys-only schools are less likely to engage in romantic relationships compared to male pupils in mixed gender schools. It could be that pupils attending boys-only schools are more likely to come from families where risk factors for antisocial behaviours are more often present, compared to boys in mixed gender schools.

Voluntary schools, which in our sample were faith schools, also seem to have a protective effect in boys. This supports the notion that elements of school values and culture are protective against CP. Also, it could be argued that faith schools might attract students from families where violent and aggressive behaviour is less common. I do not know whether a similar effect is present in girls too, because there were no girls attending voluntary schools in our sample. Future research should investigate whether faith schools are associated with lower or less persistent patterns of CP in female adolescents too.

A factor that was strongly associated with a lower risk of belonging to a persisting pattern of CP in both males and females was school climate, as indexed by the Beyond Blue scale. This finding is in line with several studies, also including qualitative ones[262,

[263], which have been conducted in relation to the theory of human functioning[114]. The theory proposes that schools with weaker relationships between staff and students and between academic learning and broader student development tend to increase the likelihood of students engaging in a wide range of risk behaviours such as antisocial activities, use of tobacco, alcohol and illicit drugs. According to theory, this would occur as a result of students not feeling committed to learning, lacking a sense of belonging and connectedness to the school. This may lead students to not share those school-wide norms that protect them from involvement in risk behaviours and antisocial activities[264].

Strengths and limitations:

To our knowledge, this is the first study to look at a wide range of school-level factors that may predict persistent antisocial behaviour in both males and females. I used a very large sample, which included nearly 4000 pupils from year 7 to year 10.

Our study presents with a number of limitations: first, I used self-report and not official measures/records of antisocial behaviour. In addition, I did not benefit from information coming from multiple informants. Also, I considered school factors that were measured at baseline and assumed they were stable over time. Although this is may be the case for some school-level factors considered (i.e. school gender), I acknowledge that others may have been subject to change over time (i.e. FSM, school climate, Ofsted). This may have had an impact on the validity of the data presented here. However, I argue that this impact would have limited effects on the data in that factors such as Ofsted and school deprivation are relatively stable over time and are not subject to sudden changes.

In addition, our sample is not a population-based sample a priori, but it is (post priori) a nationally representative sample (details in Table 21 in the Appendix).

Conclusions:

The results presented in this study have important implications for schools. I have shown that amongst several school-level factors considered, the one that shows the strongest association with persistent antisocial behaviour is school climate. The questionnaire I used takes into account several dimensions of school climate, namely student-teachers' relationships, sense of school belonging and students' level of participation in school activities. These are important aspects that researchers and schools should consider when implementing prevention and intervention programmes. Future studies should better investigate more in detail what specific components of school atmosphere may work as protective factors against aggression and antisocial behaviours.

Chapter 8

In this chapter, I will review the aims of the present work and answer the research questions that motivated this thesis. Then, I will summarise and discuss the results for each of the analyses I conducted in this work. I will also provide a summary of the strengths and limitations of each chapter and across the whole thesis. I will conclude with a section on future directions.

8.1 Summary of objectives, research questions and methods

The objectives of this work were to investigate 1) the outcomes of different CP trajectory groups, 2) differences in terms of risk factors and developmental processes across trajectory groups, 3) the role of school experience in mediating the association between CP group membership and poor education and employment outcomes, and 4) whether and what school factors predict different trajectories of CP in adolescence.

To be more specific, I tried to answer the following research questions:

1) What are the differences in psychosocial outcomes of EOP, AO and CL groups in adulthood and young adulthood?

2) Are prenatal and postnatal risk factors different for the EOP and the CL trajectory groups and across gender? Do these risk factors associate longitudinally to increase the risk of poor academic achievement in adolescence? Are these longitudinal associations different across trajectory groups and gender?

3) What is the role that school experience plays in mediating the effect of CP trajectories on later poor education and employment outcome (NEET)?

4) What is the role of structural/organisational school-factors and school atmosphere in predicting different CP trajectories from early to mid-adolescence, while controlling for individual-level factors?

In order to answer these questions, I have employed several methodologies:

1) I conducted a systematic review and meta-analysis to investigate what outcomes different CP trajectory groups face in young adulthood and adulthood.

2) I used ALSPAC data to investigate differences in terms of prenatal and postnatal risk factors between two early-onset groups of CP, namely EOP and CL, and also across gender. Using an SEM approach, I tested a developmental cascade model to investigate whether and how these risk factors related to each other longitudinally and contributed to poor academic achievement in these two CP groups and across gender.

3) I used ALSPAC data to investigate whether school experience in adolescence (specifically school enjoyment and school connectedness) acted as a protective factor towards later NEET status in different trajectory groups of CP individuals. Here, I have estimated total causal effects of each CP trajectory versus the reference group and partitioned them into natural direct effects natural indirect effects to better understand the potential that school experience has in minimising the risk for individuals belonging to different CP trajectories to be NEET at age 20.

4) I used data from the Learning Together study to investigate whether and what school-level factors (namely FSM, IDACI score of the schools, school type, school gender and school atmosphere) were associated with different developmental trajectories of CP across adolescence. Here, my analyses proceeded in two steps: in step 1, I employed LLCA to identify different trajectories of CP in the dataset (namely a “stable-low” and a “high-moderate”). In step 2, I run a series of logistic regressions to investigate what school-level factors were predictive of CP class (here considered as outcomes) while controlling for individual-level factors.

8.2 Summary of results and discussion

1) Results from my systematic review and meta-analysis showed that all three CP trajectories were associated with a higher risk of poor outcomes on a number of life domains compared to the Low trajectory. The difference I observed concerned the magnitude of risk that these trajectories showed compared to the Low trajectory at the level of several outcomes, which followed a hierarchical fashion. Specifically, EOP was the trajectory with the highest risk of poor outcomes compared to the Low trajectory, followed by AO and CL. Statistical significance was observed at the level of all outcomes when comparing the EOP against the Low trajectory. The magnitude of risk, expressed in ORs, was higher than the other two trajectories (apart from cannabis use and general health, where the risk was just slightly lower compared to AO). For the AO trajectory, seven out of eight pooled ORs were significantly higher compared to the Low trajectory, with the only exception being for poor employment outcome. CL individuals showed a trend towards being at higher risk of all outcomes considered compared to those in the Low group but statistical significance was reached only in self-reported aggression and poor education.

   The question relevant to this study was “What are the differences in psychosocial outcomes of EOP, AO and CL groups in adulthood and young adulthood?” Findings suggested that the psychosocial outcomes of these individuals are likely to be negative compared to those without a history of CP. More specifically, they will show a higher risk of mental health problems (depression/depressive symptoms), cannabis use, alcohol use, self-reported aggression, criminal behaviour, poor general health, poor education and poor employment outcomes.

