Psychopathy

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Abstract

Psychopathy is a personality disorder characterized by a constellation of affective, interpersonal, lifestyle, and antisocial features whose antecedents can be identified in a subgroup of young people showing severe antisocial behaviour. The prevalence of psychopathy in the general population is thought to be ~1%, but is up to 25% in prisoners. The aetiology of psychopathy is complex, with contributions of both genetic and environmental risk factors, and gene–environment interaction and correlation. Psychopathy is characterized by structural and functional brain abnormalities in cortical (such as the prefrontal and insular cortices) and subcortical (for example, the amygdala and striatum) regions leading to neurocognitive disruption in emotional responsiveness, reinforcement-based decision-making and attention. Although no effective treatment exists for adult with psychopathy, preliminary intervention studies targeting key neurocognitive disturbances are showing promising results. Given that psychopathy is often comorbid with other psychiatric disorders and increases the risk for physical health problems, educational and employment failure, accidents, and criminality, the identification of children and young people at risk for this personality disorder and preventive work are important. Indeed, interventions that target the antecedents of psychopathic features in children and adolescents have been found to be effective.

Dedication: This Primer is dedicated to the memory of our esteemed colleague Scott O. Lilienfeld (PhD) for his significant contribution to the field of psychopathy as a scientist and as a mentor.

[H1] Introduction

The long and controversial history of psychopathy within psychiatry and its portrait in the media have contributed to misconceptualised views of the aetiology, assessment, treatment and definition of this disorder among parts of the scientific and clinical community and general public[1,2] (Supplementary Table 1). For example, among laypeople, psychopathy is often synonymous with violence and serial killing, but not all psychopaths commit violent acts[3].

Psychopathy is a personality disorder that manifests as a syndrome characterized by a constellation of affective, interpersonal, lifestyle, and antisocial features[4,5] (Fig. 1). Affectively, individuals with psychopathy lack empathy, guilt, or remorse, are callous, and have shallow and deficient affect, whereas interpersonally they are grandiose, arrogant, deceitful, and manipulative. From an early age, individuals with psychopathy often engage in instrumental, planned acts of antisocial behaviour and aggression, but can also display impulsive and irresponsible behaviours[6]. The affective and interpersonal features of individuals with psychopathy distinguish them from those with the broader diagnosis of antisocial personality disorder[6] (ASPD; Box 1), defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)[7,8]. Although the prevalence of psychopathy in the general population is thought to be ~1%[9,10], it is associated with enormous financial and personal costs to the individual, their family, their victims and society that it has been identified by some as the most expensive mental health disorder and a major public health issue[11], with annual costs estimated to be around US$460 billion[12]. Unsurprisingly, the prevalence of psychopathy in prisons is higher than in the general population, with estimates ranging between 16% and 25%[13].

Classifying children as psychopaths would be inappropriate, and indeed inaccurate; however, most adults with psychopathy have exhibited callous and antisocial behaviour from childhood[14], which is in line with the view that personality disorders manifest developmental antecedents in childhood or adolescence[7,15]. Accordingly, a substantial body of evidence over the past 25 years shows that a subgroup of antisocial children and young people (CYP) might be at risk of developing psychopathy in adulthood[16] (Box 2), which is increasingly considered a neurodevelopmental disorder resulting from a complex interplay between genetic and environmental risk factors[17-20].

In this Primer, we adopt a developmental perspective to provide an overview of the epidemiology, aetiology, pathophysiology, diagnosis, and treatment of psychopathy. We also consider the prevalence of the disorder and its effect on physical and mental health, as well as on social, educational and occupational outcomes. We conclude by identifying gaps in knowledge, pressing challenges and future directions for the field, including how aetiological and neurocognitive data might inform management and treatment and how this should be systematically tested. It must be noted that most research on psychopathy has primarily focused on males, but more recent work has investigated female samples or compared both sexes; the importance of this line of work is noted in the Outlook section.

[H1] Epidemiology

The prevalence of psychopathy among incarcerated offenders in North America is estimated as 16%-25% in men and 7%-17% in women[13,21-23] (B. Verschuere, personal communication). The core affective and interpersonal features of psychopathy do not systematically differ between white, Black, and Hispanic offenders in North America[24]. Studies in the UK tend to find lower mean psychopathy scores among offenders than studies in North America, with prevalence estimates of 5%-8%[22,25] in men and 2%-4%[25,26] in women. Studies from other European countries have reported a prevalence of 11%-18% in

samples consisting primarily of male violent offenders from prisons and forensic psychiatric hospitals[21,22,23] (B. Verschuere, personal communication). A similar prevalence has been reported for male offenders in South America (13%-14%)[22] and Southeast Asia (12%)[27,28] (J. S. Sohn, personal communication).

Studies of the prevalence of psychopathy in the community are rare. The prevalence of 'possible' psychopathy in community samples assessed using a screening interview has been estimated as 0.6% (1.3% of men, <1% of women) in the UK[10] and 1.2% (1.0% of men, 1.2% of women) in the USA[29]. Of note, these estimates are considerably lower than the prevalence of ASPD in the general adult population in Europe, North America, Australia, and New Zealand, which is estimated as 5%-6% in men and 1%-2% in women[30].

Psychopathy co-occurs with the DSM cluster B personality disorders, particularly ASPD, narcissistic personality disorder and borderline personality disorder[13,25,31,32] (Box 1 and Fig. 2). Other conditions commonly comorbid with psychopathy include substance use disorders and attention-deficit/hyperactivity disorder (ADHD)[31]; these conditions tend to be most strongly related to the lifestyle/antisocial features of psychopathy[13] (Fig. 2).

The association between psychopathic features and symptoms of internalizing disorders tend to be relatively weak[31]. An early conceptualization of psychopathy proposed an absence of anxiety problems as a central feature of psychopathy[5], which is mirrored in the DSM-5[31]. However, when different psychopathy symptom dimensions are studied separately, the direction of the association with internalizing symptoms varies; internalizing problems are modestly, positively correlated with the lifestyle/antisocial facets of psychopathy, whereas the interpersonal/affective facets tend to be associated with lower levels of trait anxiety[31,33] (Fig. 2). Based on these data, some groups have suggested to conceptualize internalizing problems as a subtyping scheme that differentiates primary (low internalizing

problems) and secondary (high internalizing problems) variants of psychopathy[33] (Supplementary Box 1).

[H1] Mechanisms/pathophysiology

[H2] Genetic factors

Twin and adoption studies of children and adults have found robust evidence of genetic risk for psychopathic personality traits [18,34]. As the neurocognitive profile and some behaviours associated with psychopathy are at least partially distinct from those associated with antisocial behaviour in general, we might expect to find risk genes that are unique for psychopathy and those that are shared with the broader antisocial phenotype[35].

Only a handful of candidate gene studies have focused on psychopathic traits, with the majority of these investigations focusing on their putative precursor in CYP, callous-unemotional (CU) traits. These studies have identified genes involved in the serotonergic (such as *SLC6A4*) and oxytocinergic (e.g., *OXTR*) systems, which are thought to contribute to reduced emotional reactivity and capacity for attachment to others[18,34]. There is also tentative evidence for shared genetic risk between a broader antisocial phenotype and CU traits. Indeed, one study found that polygenic risk score for aggression, including variants in dopaminergic, glutamatergic and neuroendocrine signalling pathways that are thought to be important for neurocognitive function, information processing and temperament, accounted for just over 1% of the variance in CU traits[36]. Genome-wide association studies of CU traits or antisocial behaviour in combination with CU traits[37-39] have not produced any promising insights; however, the sample sizes in these studies have been small with< 3,000 participants. Sample sizes of over one million participants are needed if we want to not only detect reliable associations and also account for a meaningful proportion of genetic variance[40].