Results from my systematic review indicate the trajectory that shows the highest risk of poor outcomes is the EOP followed by the AO and by CL. A potential explanation for this is that genetic and environmental factors interact to maximise

the likelihood of developmental snares occurring across several stages of life. These developmental snares decrease the likelihood for these individuals to "recover" and shift to a healthier and adaptive course of development. I speculate that the interaction between predisposing genetic factors and negative environment is particularly relevant for explaining not only the continuity of violent and antisocial acts but also the variety of difficulties observed across several domains.

In contrast, the finding that AO individuals were at higher risk of poor outcomes compared to those in the Low trajectory conflicts with Moffitt's report that problem behaviour in adolescence is a transient and relatively normative phenomenon[95]. More specifically, given that this group also reported higher levels of self-reported aggression and higher risk of having a criminal record, I suggest that the terms Adolescent-Onset and Adolescent-Limited should not be used interchangeably. In this group, I also observed a higher risk of self-reported aggressive behaviour and official records of antisocial behaviour. This finding contrasts the notion that AO individuals tend to be more on the rule-breaking spectrum, rather than the aggressive one.

I found the CL trajectory to have the least negative outcomes compared to the EOP and AO trajectories, although those in this group had significantly poorer educational outcomes and problems with aggression in early adult life compared to those in the Low trajectory. ORs for other outcomes were in the same direction and of a similar order to other CP trajectories, although they did not reach significance. These findings support the suggestion that full recovery from CP rarely occurs and contradict the idea that CL individuals will be indistinguishable from typical individuals in adulthood[111]. These findings may be partially explained by the suggestion that CL youth have lower levels of environmental difficulties (i.e. family adversity and receiving adequate school support) and, more importantly, higher levels of effortful control (as seen in chapter 5). The interaction between these

factors may decrease internalising problems (perhaps via good levels of peer support)[111, 178]. I have not tested this hypothesis directly, but given the importance of understanding causal factors underlying changes in aggressive behaviour, I advocate further investigation.

2) Results from the developmental cascade model I tested showed that the effect of prenatal and postnatal risk factors differs across the EOP and CL trajectory groups and also across gender. Although they predict each other longitudinally, I did not observe strong evidence of an indirect effect carried through these risk factors over time that could increase the risk of poor academic achievement in a cumulative fashion (borderline significance). The strength of the association between a given risk factor and the following one in chronological order varies across groups and gender.

   The research questions relevant to this study were "Are prenatal and postnatal risk factors different for the EOP and the CL trajectory groups and across gender? Do these risk factors associate longitudinally to increase the risk of poor academic achievement in adolescence? Are these longitudinal associations different across trajectory groups and gender?" Findings suggested that the risk factors across the EOP and CL groups differ quantitatively, with EOP generally showing higher levels of risk compared to CL. With regards to gender differences, females in both trajectories showed lower levels of risk compared to males (particularly at the level of language, ADHD symptoms and poor academic achievement). These risk factors associate longitudinally but do not seem to show a strong indirect effect carried through all of them ("grand cascade"). In terms of differences observed at the level of individual paths, it appears that CL females show a stronger association coefficient on the path from ADHD to poor academic achievement compared to the other groups.

   Results from chapter 5 supported previous studies, with EOP showing significantly higher risk than CL on several domains. The co-occurrence of risk factors at the level of several domains may represent an important barrier for these individuals to be able

to shift to more typical behavioural trajectories. With regard to discrete gender differences, I observed lower levels of risk in females. This advantage may be the result of biological differences (e.g. lower levels of testosterone, which may act as a protective factor against both the development of ADHD and CP[265, 266]).

Here I also showed that the risk factors considered were longitudinally associated with one another from the prenatal period to adolescence. In other words, each predictor domain associated with the next in both EOP and CL groups. Females showed a higher coefficient than males in the path from ADHD to poor academic achievement (particularly females in the CL group). This finding suggests that prevention efforts in CP should target ADHD symptoms, particularly in females, as this strongly predicts a higher risk of poor academic achievement in adolescence in both early-onset subtypes of CP.

I also found an indirect effect from language to academic achievement via ADHD. It is of particular interest to note this coefficient was slightly higher in CL compared to EOP. This strengthens the hypothesis that ADHD plays an important role in the development of academic problems in youth with CP, particularly in the CL trajectory.

3) Results from my third study showed that CP trajectories show a higher risk compared to the Low to be NEET at age 20, with EOP showing the highest risk. In addition, I observed that school experience, given by school connectedness and school enjoyment, mediated in part the association between CP class membership and NEET status at age 20, but only in the EOP trajectory group.

   The research question relevant to this study was “What is the role that school experience plays in mediating the effect of CP trajectories on later poor education and employment outcome?” Findings suggested that school experience in mid-adolescence can decrease the risk of being NEET in particularly high-risk youth, such as EOP individuals. Therefore, a better and more positive school experience seems to have a

protective role against negative education and employment outcomes in early adulthood in individuals with persistent and pervasive patterns of CP and antisocial behaviour.

More specifically, results from chapter 6 showed that in the EOP group, school connectedness and enjoyment mediated up to 21.1% of the risk of NEET compared to the normative trajectory. This finding extends previous research and adds that school connectedness has the potential to decrease the risk of poor social outcomes not only in typical but also in high-risk youth, such as individuals with CP. Also, school enjoyment, a factor that has not been widely studied in the past, plays a role in decreasing the risk of poor outcomes in CP youth. This may suggest that adolescence may be a time where high-risk individuals are responsive to environmental changes, such as school atmosphere.

I did not observe a significant mediating effect for school connectedness/enjoyment on NEET in either the CL or the AO groups. This finding was expected for what concerns the CL group, and unexpected for what concerns the AO group. I believe this finding may reflect a high proportion of missing data, particularly at the level of mediators and confounders in this group. This may have resulted in a lack of power to detect a significant effect, or unaccounted selection bias affecting this group more than the others. These possible explanations are supported by the fact that AO individuals had a particularly high level of missing data at the level of the mediator, compared to EOP and CL individuals.

4) Results from my fourth study showed that a number of school-level factors were associated with persistent patterns of CP across early and mid-adolescence while controlling for individual-level factors. School-level factors that predicted persistent patterns of CP in females were: an Ofsted rating of “Outstanding” and high levels of FSM in the school. In males, I found that attending a Voluntary aided (faith) school (vs mainstream academy school) and attending a mixed school (vs boys-only school) were

protective factors against belonging to the persistent CP trajectory group. A factor that operated similarly across gender was school climate, with higher levels of positive school climate decreasing the likelihood of belonging to the persistent CP trajectory group.

The research question relevant to this study was “What is the role of structural/organisational school-factors and school atmosphere in predicting different CP trajectories from early to mid-adolescence, while controlling for individual-level factors?” Findings from this study suggested that school structural factors and school climate predict different trajectories of CP in females and males, with positive school climate being the only one, amongst those considered, that operates as a protective factor against persistent patterns of CP across gender.