[H2] Environmental factors

Genetic and environmental factors and their complex interplay shape how individual

development canalizes over time. (Fig. 3). Cross-sectional and longitudinal studies have identified a wide range of risk factors associated with antisocial behaviour and psychopathic features including prenatal maternal stress[41-43], child maltreatment[44] during childhood and adolescence, harsh parental discipline during childhood and adolescence, negative parental emotions[45], disorganized parent-child attachment[46] and disrupted family functioning[47]. By contrast, warm, responsive and consistent parenting has been associated with a reduced risk of antisocial behaviour and psychopathy[45,48].

Without genetically informative study designs, it is not possible to fully evaluate the causal role of postulated environmental risk factors in the development of psychopathy. Several risk factors that are thought to be 'environmental' may in part reflect genetic predispositions of people who are part of that environment, a phenomenon known as *gene-environment correlation*[49]. For example, parents with genetic variants that predispose to psychopathic behaviour have an increased risk of engaging in negative and harmful parenting practices and may also pass on some of these genetic variants to their offspring[18]; in other words, the association between dysfunctional parenting and psychopathic traits in the child may, in part, represent a genetic confound. Children also evoke different reactions in people around them or actively seek particular environments[18,50]. Data from longitudinal twin studies indicate that part of the association between harsh and negative parenting and higher levels of psychopathic traits in children may reflect genetic vulnerability within biological families[51]. However, data from adoption and twin studies have also shown that warm parenting can buffer the effects of heritable risk for psychopathic traits[52,53]. Taken together, these findings suggest that gene environment correlation, gene-environment interaction, and environmental main effects all have a role in the development of psychopathy.

[H2] Neurocognitive disruption

Three main forms of neuro-cognitive disruption are found in individuals with elevated psychopathic traits: emotional (particularly, though not limited to, empathic) responsiveness, reinforcement-based decision-making (including moral judgments) and attention. Some types of neuro-cognitive disruption seem to be disorder-specific for psychopathy (for example, deficient empathic responding), whereas others (such as response to reward or attention) are shared with other disorders, some of which can co-occur with psychopathy, such as ADHD or addiction (Box 3 and Supplementary Box 2).

[H3] Emotional responsiveness. The suggestion that psychopathic traits reflect disturbances in emotional responsiveness has a long history[54]; however, not all emotions are affected in those with psychopathy. Anger seems to be intact in individuals with psychopathic traits[55], as these individuals have an increased risk of anger-based reactive aggression **[G]**[56]. Conversely, empathic responding,[57,58] fear,[54,59] and potentially social affiliation **[G]**[60] all seem to be disrupted in those with psychopathic traits, whether they are measured through psychophysiological, cognitive, or functional MRI (fMRI) paradigms. Further research is needed to elucidate the specific aspects of fear and anxiety processing that may be affected in psychopathy. Studies have indicated problems in threat detection and responsivity, but evidence of an atypical subjective fear experience is less strong[59,61]. A reduced ability to detect and respond to others' fear and distress is hypothesized to increase the likelihood of an individual committing antisocial behaviour, particularly that which is instrumental (goal-directed[62]) in nature[62], as the individual is less bothered by the distress of others and being punished for aggressive behaviour than individuals without psychopathy[54,57].

Considerable data in adults and youths support the involvement of emotional disturbance in psychopathy. Behaviourally, individuals with psychopathic traits display reduced aversive conditioning **[G]** [63] and impaired emotion expression recognition, particularly for fear, compared with neurotypical individuals[64,65]. These behavioural findings

are complemented by data from fMRI studies that have found reduced responses in the amygdala and cortical regions implicated in responding to emotional stimuli, such as the anterior insula and ventromedial prefrontal cortices, during a variety of emotional and empathy tasks that have largely probed the processing of fear or pain (Fig. 4)[61,66-69]. Notably, reduced response in the amygdala to the distress of others mediates the relationship between CU traits and level of instrumental aggression[70].

[H3] Reinforcement-based decision-making. Adults with psychopathy and CYP at risk of psychopathy perform poorly on a variety of reinforcement-based decision-making tasks **[G]**[71-73]. This poor performance may relate to reduced reinforcement sensitivity or responsiveness, resulting in an individual who makes poorer decisions and is, therefore, more likely to be impulsive and display frustration-induced aggression[74].

Studies with CYP at risk of psychopathy have reported *reduced* neural responsiveness to reward in the striatum and ventromedial prefrontal cortex[75,76] (Fig. 4). This reduction may manifest as reduced responsiveness to drug cues in individuals with substance use disorders and psychopathic traits[77] (though see[78]). In addition, some studies have found high psychopathy scores to be related to a reduced response to monetary loss in the ventral striatum [79] and a relative failure to reduce activity within the ventromedial prefrontal and/or posterior cingulate cortex following unanticipated punishment[80,81]. However, other studies have found *increased* responses to reward in the nucleus accumbens [82].

Moral judgments involve emotional responses to the emotional content of an action and making decisions based on this content, both of which are impaired in individuals with psychopathy. Adults with psychopathy and CYP at risk of psychopathy are compromised in at least some forms of moral judgments (for example they show a reduced endorsement of care-based transgressions (involving people being harmed, such as one person hitting another) and judge care-based transgressions more like social disorder-based, conventional

transgressions (such as talking in class) relative to comparison populations; for a review, see[83]). Moral judgments also involve several brain regions, such as the ventromedial, rostromedial, and dorsomedial frontal cortices, anterior insula cortex, striatum and amygdala[84] (Fig. 4). In line with the behavioural findings, fMRI studies have relatively consistently found reduced responding within these brain regions during moral judgment tasks in adults with psychopathy and CYP at risk of psychopathy, compared with individuals without psychopathy[85,86].

[H3] Attention. Attention-based accounts were some of the earliest models of psychopathic traits[87] and suggested that individuals with psychopathy over-focus on certain features of the stimulus array (such as those associated with reward or a particular goal) at the expense of other features (such as those associated with punishment, other's distress, or contextual cues)[88]. Numerous studies have found that individuals with psychopathic traits have compromised selective attention when performing basic attentional tasks[89]. In addition, if individuals with psychopathic traits are explicitly asked to attend to the emotional content of an image or to empathize with actors in a video (rather than passively viewing the stimuli), group differences in emotional response between those with psychopathy and neurotypical individuals disappear, suggestive of an attentional abnormality in those with psychopathy[90-93]. The effect of psychopathy-related differences in selective attention on emotion responding has been documented using behavioural[94] (such as response accuracy and reaction time), electrophysiological[95,96] (for example startle potentiation, skin conductance and EEG), and neuroimaging[97] (such as amygdala and lateral prefrontal cortex activation) metrics. A few studies have extended attention-based accounts of psychopathy to antisocial CYP with CU traits, and found that manipulating attention influences emotional responding[93,98]. The larger-scale neurocognitive systems underpinning differences in attention to emotions in individuals with or at risk of psychopathy have not been widely researched. However, a resting state

fMRI study of a large incarcerated sample found that high levels of psychopathy were associated with a hyper-organised dorsal attention network[99].