More specifically, results in chapter 7 showed that a number of school-level factors were predictive of persistent forms of CP and antisocial behaviour across early and mid-adolescence. The strongest predictor of persistent patterns of CP in both boys and girls was poor school atmosphere. This is in line with previous research conducted in relation to the theory of human functioning[114]. According to this theory, schools with weaker relationships between staff and students and between academic learning and broader student development tend to increase the likelihood of students engaging in a wide range of risk behaviours, including antisocial activities. According to theory, this would occur as a result of students not feeling committed to learning, and lacking a sense of belonging and connectedness to the school. This may lead students not to share those school-wide norms that protect them from involvement in risk behaviours and antisocial activities[264]. This is an important finding in that it may guide planning and delivering school programmes that target CP and antisocial behaviour. Future research should investigate the potential causal link between school atmosphere and antisocial behaviour, as this study has only looked at their association.

8.3 Summary of strengths and limitations

1) To my knowledge, the meta-analysis in chapter 4 is the first one that investigated the psychosocial outcomes of CP trajectories and as such, it represents an accessible and useful summary of several research efforts that have been done throughout the years in different countries. I considered a wide range of health, social and educational outcomes and found consistency in the categorisation of CP trajectories across all studies. Several limitations apply to my systematic review and meta-analysis. I acknowledge that growth mixture models have limitations, which include over-fitting the number of trajectories which can lead to biased estimates of covariate effects (e.g. outcomes of trajectories)[197]. Furthermore, the measures used to construct these trajectories differed across studies (e.g. different versions of the SDQ or CBCL, or other teacher-reported measures) resulting in some degree of measurement inconsistency. I accept that the most reliable source of data should include multiple informants, and this was not often available in the studies identified for inclusion.
2) The study in chapter 5 is the first where previously identified risk factors for CP are shown to be longitudinally associated with one another from prenatal period to adolescence. Several limitations apply to my developmental cascade model. First of all, this is only one out of many potential cascades that could be tested and I acknowledge that there are differences in how the constructs used for this model were measured: while academic achievement was measured through official school records and takes into account three time points (KS1, KS2 and KS3), others (such as maternal bonding and language skills) were measured at one time point and using only one informant, thus making the measurement not particularly robust.

Also, although ALSPAC features a broad and representative sample of individuals from different socioeconomic backgrounds, the cohort has low rates of ethnic minorities. Future research should address this by employing a more ethnically-diverse sample. In addition, ALSPAC is known for its high rates of attrition over time, with children of younger and poorer mothers being more likely to be lost in follow-ups.

3) Compared to similar investigations[249] (i.e. Petras et al., 2004), the study in chapter 6 employed a large sample size and included both females and males. In addition, the outcome I considered (NEET) is associated with many others domains (e.g. health, mental health, substance use, imprisonment) and, as such, it represents a good indicator of general adjustment. Findings from chapter 6 should be considered within the context of a number of limitations. Drawing and interrogating DAGs are useful steps for identifying confounders while avoiding conditioning on colliders and hence inducing bias in the estimation of causal effects. I acknowledge that the DAG presented in this chapter may miss some potential confounding variables. I also highlight that AO presented with a considerable amount of missing data. This may have had an impact on detecting a significant mediation effect of school experience. Future research should make use of a larger sample size with lower attrition rates, and include more AO individuals. Although this group's pattern of behaviour and outcome are less negative than that of EOP, it represents a much larger portion of young people with CP.
4) To my knowledge, the study in chapter 7 is the first that looked at a wide range of school-level factors in association with persistent antisocial behaviour in both males and females. I used a large sample, which included nearly 4000 pupils from year 7 to year 10. Results from chapter 7 should be considered in the light of several limitations: first, I used self-report and not official measures/records

of antisocial behaviour and I did not benefit from information coming from multiple informants. Also, I considered school factors that were measured at baseline and assumed they were stable over time. Although this is may be the case for some school-level factors considered (i.e. school gender), I acknowledge that others may have been subject to change over time (i.e. FSM, school climate, Ofsted). However, I argue that this would have limited effects on the data in that factors such as Ofsted and school deprivation are relatively stable over time and should not be subject to change.

8.4 Strengths and limitations across the thesis

In terms of overall strengths, the work conducted to produce this thesis made use of several analytic techniques. In addition, I employed multiple longitudinal datasets of young people in the UK: both these datasets (ALSPAC and Learning Together) are very large and the Learning Together dataset is very recent. This last aspect is important, particularly when considering school-level factors. These may not necessarily reflect the same school characteristics if considered at two different time points (e.g. the same Ofsted rating may reflect certain school characteristics in 1995, but others in 2015). In this sense, I argue that the findings relative to the school-level factors examined in this work can be generalisable, to some extent, to other schools in the country at this moment in time.

In terms of limitations, I acknowledge that much of the research I conducted is based on self-report measures. To assume the validity of the data collected, researchers need to rely on the honesty of their participants. The degree to which this is a problem will vary with the topic of the questionnaire, and also with the specific respondents' characteristics (e.g. age). In this case, we included adolescent participants and asked them about their behaviour, including negative behaviour such as violence, lying etc. It is known that participants are more likely to under-report undesirable behaviour[267]. This may pose a challenge for the validity of the research findings. For what concerns the

Learning Together data, I add that the data were collected in classrooms where teachers and other classmates were present. Their presence may have further biased the results. Also, my investigations were limited to the available data. Although I was able to identify and make use of standardised scales that capture the construct of CP in both ALSPAC and Learning Together, I acknowledge that I could not use data coming from multiple sources, which would have increased validity and reliability of the results[268].

Apart from the systematic review and meta-analysis, which included studies conducted in several countries across the world (UK, US, Australia, New Zealand and Belgium), all other results presented in this thesis come from UK samples (ALSPAC and Learning Together). These are both large samples which provide good power, and I argue that most findings in my thesis are applicable to the general CP population of young people in the UK. However, there are a number of methodological aspects that limit the generalisability of these findings to other countries and to other populations of individuals with CP which have been grouped into multiple developmental trajectories.

The findings in chapter 5 and 6 rely on the statistical approach and specific variables employed to derive the trajectories. Researchers in other countries have identified similar groups of CP youth (e.g. EOP and CL), but the variables and the statistical methods employed to derive these trajectories may differ, thus resulting in groups that have a similar name (e.g. early-onset desisting or childhood-limited) but may be, in fact, slightly different.

With specific reference to chapter 5, it would be interesting to try to replicate the finding that ADHD symptoms in females on a desisting CP trajectory show higher risk of poor academic achievement, compared to other groups of CP. This would form the basis for useful knowledge that may help plan prevention and intervention programmes aimed at this specific subgroup of children and young people. Variables used in chapter 6 are more generalisable, and I would assume that NEET and school enjoyment and

connectedness are measured in a similar way across countries. However, the issue related to the generalisability of the CP trajectories remains, as these trajectories are the same as chapter 5.

For what concerns chapter 7, I argue that these findings are perhaps more difficult to generalise. This is because the school-level factors I took into account are specific to the UK. For example, the threshold for being entitled to FSM may differ in other European countries or overseas. The same can be argued for IDACI or Ofsted (assuming that similar indexes also exist in other countries). Also, some countries do not have single-gender schools. Hence, the findings related to this specific school-variable may only apply within the UK and other countries where such schools are found but not others.

8.5 General conclusions and future directions

CP are very common in children and young people and CD is the most common mental diagnosis amongst the paediatric population in the UK[34]. In this work, I have shown how different CP groups are predictive of later antisocial behaviour and crime, which carries considerable financial and societal costs[64]. Therefore, it is vital to better understand this phenomenon in order to plan and implement prevention and intervention programmes. CP is a complex and multi-determined behaviour that develops over time. For this reason, it is crucial to study it from a multidisciplinary and developmental perspective. This work represents an attempt at investigating aspects of CP using such perspectives, and to fill several gaps in the literature.

More specifically, I have summarised existing data regarding outcomes of CP by running a systematic review and meta-analysis. This was not done before and such summary was needed in the field, given the amount of primary data produced across several countries and using different datasets. Results from this work have shown a pattern of risk that highlights how continuity rather than age of onset is most predictive of poor outcomes in several domains. I have shown this in chapter 5, where EOP youth

were at higher risk of poor academic achievement in adolescence, and in chapter 6, were EOP youth displayed higher rates of NEET in early adulthood compared to other CP trajectories. In this sense, there was a consistency of findings across the thesis. Findings were also consistent between chapter 6 and chapter 7. Here, I have shown that students' feelings towards the school are important in predicting their developmental course of CP and also their adult outcome (e.g. education and employment outcomes).

Although risk factors underlying CP have long been studied by researchers, there have not been many attempts at theorising how the longitudinal association between these may lead to poor academic achievement, a common risk factor in this population. My developmental cascade model did not show an indirect effect being carried through postnatal factors until adolescence but showed that all risk factors were predicting each other down the chronological line and highlighted smaller indirect effects which may be the object of further investigations in the future. In addition, I have observed a strong association between ADHD and poor academic achievement, particularly in females with a desisting pattern of CP. This may serve as a potential area to target for prevention and intervention programmes that aim to improve academic achievement, particularly in this subtype of young people with CP.

Previous work to investigate the role of schools in potentially modifying the course of development of CP has been undertaken; however, a systematic investigation of specific school factors and their potential mediating role across different developmental trajectories of CP was missing. Results from chapter 6 and chapter 7 have filled this gap and offer important insights into how to implement and deliver interventions for youth with CP.

These findings are supported by emerging literature which indicates that school atmosphere represents an important predictor of students' behaviour. Particularly, students' sense of commitment and belonging to the school have been theorised to be

important in protecting young people from engaging in health risk behaviour and violence. As mentioned in the previous chapter, this could be because commitment and sense of belonging to the school may encourage school-wide norms supportive of positive behaviour. On the contrary, lack of commitment and sense of alienation to the school may increase the likelihood of young people looking for a sense of identity elsewhere, often performing behaviours that are in contrast with those promoted by schools.

The importance of schools in promoting young people's health and positive behaviour has received support by the results of several trials, including the Learning Together study, mentioned in chapters 3 and 7[124, 269, 270]. In this trial, a three-year intervention based on several components such as restorative practices to resolve conflict and social and emotional education proved to be effective in reducing the number of bullying victimisation episodes, improving health and mental health, and decreasing substance use and contact with the police. Interestingly, results did not show a significant decrease in self-reported antisocial behaviour scores in the intervention schools.

In one of the aforementioned trials[270], however, authors found that two school programmes designed to reduce high-risk behaviours among inner-city African American youth yielded significant results in terms of reducing violence and provoking behaviour and school delinquency.

The two interventions were the social development curriculum (SDC) and the school community intervention (SCI). SDC was designed to teach cognitive-behavioural skills to build self-esteem and empathy, manage stress and anxiety, develop interpersonal relationships, resist peer pressure, and develop decision-making skills. It was structured to teach the application of these skills to avoid violence and school delinquency. SCI included the SDC with the addition of parental support, school climate, and community components to impact all social domains of influence on

children. In particular, the school staff and school-wide youth support programmes integrated skills into the school environment. Researchers found that the SCI had stronger effects than the SDC, which may suggest that targeting school policy and changing its climate may yield better outcomes than targeting students alone.

To better understand and identify factors that may play a role in CP development, I would suggest incorporating qualitative data in future work. The combination of quantitative and qualitative data can lead to a better understanding of the factors underlying engagement in antisocial activities. Authors[262] conducted four group interviews with 24 institutionalised offenders aged 11–18. They investigated, amongst others, what they thought were the main risk and protective factors for their engagement in antisocial activities. Risk factors mentioned by individuals include delinquent friends, poor parent-child relationships, and school factors such as low commitment and poor academic performance. Amongst protective factors, young people mentioned non-delinquent friends and good relations with teachers and school staff who can simultaneously give them advice and supervise them. These findings are in line with quantitative research literature and with the results presented in this thesis, and stretch the fact that multiple interrelated domains (e.g. family and school environment) play an important role in the development of CP and antisocial behaviours.

In addition, qualitative research should be conducted with those who work closely with young people with CP such as psychologists, therapists and teachers. More specifically, I argue that useful data may come from asking these professionals about the most effective strategies and interventions. In particular, teachers' views and insight may be very useful to understand the mechanisms that promote change in this high-risk population, for example, within the context of a school intervention.

This last chapter highlights that it is important for research to continue to produce findings that shed light on risk factors, processes and outcomes of CP. These findings

should be used to design and implement interventions that are most effective for youth with CP. In this sense, researchers from several backgrounds (e.g. social scientists, psychologists and psychiatrists) should think pragmatically about how to make use of their findings to achieve such a goal.

Finally, I hope that my efforts and those of other colleagues will result in our findings going beyond academia and reach the public, particularly schools, and raise awareness of the potential that they have to improve students' behaviour, health and mental health. I hope that the findings produced by researchers in this field will reach funders and policymakers, and increase the likelihood of resource allocation to relevant professionals and organisations (e.g. academics who study the effectiveness of prevention/intervention programmes and schools). Science can be considered the foundation of progress, but this can hardly be achieved without the will of different parties to collaborate, and, importantly, without a strategic allocation of resources.