[H2] Structural MRI studies

[H3] Grey matter. Structural abnormalities in a network of subcortical and cortical regions have been found in those with psychopathy, likely accounting for the atypical neurocognitive functioning discussed above (Fig. 4). Early studies exclusively focusing on specific lobes/regions of interest identified *a priori* showed that psychopathy is associated with reduced volume of the prefrontal cortex and reduced volume and abnormal shape of the hippocampus and amygdala, likely underpinning the impaired classical fear conditioning and stimulus-reinforcement learning in psychopathy[100,101]. Increased and reduced volume of the dorsal and the ventral striatum[100,101] have also been found and are consistent with data from neuropsychological and fMRI studies that found abnormal processing of reward and punishment information in individuals with psychopathy and CYP at risk of developing psychopathy[17]. In addition, large cavum septum pellucidum, a marker of abnormal limbic brain development, is associated with psychopathy[101] (but, see[102] for a failed replication) lending further support to the view that psychopathy might have a neurodevelopmental origin[19]. However, one study in youths found that large cavum septum pellucidum may increase the risk for antisocial behaviour, but does not seem to be a neurodevelopmental marker for psychopathy *per se*[103].

Studies that have focused exclusively on *a priori* regions of interest may have missed abnormalities in other regions that are affected in psychopathy[104]. Therefore, more recent structural MRI studies have used automated and unbiased methods that are carried out using algorithms and do not depend on manual tracing or subjective assessments, such as voxel-based morphometry[105] (VBM). Intriguingly, no overall differences between people with psychopathy and controls have been reported for total intracranial volume, or total grey

matter volume, but psychopathy is characterized by reduced grey matter volume across several cortical and subcortical regions, including frontal, temporal, parietal, and occipital regions, in addition to the anterior and posterior cingulate, anterior and posterior insula, amygdala, hippocampus and the caudate and putamen (although other studies have found increased grey matter volume in the caudate and amygdala)[100].

Based on evidence that psychopathy lies on a continuum of severity[106], five VBM studies have examined the association between the severity of psychopathy in prisoners and grey matter volume[100,101]. The most consistent finding from these studies is that total psychopathy scores are negatively correlated with grey matter volume in temporal and limbic or paralimbic regions[100,101]. A meta-analysis of studies in CYP found that the severity of CU traits is positively related to grey matter volume in the putamen[107], whereas more recent studies have found negative associations between CU traits and grey matter in the amygdala[108,109]. These findings provide support to an influential neurocognitive model of the development of psychopathy, which posits amygdala disruption as central to the development of disorder[62]. However, the large ABCD study[110] has found that volume reductions of the amygdala and the hippocampus occur in antisocial youths, irrespective of the levels of CU traits, compared with typically developing youths, but that volume reduction in the insula might be unique to those with high CU traits. The latter finding could partly explain difficulties in empathy and decision-making in this population.

Grey matter volume in VBM is thought to reflect several properties of the cerebral cortex, including its thickness, surface area, and gyrification (folding)[111]. Given evidence in neurotypical individuals that these properties are under distinct genetic influences in adults[111] and follow divergent developmental trajectories[112], some studies have used surface-based morphometry (SBM) to investigate these different metrics in psychopathy. The majority of studies have focused on cortical thickness, of which the most consistent findings are reduced

cortical thickness in the frontal and temporal lobes in individuals with psychopathy, with some evidence that those reductions are associated with the affective facet of the disorder[113] and partially account for the commonly observed increased response perseveration on neuropsychological tasks[114]. In one study of 716 male prisoners psychopathy was associated with reduced gyrification in the middle cingulate cortex extending into the dorsomedial frontal and parietal cortices[115], a network of regions that are central to a host of cognitive and emotional processes that are impaired in psychopathy, such as, for example, error detection and emotional processing of negative images. Few SBM studies have examined CYP at risk for psychopathy[116]; in one study CU traits were found to be positively correlated with insula folding[117], while in two other studies CU traits were negatively correlated with cortical thickness in the right superior temporal cortex[118,119] and the lingual and fusiform gyri[117,119], which are involved in decision-making and face processing, respectively.

[H3] White matter volume and microstructure. Studies that have examined white matter in people with psychopathy have focused on its volume or the microstructure of white matter tracts[100,101]. Increased volume of the corpus callosum, cerrebellum, and frontal, parietal, and occipital lobes have been found in individuals psychopathy compared with neurotypical individuals[101]. Studies on males and females using diffusion neuroimaging to examine white matter tracts have consistently demonstrated that psychopathy is associated with higher diffusivity (for example reduced fractional anisotropy) in the uncinate fasciculus, a tract connecting the ventromedial prefrontal cortex and the anterior temporal lobe including the amygdala[100,101,120] (Fig. 4). However, some studies have also found higher diffusivity within other tracts implicated in interhemispheric (corpus callosum) and frontal lobe connectivity as well as within striato-thalamo-frontal and dorsal default mode networks, with the latter specifically related to the affective dimension of the disorder[100,101]. Intriguingly, an

emerging body of research[121-123] in antisocial youths has identified microstructural changes that are associated with high CU traits in similar tracts to those identified in adults with psychopathy (such as uncinate fasciculus, corpus callosum, dorsal cingulum), but these microstructural changes are in opposite directions to those observed in adults, wherein in youths lower diffusivity is observed (often interpreted as greater integrity), with higher diffusivity observed in adults (commonly seen to reflect reduced integrity). The reasons for the discrepancy between youth and adult data are not fully understood, but likely reflect differences in maturational stage, sample composition, and analytic approaches (Box 3).

In sum, there is increasing evidence from behavioural and fMRI studies suggesting that CYP at risk of psychopathy share some of the same neurocognitive disruptions as those observed in adults with psychopathy. However, although grey matter abnormalities have to some extent been observed in similar cortical and subcortical regions, evidence from structural connectivity studies indicates that these might present differently between childhood and adulthood. Crucially, the pattern of results in these studies also suggests that psychopathy, like most psychiatric disorders[124], is likely to be a disorder that affects brain *circuits* rather than isolated regions[62]. Finally, despite the lack of prospective longitudinal studies, these data provide tentative support to the view that psychopathy has a neurodevelopmental origin.

[H1] Diagnosis, screening and prevention

[H2] Diagnosis

The construct of psychopathy was well-known to many mental health professionals prior to the advent of specific measures for its assessment, but no consensus existed on which specific traits or behaviours should be included in an assessment leading to a diagnosis. The DSM-5 does not include psychopathy as a personality disorder; however, the Cluster B

personality disorders (ASPD, borderline, histrionic, and narcissistic), particularly ASPD, are the disorders that are most strongly associated with psychopathy[25,31,32].

The most commonly used measure to assess psychopathy in clinical and forensic settings is the Hare Psychopathy Checklist – Revised (PCL–R, Fig. 1)[9,125]. The PCL-R was designed to capture a constellation of traits and behaviours consistent with early conceptions of psychopathy, particularly those described by psychiatrist Hervey Cleckley[5] (Supplementary Table 1). The 20 items included in the PCL-R are weighted equally and are assessed on a three-point ordinal scale (0, 1, 2) based on information from a semi-structured interview and review of collateral information, such as police reports, criminal and court records, institutional records, medical, social work, psychological assessments, and parole and probation records. The interview can last up to 3 hours. It should only be conducted by a suitably qualified and experienced clinician or researcher who is specifically trained to administer the PCL-R under standardized conditions. For clinical purposes, the PCL-R assessment should not be based solely on information learned through interview, as many individuals with psychopathic traits engage in impression management and lying. Although it is possible to conduct a PCL-R assessment for clinical purposes using only collateral information (information from different people, that spans temporal periods, and across diverse life domains, such as family, work/school, and community), clinicians and researchers often rely on how the individual interacts with them to help assess the interpersonal features of psychopathy. A large number of studies have used the PCL-R and it has undergone rigorous psychometric evaluation.

The PCL-R and its derivatives were designed to measure the construct of psychopathy. However, data showing that psychopathy is a risk factor for violence[126] (but see[127]) have contributed to the use of the PCL-R and its derivatives in the criminal justice system to inform decisions about future violence risk in sentencing and parole hearings[128], in

the death penalty and sexually violent predator hearings in the United States[129], and dangerous offender hearings in Canada[130].

Psychopathy as assessed by the PCL-R and various other measures (Table 1) is a dimensional construct[106,131], but for research and clinical purposes, a categorical cut-off score of 30 or greater[9] (out of a maximum possible score of 40) is commonly used on the PCL-R for a diagnosis of psychopathy to North American male offenders. Different cut-off scores of 25 or 26 or higher have been used for classifying forensic psychiatric patients or sexual offenders as high risk[132,133] and in some European countries where the mean score on the PCL-R is lower[134]. Of note, an individual with no criminal record would normally score no more than 4 and most prisoners would score ~20-22[9]. Having a high score on a couple of items would not be indicative of psychopathy, as having elevated scores across all facets of psychopathy is reflective of this disorder.

In addition to the rater-based approaches for the assessment of psychopathy, such as the PCL-R and similar rating scales, psychopathic traits can also be evaluated using self-report, which is used widely in research and measures have proliferated over the past 20 years (Table 1). One relatively recent self-report measure of psychopathy that has garnered a considerable amount of research is the Triarchic Psychopathy Measure (TriPM)[135]. This measure was developed to assess the triarchic model of psychopathy[136] which operationalises psychopathy as 3 distinct domains: boldness, meanness, and disinhibition. Importantly, given the propensity of individuals with psychopathic traits to engage in impression management or dissimulation, self-report measures should not be used on their own when assessing psychopathic traits for clinical purposes[137].

[H2] Children and adolescents

Several measures can assess psychopathic traits in youths (Table 1**)**; the decision regarding which measure to use should be guided by the main goals of the assessment (Supplementary Box 3). DSM-5[7] and the 11th Revision of the International Classification of Diseases (ICD-11)[138] were focused on using dimensions of psychopathy to differentiate between persons with conduct problem diagnoses (conduct disorder (CD) in DSM-5, oppositional defiant disorder and conduct-dissocial disorder in the ICD-11), and both diagnostic systems added a specifier of 'with Limited Prosocial Emotions' (Supplementary Box 4) that only includes CU traits. The rationale for this inclusion is because this CU/affective dimension of psychopathy seems most useful for the specific purpose of differentiating between persons with conduct problem diagnoses who show distinct aetiological, neurocognitive and social characteristics (Supplementary Box 3). Thus, for the purposes of designating an important subgroup of children with conduct problems, it would be important to include comprehensive measurement of CU traits, such as the widely used 24-item Inventory of Callous-Unemotional Traits (ICU), which exists in self-report, parent-report and teacher-report versions.

It is pertinent to note a few important cautions in using these criteria for making the diagnosis in children. First, given the pejorative connotations associated with the term 'psychopathy'[139] and the evidence that these traits are highly changeable in children[140], clinicians should avoid using the term 'psychopathy' when referring to CYP. Instead, 'limited prosocial emotions' is descriptive of the limitations in the child's emotions that can lead to his or her behaviour problems without necessarily having the same connotations as psychopathy. Second, this designation captures a subgroup of CYP that have distinct neurocognitive characteristics from other CYP with behavioural problems who are similar to adults with psychopathy, and that could be important for designing more effective treatments for these CYP. Further, there is evidence that children with high levels of CU traits are at risk

for showing later psychopathic traits. However, it is important to note that more research is needed on the level of this risk and how this may be influenced by different ways of defining CU traits. Most importantly, the available evidence suggests that most children with elevated CU traits will not meet traditional definitions of psychopathy in adulthood[141].

[H2] Prevention

Prevention of psychopathy in adulthood is likely to necessitate timely and effective intervention for CYP at risk of psychopathy. Findings from meta-analyses support parent management training **[G] (**PMT; also known as behavioural parent training) as the recommended treatment for reducing childhood conduct problems, with treatment gains that are maintained over three or more years after intervention[142]. Other evidence-based psychosocial treatments for conduct problems, include PMT with problem-solving skills training, anger control and social skills training, contingency management **[G]**, cognitive-behavioural interventions **[G]**, family therapy and multisystemic therapy **[G]**)[143,144]. Across treatment modalities and versions of PMT, several studies have found that although antisocial CYP with high CU traits do show improvements in CU traits[45,145] and antisocial behaviour, they often begin and end treatment with more severe parent-rated and teacher-rated conduct problems relative to CYP with lower levels of CU traits[45,145-147]. This pattern of continued impairment post-treatment is consistent with findings in adults with psychopathic traits[148] (see Management below).

The leading explanation for why first-line PMT treatments produce unequal outcomes depending on the severity of CU traits is that these treatments do not address the distinct familial and neurocognitive processes underlying the behavioural problems of individuals with psychopathic traits. PMT is underpinned by established causal models of conduct problems that emphasize the importance of improving the effectiveness and consistency of

parental discipline to produce child behavioural change. These strategies are undermined by the temperamentally fearless and punishment-insensitive learning styles of antisocial CYP with CU traits who experience core behavioural discipline strategies, such as time-out, as less aversive than antisocial CYP with low CU traits[151,152]. By contrast, using positive reinforcement within PMT was rated by parents of clinic-referred children with disruptive behavioural disorders as equally effective for reducing conduct problems across varying levels of child CU traits[152]. Indeed using reward-oriented contingency management strategies that target the self-interests of incarcerated adolescents with high psychopathic traits, within an intensive treatment that placed less emphasis on sanctions, reduced recidivism over a 2-year period following release, compared with treatment-as-usual[153,154] These findings suggest that modifying traditional behavioural therapies to emphasise individualized positive reinforcement over punishment may enhance some treatment outcomes for CYP at risk of psychopathy, with evidence for sustained effects over a 6-year follow-up[155]. It should also be noted that a number of studies have found that CU and psychopathic traits do not affect children's response to interventions for conduct problems when the treatment is multimodal (including medication management for comorbid ADHD), intensive (average of >20 weekly sessions), personalized to address the family's unique needs and risk factors, and/or is delivered as preventive family-based intervention to toddlers and preschoolers at risk for early starting conduct problems[149,150]. This suggests that CYP with CU traits can benefit from some generic conduct problem interventions, particularly when these are preventative or include some individualization.