Appendix

Table 13 Summary of health and substance use outcome measures

Author	Assessment measures	Mental health	General health	Cannabis use	Alcohol use
Alink and Egeland, 2013	CBCL, Teacher Report Form (TRF) and Youth Self-Report (YSR), TRF				
Bor, McGee, Hayatbakhsh, Dean, and Najman, 2010	CBCL (short form at age 5), while the Youth Self Report CBCL was used at age 14	Anxiety and depressive symptoms were assessed using the YASR anxiety/depression subscale. Scores exceeding one standard deviation above the mean were considered to represent "caseness." Delusional symptoms were assessed using the 21-item Peters Delusion Inventory (PDI-21). Questions are derived by the Present State Examination. Individuals were put into three categories: 0-3 items, 4-10 items, 11 or more items	General health problems: participants were asked whether they had been told by a doctor that they had a range of physical problems; participants were grouped as follows: no problems at all, one to three problems, four problems or more	Cannabis consumption: never used, every day, every few days, used it once or so, not used in the past month. Participants were then put into the following categories: never used, occasional users, and frequent users	Binge drinking: number of standard drinks drunk on a typical drinking occasion (+6 on a typical drinking occasion, 1-6, 0)
Kretschmer et al., 2014	Mother-reported conduct problems, using the "conduct problem" subscale of the SDQ. The sum score was dichotomised using the standard threshold of scores of 4 or more, yielding 6 binary indicators for the latent growth classes	Depression and anxiety measured using the clinical interview schedule-revised (CIS-R), a self-administered computerised interview that derives diagnoses based on ICD-10 criteria for depression and anxiety disorder (GAD, panic, phobia, social anxiety)	Risky sexual behaviour: respondents were asked how many sexual partners they had had in the last year and were assigned a score of one if they reported three or more different partners	Cannabis use: respondents completed the six-item cannabis abuse screen test asking about cannabis use in the previous 12 months. The sum-score was derived by assigning one to the responses "fairly often" and "often" and 0 to the other response options and summing the responses.	Alcohol use: AUDIT. Authors used a cut-off of 16 points and above on the AUDIT scale to indicate harmful use

				This scale was then dichotomised to indicate those scoring one or more points	
Moffitt, Harrington, and Milne, 2002	Antisocial behaviour: Rutter Child Scale (11-item antisocial scale) completed by parents and teachers when child was 5, 7, 9, 11	Psychopathology: the mental health assessment was a 50-minute module using the Diagnostic interview schedule for DSM-IV disorders with a reporting period of 12 months. Authors classified disorders in anxiety disorders, social phobia, post-traumatic stress disorder, major depression, schizophreniform disorder		Alcohol dependence, other drugs dependence (requiring physiological criteria for withdrawal and tolerance)	Alcohol dependence, other drugs dependence (requiring physiological criteria for withdrawal and tolerance)
Moffitt, Caspi, Dickson, Silva, and Stanton, 1996	Antisocial behaviour: Rutter Child Scale (11-item antisocial scale) completed by parents and teachers when child was 5, 7, 9, 11 (more details in Moffitt et al., 1993). In mid-adolescence authors used self-reported Delinquency Structured Interview (vandalism, shoplifting, buying or selling stolen goods, selling marijuana, drunk driving, beating a family member, beating a non-family member)		WHO sexuality instrument. Unsafe sexual behaviour was considered if the participant had had sexual intercourse with three or more different partners in the last 12 months and never used a condom	DSM-III diagnosis given using the Diagnostic Interview Schedule	DSM-III diagnosis given using the Diagnostic Interview Schedule
Odgers et al., 2008	Conduct problems symptoms (6 key symptoms): physical fight, bullying others, destroying property, telling lies, truancy, and stealing	Mental health: psychiatric disorders (Diagnostic Interview Schedule was used and diagnoses over past year were made according to		Diagnostic Interview Schedule for DSM-IV	Diagnostic Interview Schedule for DSM-IV

		DSM-IV criteria), suicide attempts (using Life History Calendar), informant reports of internalising symptoms and substance use, informant reports of substance use problems			
Odgers et al., 2007	Conduct problems symptoms (6 key symptoms): physical fight, bullying others, destroying property, telling lies, truancy, and stealing	Psychiatric disorders assessed using Diagnostic Interview Schedule (GAD, OCD, phobias, MDD, cannabis and other drugs dependence, PTSD). Indicators of mental health: study members reported whether they had a history of outpatient treatment for mental health or substance abuse, periods when they had psychiatric medication, periods of homelessness, and suicide attempts	Physical health outcomes at age 32: study members provided reports of their overall health on a 5-point Likert scale	Diagnostic Interview Schedule for DSM-IV	Diagnostic Interview Schedule for DSM-IV
Roisman, Aguilar, and Egeland, 2004	Age: grades 1, 2, 3, 6, and age 16: teacher-reported (TRF) CBCL. Parent versions and youth (YSR) versions at age 16	CBCL (Young Adult Self-Report, YSR)		Young Adult Health Survey (frequency of substance use)	Young Adult Health Survey (frequency of substance use, risk-taking behaviour, various forms of antisocial behaviour)
Xie, Drabick, and Chen, 2011	Interpersonal competence scale – teacher administered (which assesses aggression, popularity, and academic competence)				
Hayatbakhsh et al., 2008	Externalising behaviour subscale of CBCL (age 5) and Youth Self Report version of CBCL (age 14)			Cannabis use assessed using CIDI-Auto (age 21)	Cannabis use assessed using CIDI-Auto (age 21)
Stringaris, Lewis, and	Mother-reported SDQ (conduct	Depression assessed using			

Maughan, 2014	problems subscale)	the Revised Clinical Interview Scale (CIS-R), a self-administered computerised interview administered at age 18	
McGee et al., 2011	CBCL (aggression scale, completed by mother) administered at age 5 and the externalising scale of YSR (self-reported version of CBCL) at age 14	Young adult anxiety and depression were assessed using the 17-item anxiety and depression subscale of Young Adult Self-Report (YASR) version of the CBCL	General health was assessed by asking participants whether they had ever been told by a doctor that they had any of the following health problems: diabetes, hypertension, eczema, asthma, depression, anxiety disorder, autism, schizophrenia, migraine, tension headache, attention deficit hyperactivity disorder, liver disease, gall bladder disease, and/or obstructive sleep apnoea
Sentse, Kretschmer, Haan, and Prinzie, 2016	Dutch version of CBCL	Youth Self-Report (YSR). Syndrome scores were created for anxious/depr., withdrawn/depressed, thought problems, attention problems	YSR: somatic complaints

Note. CBCL= Child Behavior Checklist; TRF= Teacher-reported form; YSR= Young person Self-report; PDI= Peters Delusion Inventory; SDQ= Strengths and Difficulty Questionnaire; DSM= Diagnostic and Statistical Manual of Mental Disorders; GAD= Generalised Anxiety Disorder; MDD= Major Depressive Disorder; ODD= Obsessive-Compulsive Disorder; PTST= Post-Traumatic Stress Disorder; CIS-R= Clinical Interview Scale Revised;