Contemporary treatment research increasingly focuses on adapting established behavioural treatments to target the specific risk factors in CYP at risk of psychopathy. For example, augmenting PMT with parent-child emotion recognition training was superior to PMT alone in improving empathy and reducing conduct problems for antisocial children with

elevated CU traits[156]. However, improvements in children's emotion recognition or affective empathy did not explain the positive effect of this enhancement on reducing conduct problems in children with high levels of CU traits. An alternative focus on enhancing warm, responsive and consistent parenting within family-based interventions has been spurred by findings that this style of parenting is associated with a reduced risk of antisocial behaviour and psychopathic traits[45,48], with encouraging findings of improved antisocial outcomes for CYP at risk of psychopathy[150,157]. An intriguing but yet unanswered question is whether PMT programs that integrate a positive parent-child relationship building component (44% of programs examined in a meta-analysis[158]) are superior to programs that teach behavioural management alone in reducing conduct problems for children high on CU traits and counteracting the tendency for those with an inherited risk for psychopathy (based on biological mothers' fearlessness and low interpersonal affiliation) to evoke increasingly harsh parenting in the toddler to preschool years, which undermines empathy and conscience development and further increases levels of CU traits[159]. This knowledge can be used to guide the selection of treatment programs, from the many available options, to adapt for children at risk of psychopathy.

The efficacy and efficiency of delivering these nuanced interventions will be greatest when provided to children with early starting conduct problems who are identified as being at risk based on validated tools for assessing CU and psychopathic traits (Table 1). Interventions for the prevention of psychopathy have use only insofar as individuals engage in, complete and benefit from treatment. Among CYP identified as at risk for developing psychopathy, there is likely to be variation in treatment response, necessitating further research into moderating variables. Tailoring treatment programs or their components to subpopulations that respond positively to these interventions, such as those sharing specific phenotypes, genotypes, or other biomarkers, may further optimize intervention efficiency[160]. However, the

willingness to engage in intervention and/or develop the important therapeutic alliance may be detrimentally affected by traits such as low interpersonal affiliation that are shared in common between parents and their CYP with CU traits[161]. Alternatively, some parents of children with high levels of CU traits may be highly motivated for change because of the greater severity and burden of their children's conduct problems relative to their low CU counterparts. Findings on treatment engagement within family-based interventions are mixed, with some, but not all, studies reporting greater dropout and less parent-reported treatment satisfaction for children with high levels of CU traits compared with those with low levels of CU traits[146,162,163]. Among older CYP involved in treatment, psychopathic traits are modestly associated with treatment noncompliance, poor attendance, lower quality participation, and premature treatment dropout[164]. Further areas of concern for therapists include poor motivation to change, manipulation or deceit, and high rates of aggression and violence among CYP with or at risk for developing psychopathic traits that require safeguarding considerations. An important avenue for future research will be to investigate factors that may motivate engagement in and reduce risk of safeguarding concerns during interventions.

In sum, CYP with early starting conduct problems and high levels of CU traits, and at potential risk of psychopathy, may benefit most from psychosocial treatments for conduct problems that are either enhanced to target their specific vulnerabilities or that flexibly address their individual needs using multiple tailored modules determined from a comprehensive initial assessment. The durability over time of gains from these treatments in CYP with different levels of psychopathic traits, and whether treatment curtails the later development of psychopathy, requires further investigation using randomized controlled trials with long-term follow-up periods. Where trials have followed children treated for conduct problems into early adulthood, findings are inconsistent and no studies examined moderation by CU or psychopathic traits[165,166]. Continued translational psychological and neuroscience

research that applies knowledge on the causes of psychopathy to strengthen established treatments or to develop novel interventions targeting these processes is critical to preventing the development of psychopathy in at-risk CYP.

[H1] Management

Finding appropriate ways to manage and treat the harmful behaviour displayed by adults with psychopathic traits has been particularly challenging. Indeed, those individuals often exhibit higher rates of institutional violence when in correctional and forensic psychiatric settings[167] and are placed in solitary confinement in correctional settings at a higher rate than individuals with lower psychopathy scores[25]. Elevated psychopathic traits have been associated with reduced treatment cooperation, including bonding and the inclination to complete tasks as part of treatment[168]. It also has been suggested that psychopathy may have a substantial effect on interpersonal relationships with staff[169], but empirical research into this topic is lacking. Given the severity and chronicity of their antisocial behaviour, both in the community and within correctional and forensic psychiatric settings, individuals with high levels of psychopathic traits are regularly referred for treatment in these supervised settings. Indeed, the Netherlands have developed a forensic psychiatric system for treatment and management of severe antisocial behaviour and personality disorders, including psychopathy[170].

Several different pharmacotherapy and psychological approaches have been used to try to address the behaviour of adults with psychopathic traits. Some approaches that are useful for treating different types of antisocial individuals seem to be less effective in adults with high psychopathic traits[145,171,172].

[H2] Medication

In general, administration of psychotropic medication has been an important tool for managing undesirable and maladaptive behaviour in individuals with psychiatric disorders. However, there has been very little work on psychopharmacological treatment for psychopathy, with only a handful of anecdotal reports and no reliable systematic investigation conducted. One report of pharmacotherapy in four individuals diagnosed with psychopathy and ASPD has been published, and found a reduction in irritability, aggressiveness, and impulsivity with the antipsychotic quetiapine[173]. A few other studies of individuals with high levels of impulsive-aggression without a formal diagnosis of psychopathy, found that that lithium[174], phenytoin (an anticonvulsant)[175], and serotonin reuptake inhibitors[176] may reduce aggression in these individuals compared with their pre-medication behaviour. Notably, none of these studies were large, rigorous randomized controlled trials and none targeted psychopathy specifically.

[H2] Psychological interventions

The vast majority of psychological interventions for adults with psychopathic traits focus on addressing their thoughts and behaviours. Many treatments encompass some variant of cognitive-behavioural therapy, behaviour therapy, and/or milieu therapy **[G]**. Psychological interventions focusing on cognitive, behavioural and interpersonal functioning can take many forms and be administered over the course of a few months to years in order to address the needs of individuals.

There is general pessimism regarding the treatment of psychopathy in adults. One study compared the usefulness of CBT in 20 offenders with psychopathy and 20 offenders without psychopathy and found that it had little effect in either group[177]. Subsequent studies found that cognitive-behavioural therapy and milieu therapy had either minimal effects in individuals with psychopathy or, in some cases, that intervention worsened symptoms. For

example, one study reported a negative association between improvement in clinical symptoms and psychopathy[178]. In addition, psychopathic traits are negatively associated with treatment-related outcome measures[179]. Indeed, a handful of studies have found that adults with psychopathy are more likely to drop out of cognitive-behavioural treatments or milieu treatment compared with controls without psychopathy[180-182], which might suggest that individuals with psychopathy do not have the opportunity to benefit from treatment. In support of this conclusion, some studies have found improvements in clinical outcomes (such as antisocial behaviour) in adults with psychopathy when they complete psychological treatment[180,182]. However, other studies indicate that following treatment (regardless of drop-out or completion) adults with psychopathy have higher rates of re-offense compared with individuals withoutpsychopathy[171]. Of note, only a small number of studies have been conducted on this topic, no studies have included large samples, and they rarely reported appropriate methodological controls (such as a control group or randomization)[183]. Therefore, strong conclusions about the treatability of adults with psychopathy are tenuous at best.

Common psychological interventions, such as cognitive-behavioural, behavioural, and milieu therapies, may be less effective for treating adults with psychopathic traits than individuals without psychopathy. Although these therapies may yield some improvements in those with psychopathy, these treatments rarely result in desired clinical outcomes or return the individual to a 'normative' level of functioning. Moreover, it is hard to ignore the evidence suggesting that traditional interventions may have a negative effect on individuals with psychopathic traits. This conclusion underscores the pessimism about treating individuals with psychopathic traits; however, it is quite likely that individuals with psychopathic traits are treatable, but the right treatment has not yet been identified. In this regard, decades of research on the biological and cognitive mechanisms supporting

psychopathic behaviour provide grounds to be optimistic, as they may provide insights into novel intervention approaches (see Outlook, below).

[H1] Quality of life

Quality of life (QOL) assessment measures an individual's subjective satisfaction with life across several domains[184]. No studies have investigated QOL in adults with a psychopathy diagnosis compared with controls matched on key demographic variables, precluding a rigorous assessment of how individuals with psychopathy experience their life relative to others. Only two studies have examined the association between psychopathic traits and self-rated QOL in adults. In one study, a sample of Belgian forensic patients divided into low (PCL-R total score < 15, moderate (PCL-R between 15 and 24.9) and high (PCL-R > 25) psychopathy groups did not differ on self-ratings of physical health, psychological health or their environment[185].Furthermore, patients with moderate and high psychopathy scores rated their social relationships more positively compared with patients with low psychopathy scores. By contrast, in a Swedish community sample of adults with a varied history of youth crime[186], individuals higher in psychopathic traits reported less satisfaction with their work, psychological health, and with family relationships. These contradictory findings indicate a need for more research on QOL in individuals with psychopathy. Reliance on the individuals' subjective perception of their QOL might be problematic in this population because individuals with psychopathy often have a profound lack of insight in the nature and extent of their problems[137] and, therefore might not view their lives through the same lenses as the rest of us. Given the paucity of research on QOL in psychopathy, this section mostly focuses on the effect of psychopathy on important domains of functioning. Psychopathy is devastating for individuals and society due to its association with diverse negative outcomes across the lifespan, including legal problems, social and

family impairments, educational and employment problems, and mental and physical health problems (Fig. 5).

CYP at risk of psychopathy have difficulties in a number of domains that suggest reduced QOL. They have lower school and academic performance[187] , and conflicted relationships with peers, parents, and teachers[188]. In addition, these individuals have increased conduct problems[189], bullying[190,191,], instrumental and reactive aggression [192], frequent and diverse criminal behaviours[193], institutional aggression[194], lack of program noncompliance[195], substance abuse[196], risky sexual behaviours[197] and high rates of unplanned pregnancy[197], and increased suicidality[198,199]. They are also more likely than their peers to have experienced peer victimization[200], parenting that is harsh, negative, and low in warmth, physical/emotional abuse and neglect[201], increased exposure to violence at home and within the community[202], lack of parental supervision[203] and gang involvement[204]. A large (*N*=1,215) prospective longitudinal study in the USA found that CU traits at baseline in first-time adolescent arrestees increased both the frequency of gun carrying and the likelihood of using a gun when committing a crime during a 4 year follow-up period[205].

Psychopathic and CU traits are moderately stable from childhood or adolescence into adulthood[206-208], and, without intervention, a number of negative outcomes occur in adulthood. Indeed, legal problems are very common, often starting at a young age and persisting across the lifespan[209]. Individuals with psychopathy commit both reactive and instrumental violence[210] and researchers have found a link between sadistic motives and psychopathy in sexual offenders[211]. In the community, individuals with psychopathy have higher rates of substance abuse[212], smoking quantity[213], employment problems[214], homelessness[10], problematic intimate relationships[215], divorce[216], engage in risky sexual behaviours[217], and negative parenting behaviours[218], compared with individuals without psychopathy. In addition, in a longitudinal community sample, psychopathic traits were

associated with a reduction in general health and an increase in prevalence of diabetes mellitus, high blood pressure, high cholesterol, and neurological disorders (epilepsy, migraines, stuttering, tinnitus, ADHD, anxiety, and depression) in early adulthood[219]. Other studies have reported a positive relationship between psychopathic traits and suicidality with stronger associations in women compared with men[220,221]. A large global study of adults found an association between psychopathic traits in women and maternal and infant mortality[222]. Likely as a result of their impulsive and reckless behaviours, a Finnish study with a 30 year follow-up found that offenders with psychopathy die younger than the general population with a fivefold mortality rate, and their causes of death are more violent than for other offenders without psychopathy[223].

Unsurprisingly, the societal and economic effects of psychopathy across the lifespan are substantial. In Missouri, researchers concluded that juvenile offenders with psychopathic traits were responsible for a disproportionate amount of crime costs[224]. More broadly across the USA, the estimated annual costs of psychopathy to the criminal justice system has been estimated to be US$460 billion[12]. This does not include the considerable emotional costs to those who have a family member, who work with, or who are intimately involved with someone with psychopathy. In this context, we agree with Reidy and colleagues[225] that psychopathy should be considered 'a serious public health problem' and that more research needs to be conducted on primary prevention strategies in at-risk CYP.

[H1] Outlook

We have learned so much about psychopathy and its development over the past 40 years and, although small, this field of research is progressing rapidly. Yet, many outstanding questions and challenges lie ahead.

[H2] Lack of funding and advocacy

As highlighted in this *Primer*, psychopathy is associated with an enormous personal, societal, and economic effects across the lifespan, which calls for substantial funding for its prevention, research, and treatment. However, this is not the case. Indeed, in the Anatomy of NIMH Funding in the USA, borderline personality disorder is the only personality disorder mentioned and it receives the least amount of funding of all the psychiatric disorders and psychopathy is not included at all. Similarly, in the UK, ASPD is not mentioned in the UK Mental Health Research Funding (https://www.mqmentalhealth.org/our-work/research-reports/) and personality disorder research more broadly received one of the smallest shares of support between 2014-2017. As noted in a recent *Primer*, the same can be said for conduct disorder, meaning that there is a lack of funding at every developmental stage. This state of affairs is indefensible and likely results from several interlinked factors, including stigma, challenging family circumstances that reduce the ability of family members to lobby for funding, and the fact that adults with psychopathy and CYP at risk for psychopathy do not elicit sympathy due to the very nature of their disorder. Consequently, from a young age, these individuals do not have natural advocates, unlike individuals with other disorders that are arguably much less costly and concerning to society. Given that psychopathy is a serious public health problem, more research funding should be devoted to this disorder and on an equal basis to other psychiatric disorders.

[H2] Epidemiology and quality of life

Likely due to its absence from the DSM-5 as a disorder, limited epidemiological data exist on psychopathy and those are confined to North American and UK samples. Given the potential impact of the disorder worldwide and evidence that psychological and neurobiological findings based on Western populations often do not replicate in other

cultures[226], more large-scale global epidemiological research should be conducted. This line of work would clarify if the effect of psychopathy as a public health issue varies across countries that differ, for example, in terms of income or rates of antisocial and violent behaviour/crimes. More research is also needed on the QOL of this population and its primary and secondary variants that includes both subjective and objective measures of distress and discomfort.