Table 14 Summary of conduct, educational and social outcome measures

Author	Assessment measures	Self-reported aggression	Criminal records	Education	Employment
Alink and Egeland, 2013	CBCL, Teacher Report Form (TRF) and Youth Self-Report (YSR), TRF				Unemployment at age 26. Interview about work and education. One of the questions concerned whether and for how many months the participant had been unemployed during the past three years. Score was based on number of months of unemployment
Bor, McGee, Hayatbakhsh, Dean, and Najman, 2010	CBCL (short form at age 5), while the Youth Self Report CBCL was used at age 14	Youth Adult Self Report of CBCL	Court attendance: yes/no		
Kretschmer et al., 2014	Mother-reported conduct problems, using the "conduct problems" subscale of the SDQ. The sum score was dichotomised using the standard threshold of scores of 4 or more, yielding 6 binary indicators for the latent growth classes	Items similar to the core offenses in the 2005 Offending, Crime, and Justice Survey (mugging, shoplifting, break and enter, selling drugs, fire setting, selling or buying stolen goods) were presented to respondents who indicated whether or not they had engaged in these behaviours in the past year. A score of one was assigned following a positive response to one or more of the items	Respondents indicated whether they had been arrested or convicted of a criminal offense, put on trial in court, got police caution, got court fine, got community service order, received an ASBO (antisocial behaviour order). A score of one was assigned following a positive response to one or more of the items		
Moffitt, Caspi, Harrington, and Milne, 2002	Antisocial behaviour: Rutter Child Scale (11-item antisocial scale) completed by parents and teachers when child was 5, 7, 9, 11		Criminal offending (mean number of convictions)	Education completed	Mean months unemployed

Moffitt, Caspi, Dickson, Silva, and Stanton, 1996	Antisocial behaviour: Rutter Child Scale (11-item antisocial scale) completed by parents and teachers when child was 5, 7, 9, 11 (more details in Moffitt et al., 1993). In mid-adolescence the self-reported Delinquency Structured Interview was used (vandalism, shoplifting, buying or selling stolen goods, selling marijuana, drunk driving, beating a family member, beating a non-family member)		Criminal offending (mean number of convictions)	Age when participant left high school	
Odgers et al., 2008	Conduct problems symptoms (6 key symptoms): physical fight, bullying others, destroying property, telling lies, truancy, and stealing	Violence towards others, partner abuse (measured using a standardized interview with 13 physical abuse acts such as hitting, slapping, or kicking and 13 controlling abuse acts such as stalking or stopping contacts with friends or family), hitting a child (measured using the Self-Report Crime Interview), self-reported violence in the past year (using the US national Youth Survey Self-Report Crime Interview), informant-reported fighting	Official violence convictions using the computerized New Zealand Police database. Convictions included, but were not limited to: common assault, rape, indecent assault of a female, robbery, and arson	No educational qualification obtained	Economic problems: SES. Household income, unemployed, informant-rated financial problems, no money for food or other necessities, homeless/taken
Odgers et al., 2007	Conduct problems symptoms (6 key symptoms): physical fight, bullying others, destroying property, telling	Violence towards others, partner abuse (measured using a standardized interview with 13 physical abuse acts such as hitting, slapping,	Official violence convictions using the computerised New Zealand Police database. Convictions included, but were not limited to: common assault,		

	lies, truancy, and stealing	or kicking and 13 controlling abuse acts such as stalking or stopping contacts with friends or family), hitting a child (measured using the Self-Report Crime Interview), self-reported violence in the past year (using the US national Youth Survey Self-Report Crime Interview), informant-reported fighting	rape, indecent assault of a female, robbery, and arson		
Roisman, Aguilar, and Egeland, 2004	Age: grades 1, 2, 3, 6, and age 16: teacher-reported (TRF) CBCL. Parent versions and youth (YSR) versions at age 16	CBCL (Young Adult Self-Report, YASR)		School/work status: self-rated, educational attainment. At age 23, participants indicated how far they had gone in school (0 = no degree, 1 = graduate equivalent degree, 2 = high school diploma, 3 = technical school degree, 4 = 2-year degree, 5 = 4-year degree, 6 = postgraduate degree).	Individuals rated at the high end of the scale spent the "dominant pattern" no less than 75% of the time since they turned 21 in fulltime work, school, or a combination thereof. Participants rated at the middle of the scale were engaged in some combination of part-time work or school for the dominant pattern of the year. Those rated at the low end reported little or no work experience. This rating – as well as the work ethic scale described below – was independently rated by one of two coders, both of whom were trained graduate students or staff on the Parent–Child Research Project

Xie, Drabick, and Chen, 2011	Interpersonal competence scale – teacher administered (which assesses aggression, popularity, and academic competence)		Criminal arrest in early 20s	Education failure (between age 20 and 24), defined as not completing high school or an equivalent degree	
Hayatbakhsh, McGee, Bor, Najman, Jamrozik, and Mamun, 2008	Externalising behaviour subscale of CBCL (age 5) and Youth Self Report version of CBCL (age 14)				
Stringaris, Lewis, and Maughan, 2014	Mother-reported SDQ was used (conduct problems subscale)				
McGee et al., 2011	CBCL (aggression scale, completed by mother) administered at age 5 and the externalising scale of YSR (which is a self-reported version of CBCL) at age 14				Young adults were asked whether they had a “paid job” at the time the survey was conducted. They were grouped into the categories paid job (76.6%) and no paid job (23.4%)
Sentse, Kretschmer, Haan, and Prinzie, 2016	Dutch version of CBCL	Aggressive behaviour, rule-breaking behaviour (using CBCL YSR)			

Note. CBCL= Child Behavior Checklist; TRF= Teacher-reported form; YSR= Young person Self-report; SDQ= Strengths and Difficulty Questionnaire; SES= Socioeconomic Status.

Table 15 Summary of results for each meta-analysis

Outcome	Trajectories	N. of studies	Pooled OR (95% CI)	I-squared (p-value)
Mental health (depression)		7		
	Low		1	
	EOP		2.24 (1.67 - 3.01)	38.3% (0.137)
	AO/AL		1.58 (1.19 - 2.08)	46.8% (0.080)
	CL/Desisting		1.29 (1.00 - 1.66)	29.7% (0.201)
Cannabis use		7		
	Low		1	
	EOP		3.34 (2.53 - 4.41)	0.0% (0.524)
	AO/AL		3.78 (2.54 - 5.63)	65.4% (0.008)
	CL/Desisting		1.14 (0.89 - 1.47)	7.7% (0.369)
Alcohol use		5		
	Low		1	
	EOP		1.85 (1.04 - 3.28)	47.8% (0.105)
	AO/AL		1.72 (1.23 - 2.41)	0% (0.490)
	CL/Desisting		1.14 (0.80 - 1.63)	0% (0.650)
Self-reported aggression		7		
	Low		1	
	EOP		5.40 (2.80 - 10.43)	86.9% (<0.000)
	AO/AL		3.55 (2.07 - 6.08)	84.1% (<0.000)
	CL/Desisting		1.75 (1.21 - 2.53)	60.2% (0.020)
Criminal behaviour		6		
	Low		1	
	EOP		3.18 (1.73 - 5.85)	70.4% (0.005)
	AO/AL		2.29 (1.43 - 3.67)	67.3% (0.009)
	CL/Desisting		1.28 (0.99 - 1.66)	16.2% (0.309)
General health		4		
	Low		1	
	EOP		2.35 (1.48 - 3.73)	0% (0.655)
	AO/AL		2.38 (1.25 - 4.53)	70.9% (0.016)
	CL/Desisting		1.36 (0.89 - 2.10)	59.9% (0.058)
Poor education		6		
	Low		1	