[H2] Mechanisms/pathophysiology

Defining the precise environmental and neurobiological risk factors and how they interact to contribute to the onset and course of psychopathy and its different facets is important. Despite the clear epidemiological phenomenon of sex differences in the prevalence of psychopathy and youth data suggesting that the aetiology for high CU traits might differ between the sexes[227], the mechanisms that underpin these differences in prevalence and aetiology are poorly understood. Accordingly, more multilevel research (such as investigating environmental, genetic, neuroimaging, and behavioural factors) including both sexes should be conducted. Relatedly, there are no large international scientific consortia that specifically focus on the genetic underpinnings of psychopathy and its facets to conduct well-powered genome-wide association, epigenetic, or gene-environment interplay studies. Furthermore, the extant large-scale studies with genetic data do not include psychometrically-sound measures of psychopathy. Crucially, no systematic investigations exist at different stages of development, although data from twin studies indicate that different genetic risk factors may be important for the initial risk versus the developmental course of psychopathic traits[228]. If molecular genetic research on psychopathy is to advance, larger samples and careful phenotyping are required. In addition to efforts focusing on common genetic variants, it is also important to study rare variants that may have more substantial effects but that only

affect a very small subset of the population. Gene expression studies also hold potential promise to the field. One study[229] focused on gene expression patterns in a small sample of psychopathic offenders (N = 6), substance abusers (N=3) and healthy controls (N=6), and implicated gene expression in several genes and immune related pathways in psychopathy. Replication of these findings in larger samples, as well as the degree to which these gene expression results reflect heritable genetic variation versus the organism's response to environmental inputs, will be an important avenue for further research.

Four key challenges, shared with other fields, will have to be tackled to more accurately understand the neurocognitive features of psychopathy and its facets. First, task parameters and demands often vary considerably between studies purporting to assess the same cognitive or affective constructs, which is problematic for meta-analytic studies. Thus, the field should agree on a core set of paradigms that more precisely and reliably measure a set of clearly defined candidate cognitive or affective functions. Second, psychometric validation of functional neuroimaging and experimental measures is needed if we want to advance the longitudinal study of psychopathy. Indeed, these paradigms have not been psychometrically validated to sensitively and reliably capture individual differences, thereby limiting their utility for inclusion in large-scale longitudinal studies. Third, more work is needed to validate paradigms that could be used to assess the same neurocognitive domains in different age groups. Fourth, the substantial variability in analysis pipelines for fMRI data, combined with the degrees of freedom of researchers, have likely contributed to a lack of replicability across studies and, therefore we call for data sharing (where ethically feasible) and codes between researchers along with pre-registration and registered reports[230]. A final challenge specific to this field will be to systematically research neurocognitive processes related to empathy and social affiliation in individuals with secondary psychopathy (Supplementary Box 1) and investigate how their social cognition develops. In other words,

we must be open to investigating different developmental pathways (equifinality) to psychopathy.

Although personality disorders were not mentioned in the Grand Challenges in Global Mental Health Initiative[231], its call for large-scale prospective longitudinal studies that start in the prenatal period and include multiple levels of analysis is also relevant to psychopathy. Such research is needed to identify and quantify how and when different risk factors operate to cause psychopathy. Some researchers have suggested that significant progress in understanding the pathophysiology of psychiatric disorder necessitates good animal model[232]; in this respect recent genetic work on a non-human primate model of psychopathy might prove fruitful[233]. Finally, grey matter volume differences associated with psychopathy are present in the four lobes of the brain and in subcortical structures, possibly accounting for some of the neurocognitive disruptions seen in psychopathy. However, it is important to note that there are marked inconsistencies across studies in the loci and direction of the effects, likely due to methodological factors as well as differences in the demographic and clinical characteristics of the samples[234](Box 3), which have been small, with a few notable exceptions[235,236]. In this context, data sharing and harmonisation in international and interdisciplinary collaborations (such as Enhancing Neuro-Imaging and Genetic research through Meta-Analysis [237] (ENIGMA)'s *Antisocial Behaviour* working group (http://enigma.ini.usc.edu/ongoing/enigma-antisocial-behavior/) and the Psychiatric Genomics Consortium (https://www.med.unc.edu/pgc/)) will be important and should help to overcome the small sample size of existing neuroimaging and genetic studies. Addressing the above gaps, pressing challenges, and future directions for the field will ultimately help refine existing models of psychopathy, its diagnosis, and promote the development of targeted treatment and prevention approaches.

[H2] Diagnosis

As the DSM-5 includes the limited prosocial emotions specifier for the diagnosis of CD (Supplementary Box 3) to recognise that there is a subgroup of CYP at risk of developing psychopathy (Box 2), we, like others[19], believe that, from a developmental perspective, psychopathy should also be included within the DSM-5 as a specifier for the related, but broader, diagnosis of ASPD (Box 1) for which a diagnosis of CD before age 15 is a prerequisite[7]. More work needs to be carried out to understand the variants of psychopathy, but it is unclear if diagnosis based solely on clinician's ratings of observable symptoms will be able to differentiate them; in the future, the identification of biomarkers for psychopathy variants could improve their identification by providing more objective biological and neurocognitive measures to complement clinical judgment. This may in turn reduce stigma and contribute to advancing the field towards a 'precision psychiatry' approach tailored to specific individuals. The discovery of reliable structural neuroimaging biomarkers could also potentially contribute to reconceptualising psychopathy as a neurodevelopmental disorder[19]. However, no reliable biomarkers for psychopathy have been identified, but advanced statistical methods such as machine learning applied to structural neuroimaging and genetics data[238] within prospective longitudinal research have potential for identifying reliable and predictive biomarkers. Ultimately, improved diagnostic and potential stratifications of patients based on reliable biomarkers and environmental risk factors could pave the way for better treatments and outcomes for psychopathy.

[H2] Treatment

The continued translation of research findings to improve the treatment of psychiatric disorders is a central goal of psychological and neuroscience research. Novel, cross-disciplinary, therapeutic frameworks propose that psychopathy could be treated using

interventions designed to specifically target disturbances in biological and cognitive mechanisms relevant to this disorder[171]. One study[239] of prisoners used computerized training designed to target cognitive deficiencies related to psychopathy, and found training-related improvements after six weeks of training using computerized tasks, compared with individuals who received the alternative mechanistically unmatched training, and these training effects generalized to other tasks that were not practiced. A key shift in the treatment focus was to identify and target putative cognitive-affective mechanisms related to psychopathy. This focus might allow for more direct change in the mechanisms supporting psychopathic behaviour. Alternatively, a mechanistic focus might allow individuals with psychopathic traits to build or harness compensatory strategies that allow them to circumvent their cognitive-affective deficits, and to engage in more prosocial behaviour supported through alternative strategies. This is consistent with our understanding of neural plasticity and behaviour change.

Another potential treatment approach for future investigation is biofeedback. Biofeedback interventions involve measuring physiological responses (such as heart rate or skin conductance response) and relaying this information in real-time to the patient[240]. The assumption is that the patient will use this information to willingly regulate internal states and behaviour. This approach has shown promise for treating individuals with inattention and impaired behavioural regulation[241,242], which are also problems seen in psychopathy[89]. One study[243] developed a biofeedback training that required offenders with psychopathy to learn to regulate their brain activity to improve behavioural control. Preliminary findings in a small sample suggest that this type of training reduced aggressive and maladaptive behaviour, but results require replication in much larger samples to determine their robustness. Of note, a biofeedback approach requires some consideration of the different variants of psychopathy and their distinct underlying aetiology, as it is likely that different mechanisms will have to

be targeted using techniques and measures tailored to the characteristics of each variant. It will also be important for future clinical research to examine how the effects of such interventions are reflected by changes in potential biomarkers for psychopathy.