	EOP	4.14 (1.95 - 8.82)	81.3% (<0.000)
	AO/AL	2.35 (1.44 - 3.82)	73.3% (0.002)
	CL/Desisting	1.83 (1.26 - 2.65)	52.9% (0.060)
Poor employment outcome	5		
	Low	1	
	EOP	2.00 (1.43 - 2.79)	0% (0.469)
	AO/AL	1.22 (0.95 - 1.55)	0% (0.936)
	CL/Desisting	1.14 (0.90 - 1.45)	0% (0.795)

EOP= Early-Onset Persistent; AO/AL= Adolescent-Limited or Adolescent-Onset; CL= Childhood-Limited

Table 16 Fit statistics and nested model comparisons

Step 1 Nested model comparisons: CL vs EOP	**df**	**Scaling Factor**	**x2**	**CFI**	**TLI**	**RMSEA**	**Model Comparison**	**x2 diff**	**df diff**	**p**
1. Fully constrained	207	1.0525	460.347	0.973	0.969	0.04	.	.	.	.
2. Freely estimated (full)	197	1.0442	453.086	0.973	0.967	0.041	2 vs 1	9.377	10	**0.002**
3. Freely estimated cascade	203	1.0478	456.885	0.973	0.968	0.04	3 vs 1	4.485	4	**0.034**
3a. Free path MatPsy --> MatBond	206	1.0512	460.913	0.973	0.969	0.04	3a vs 1	0.002	1	0.959
3b. Free path MatBond --> Lan	206	1.0522	459.654	0.973	0.969	0.04	3b vs 1	0.778	1	0.378
3c. Free path Lan --> ADHD	206	1.0502	461.23	0.973	0.969	0.04	3c vs 1	0.086	1	0.769
3d. Free path ADHD --> Aca	206	1.0518	456.118	0.974	0.969	0.04	3d vs 1	3.986	1	**0.046**
4. Direct effects: EOP vs CL (grand test)	204	1.05	459.716	0.973	0.968	0.04	4 vs 1	1.48	3	0.223
4a. Free path MatPsy --> Aca	206	1.0525	459.654	0.973	0.969	0.04	4a vs 1	0.693	1	0.405
4b. Free path MatBond --> Aca	206	1.0524	460.389	0.973	0.969	0.04	4b vs 1	0.001	1	0.697
4c. Free path Lan --> Aca	206	1.0501	460.563	0.973	0.969	0.04	4c vs 1	0.567	1	0.451
Step 2 Nested model comparisons: sex diff. CL vs EOP										
1. Fully constrained	435	1.0376	785.544	0.963	0.96	0.046	.	.	.	.
2. Freely estimated (full)	405	1.0247	755.912	0.963	0.957	0.047	2 vs 1	33.42	30	**<0.000**
3. Freely estimated Cascade	423	1.0297	779.154	0.963	0.958	0.047	3 vs 1	9.71	18	**0.002**

3a. Free path MatPsy --> MatBond	432	1.0357	785.136	0.963	0.959	0.046	3a vs 1	1.46	3	0.227
3b. Free path MatBond --> Lan	432	1.0369	785.47	0.963	0.959	0.046	3b vs 1	0.55	3	0.458
3c. Free path Lan --> ADHD	432	1.0304	786.772	0.963	0.959	0.046	3c vs 1	1.001	3	0.317
3d. Free path ADHD --> Aca	432	1.0362	778.579	0.964	0.96	0.046	3d vs 1	6.711	3	**0.01**
3d1: CL female vs CL male	433	1.0365	778.69	0.964	0.96	0.046	3d1 vs 1	6.645	2	**0.012**
3d2: CL female vs EOP female	433	1.0367	781.079	0.964	0.96	0.046	3d2 vs 1	4.329	2	**0.037**
3d3: CL female vs EOP male	433	1.0367	779.143	0.964	0.96	0.046	3d3 vs 1	5.657	2	**0.015**
4. Direct effects: EOP vs CL sex differences (grand test)	426	1.0349	773.428	0.964	0.959	0.046	4 vs 1	12.579	9	**<0.000**
4a. Free path MatPsy --> Aca	432	1.0375	782.549	0.963	0.959	0.046	4a vs 1	3.028	3	0.081
4b. Free path MatBond --> Aca	432	1.0374	782.766	0.963	0.959	0.046	4b vs 1	2.843	3	0.091
4c. Free path Lan --> Aca	432	1.0349	783.253	0.963	0.959	0.046	4c vs 1	3.149	3	0.076

Table 17 Fit statistics and nested model comparisons (using impulsivity, hyperactivity and inattention individually for each model)

Step 1 Nested model comparisons: CL vs EOP (Impulsivity, Hyperactivity, Inattention)	**df**	**Scal Factor**	**x2**	**CFI**	**TLI**	**RMSEA**	**Model Comparison**	**x2 diff**	**df diff**	**p**
1. Impulsivity Fully constrained	211	1.0699	2394.964	0.77	0.738	0.116	.	.	.	.
2. Hyperactivity Fully constrained	211	1.0689	2344.754	0.775	0.745	0.115	.	.	.	.
3. Inattention Fully constrained	211	1.0692	2283.424	0.782	0.752	0.113	.	.	.	.
4. Free path Impulsivity --> Aca	210	1.0694	2388.834	0.771	0.738	0.116	4 vs 1	6.598	1	**0.01**
5. Free path Hyperactivity --> Aca	210	1.0688	2338.914	0.776	0.744	0.115	5 vs 2	6.481	1	**0.015**
6. Free path Inattention --> Aca	210	1.0683	2277.757	0.782	0.751	0.113	6 vs 3	6.445	1	**0.011**
Step 2 Nested model comparisons: sex differences CL vs EOP (Impulsivity, Hyperactivity, Inattention)										
1. Impulsivity Fully constrained	441	1.0528	2652.603	0.77	0.749	0.114	.	.	.	.
2. Hyperactivity Fully constrained	441	1.0518	2609.795	0.774	0.754	0.113	.	.	.	.
3. Inattention Fully constrained	441	1.0514	2544.871	0.781	0.762	0.111	.	.	.	.
4. Free path Impulsivity --> Aca	438	1.0519	2643.852	0.77	0.748	0.114	4 vs 1	9.783	3	**<0.001**
5. Free path Hyperactivity --> Aca	438	1.0516	2599.727	0.775	0.753	0.113	5 vs 2	10.277	3	**0.001**
6. Free path Inattention --> Aca	438	1.0494	2538.539	0.781	0.76	0.112	6 vs 3	8.734	3	**0.003**

Table 18 Predictors of data missingness

	Odds Ratio	P-value	95% CI lower	95% CI upper
LOW				
AO	**1.554**	**0.005**	**1.145**	**2.109**
CL	1.020	0.869	0.808	1.287
EOP	1.020	0.889	0.767	1.358
NEET (No)				
NEET (Yes)	1.073	0.631	0.805	1.429
Male				
Female	0.964	0.63	0.831	1.119
White				
Non-White	1.387	0.145	0.894	2.153
KS4_IDACI	**2.442**	**0.009**	**1.252**	**4.761**
High/Mid-high social class				
Low/Mid-Low social class	**1.222**	**0.055**	**0.995**	**1.501**
Depression (No)				
Depression(Maybe/Yes)	**1.252**	**0.015**	**1.045**	**1.499**
School connectedness	1.026	0.075	0.997	1.057
School enjoyment	**0.924**	**0.002**	**0.878**	**0.972**

AO= Adolescent-Onset; CL= Childhood-Limited; EOP= Early-Onset Persistent.
Highlighted in bold significant results

Table 19 Analyses run using a restricted sample (N=1077) where there were no missing data at the level of confounders and mediators

	G-comp est. (expRR) N= 1077	P-value	L 95% CI	U 95% CI
TCE(2) AO	2.627	0.032	1.087	6.356
NDE(2)	2.624	0.033	1.081	6.366
NIE(2)	1.002	0.984	0.831	1.209
PM(2)	0.002	0.998	-1.533	1.537
TCE(3) CL	3.023	0.001	1.604	5.698
NDE(3)	2.907	0.001	1.530	5.524
NIE(3)	1.040	0.664	0.871	1.241
PM(3)	0.035	0.759	-0.191	0.261
TCE(4) EOP	3.916	0.000	2.084	7.359
NDE(4)	3.206	0.001	1.638	6.277
NIE(4)	1.221	0.041	1.008	1.480
PM(4)	0.146	0.118	-0.037	0.330

TCE= Total Causal Effect; NDE= Natural Direct Effect; NIE= Natural Indirect Effect; PM= Percentage Mediated; AO= Adolescent Onset; CL= Childhood-Limited; EOP= Early-Onset Persistent. Note that PM is expressed in log terms

Table 20 Estimated total, direct and indirect effects of CP trajectory expressed in relation to the reference L (Low) trajectory and including truancy as an intermediate confounder (N=3288)

	G-comp est. (expRR) 3288	P-value	L 95% CI	U 95% CI
TCE(2) AO	1.500	0.078	0.956	2.353
NDE(2)	1.589	0.043	1.015	2.489
NIE(2)	0.944	0.263	0.852	1.045
PM(2)	-0.143	0.804	-1.273	0.987
CDE(2)				
TCE(3) CL	1.690	0.006	1.165	2.452
NDE(3)	1.709	0.009	1.143	2.553
NIE(3)	0.989	0.868	0.870	1.125
PM(3)	-0.021	0.906	-0.366	0.325
CDE(3)				
TCE(4) EOP	2.573	0.000	1.642	3.187
NDE(4)	2.112	0.001	1.379	3.234
NIE(4)	1.218	0.012	1.044	1.422
PM(4)	0.209	0.074	-0.020	0.438

TCE= Total Causal Effect; NDE= Natural Direct Effect; NIE= Natural Indirect Effect; PM= Percentage Mediated; AO= Adolescent Onset; CL= Childhood-Limited; EOP= Early-Onset Persistent. Note that PM is expressed in log terms

Table 21 Comparison of Inclusive study schools with non-recruited schools and average for secondary schools in England

	England average	**Inclusive trial schools**				**Non-recruited schools**			**Comparison of recruited and non-recruited schools**
		N	***Mean (SD)***	***Median***	***Range***	***N***	***Mean (SD)***	***Median***	***Range***	***p-value***
School IDACI (mean)	not available	40	0.262 (0.198)	0.239	0.028-0.698	427	0.251 (0.186)	0.199	0.007-0.765	0.5*
School population size (mean)	939	40	1081 (324)	1075	446-1786	427	1073 (379)	1058	60-2405	0.9
Special educational need (SEN) (%)	2.8	40	5.2 (4.4)	5.9	0.03-14.4	422	5.6 (5.9)	5.1	0.1-42.7	0.5*
English as a foreign language (%)	13.60%	40	34.7 (25.9)	29.5	3.3-90.3	424	30.5 (25.0)	23.3	0-92.8	0.2*
Eligible for free school meals (%)	16.30%	40	36.8 (19.4)	38.1	3.9-75.8	427	34.7 (20.8)	31.2	1.6-94.0	0.3*
No. with ≥5 GCSEs at A to C grade (%)	59.30%	40	60.6 (14.5)	56.5	35-99	399	63.4 (16.0)	63.0	14-100	0.3
Value added (best 8) (median score)	1000	40	1013 (24)	1014	925-1064	399	1015 (22)	1016	949-1081	0.3
Student absence (annual) (%)	5.8	40	5.2 (1.2)	5.1	2.7-9.1	419	5.0 (1.0)	4.9	2.1-10.5	0.3

OFSTED rating						
Outstanding	12%	13	32.5%	144	33.8%	
Good	60%	23	57.5%	194	45.5%	
Requires improvement	15%	3	7.5%	68	16.0%	
Inadequate	13%	0	0%	3	0.7%	
Not available	-	1	2.5%	17	4.0%	
Combined either outstanding or good	72%	40	90%	426	79.3%	0.04
School sex makeup		***40***	***%***	427	***%***	
Boys only		2	5.26	28	6.6	0.9
Mixed sex		33	86.84	356	83.4	
Girls only		6	7.89	43	10.1	

Table 22 Pattern of missing data across waves and gender

	0		1		2		Total	
Girls	N	%	N	%	N	%	N	%
Stable low	946	52.64	467	25.99	384	21.37	1,797	100
Moderate/High	71	39.44	49	27.22	60	33.33	180	100
Total	1,017	51.44	516	26.1	444	22.46	1,977	100
Boys	N	%	N	%	N	%	N	%
Stable low	931	53.02	475	27.05	350	19.93	1,756	100
Moderate/High	49	29.17	67	39.88	52	30.95	168	100
Total	980	50.94	542	28.17	402	20.89	1,924	100

0= data available at all 3 time-points, 1= data available on at least two of the three time-points, 2= data available at only one of the three time-points

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