Despite the promise of a shift toward a more mechanistic and neurocognitive focus for treatment in individuals with psychopathy, a key challenge will be to address the extent to which these individuals would be motivated to engage in more normative and prosocial thinking and behaviour. Additionally, given the effortful nature of engaging certain cognitive-affective processes, there is a question of how reliably individuals with psychopathy will be able to deliberately call upon these resources to promote more prosocial responding. However, even if automatic affective responses can be trained or evoked in individuals with psychopathy, finding the right interventions to achieve this (for each variant) will be difficult. It is likely that multi-modal treatments will be needed to help psychopathic individuals build compensatory strategies for navigating their social world such that their own needs are met, but also of those they encounter.

As it is unlikely that psychopathy will ever be completely eradicated, one interesting avenue for future research to reduce its harmful effect on others might be to focus research and advocacy on the victims[244]. Given findings that individuals with psychopathy are particularly good at identifying potential victims[245], and that the likelihood of being victimized is not random[246], this avenue of research presents potential to alleviate much suffering. This line of work could increase the public's awareness of who may be vulnerable and how those with psychopathy manipulate their victims, thereby decreasing people's risk of forming, or staying in, a toxic personal or professional relationship with an individual with psychopathy. This line of work needs to be conducted sensitively and has to be unequivocal in not placing any blame on victims. In this respect, the work of the Aftermath: Surviving

Psychopathy Foundation (https://aftermath-surviving-psychopathy.org/) has been instrumental for the past 10 years.

[H2] Prevention

Given that psychopathy has such a deleterious impact on all aspects of life (Fig. 5), its associated personal and societal costs, and the difficulty in treating it, improving efforts at preventing the disorder should be a key public health priority. For such preventative work to be effective it must be family-based focusing on both parent or caregivers and CYP. As the brain and personality are more adaptable early in life and work indicating that the precursors of CU traits can be identified in the first three years of life (Box 4), prevention work must start early, focusing on putative causal mechanisms thought to be specific to the development of psychopathy and its variants, and must involve long-term follow-ups. Given the low prevalence of the disorder in the community, such work might have to be carried out on 'at-risk' individuals that are enrolled in well-designed randomized controlled trials within prospective longitudinal studies causal risk and, crucially, protective factors for the disorder are to be identified. However, such work based on deemed 'at-risk' populations will have to be carried out sensitively and with careful ethical consideration, protecting the rights of the individuals, both adults and CYP, and avoiding the potential negative impacts of labelling.

When Aristotle allegedly said, "Give me a child until he is 7 and I will show you the man" he was partially correct. He was right because there is indeed some degree of continuity between the temperament of the child and the personality of the adult. However, Aristotle was also wrong on several fronts that are particularly relevant to what this *Primer* has shown about the development of psychopathy. First, although some features of psychopathy can be identified in a subgroup of CYP who show severe antisocial behaviour and may be genetically vulnerable, we now know that not all of those CYP will develop the syndrome as adults. In fact, only a minority of them will[141]. Second, Aristotle neglected the influence of

the environment, but the aetiology of psychopathy is complex, with contributions of both individual (such as genetic) and environmental (such as parenting) risk factors and different forms of interplay between the two. The exact timing and nature of those interplays remain poorly understood, partly due to a limited prospective longitudinal, multi-method body of research on the development of psychopathy. However, we are optimistic that methodological advances, combined with large-scale prospective international and interdisciplinary collaborations, can lead to radical changes in our understanding of the aetiology of psychopathy. Such progress could, in turn, contribute to improved diagnosis, treatment, and prevention of the disorder, thereby decreasing its public health toll and conferring major benefits for the individual, their family, and society.

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A.F. receives royalty payments from the sale of the Psychopathy Checklist: Youth Version, which is an instrument listed in Table 1. All other authors declare no competing interests.

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Related links

Mental Health Research Funding: https://www.mqmentalhealth.org/our-work/research-reports/

Enhancing Neuro-Imaging and Genetic research through Meta-Analysis (ENIGMA)'s *Antisocial Behaviour* working group: http://enigma.ini.usc.edu/ongoing/enigma-antisocial-behavior/

Psychiatric Genomics Consortium: https://www.med.unc.edu/pgc/)

Aftermath: Surviving Psychopathy Foundation: https://aftermath-surviving-psychopathy.org/

Table 1. Assessment measures of psychopathic traits in adults and youths

Measure	Method	Items and scale Scale	Dimensions, domains, facets and factors assessed	Refs
Measures primarily for adults				
Business Scan-360 (B-Scan-360)	Informant rater or self-report	20 items, 5-point scale	Manipulative or unethical, callous or insensitive, unreliable or unfocused and intimidating or aggressive	[247]
Comprehensive Assessment of Psychopathic Personality (CAPP)	Professional rater or Self-report	33 items, 7-point scale	Attachment, behavioural, cognitive, dominance, emotional and self	[248]
Elemental Psychopathy Assessment (EPA) [a]	Self-report	178 items, 5-point scale	Antagonism, emotional stability, disinhibition and narcissism	[249]
Levenson Self-Report Psychopathy Scale (LSRP)	Self-report	26 items, 4-point scale	Primary and secondary variants	[250]
Psychopathy Checklist-Revised (PCL-R)	Professional rater	20 items, 3-point scale	Interpersonal, affective, lifestyle and antisocial	[9]
Psychopathy Checklist: Screening Version (PCL:SV)	Professional rater	12 items, 3-point scale	Interpersonal, affective, lifestyle and antisocial	[251]
Psychopathic Personality Inventory-Revised (PPI-R) [a]	Self-report	154 items, 4-point scale	Fearless dominance, self-centered impulsivity and coldheartedness	[252]
Self-report Psychopathy Scale (SRP-4) [a]	Self-report	64 items, 5-point scale	Interpersonal, affective, lifestyle and antisocial	[253]

Triarchic Psychopathy Measure (TriPM) [a]	Self-report	58 items, 4-point scale	Boldness, meanness and disinhibition	[136]
Measures primarily for children and/or adolescents				
Antisocial Process Screening Device (APSD)	Parent-report, teacher-report or self-report	20 items, 3-point scale	Narcissism, callous-unemotional and Impulsivity	[254]
Clinical Assessment of Prosocial Emotions, Version 1.1 (CAPE 1.1)	Professional rater	4 items, 3-point scale	LPE Specifier	[255]
Child Psychopathy Scale (CPS)	Parent-report, teacher-report or self-report	52 items, 2-point scale	Interpersonal, affective and impulsive	[256]
Child Problematic Traits Inventory (CPTI)	Parent-report or teacher-report	28 items, 4-point scale	Grandiose-deceitful, callous-unemotional and impulsive-need for stimulation	[257]
Inventory of Callous-Unemotional Traits (ICU)	Parent-report, teacher-report or self-report	24 items, 4-point scale	Callous-unemotional	[258]
Psychopathy Checklist: Youth Version (PCL:YV)	Professional rater	20 items, 3-point	Interpersonal, affective, behavioural and antisocial	[259]
Youth Psychopathic Traits Inventory (YPI) [a]	Self-report	50 items, 4-point scale	Grandiose-manipulative, callous-unemotional and impulsive-irresponsible	[260]
Youth Psychopathic Traits-Child Version (YPI-CV) [a]	Self-report	50 items, 4-point scale	Grandiose-manipulative, callous-unemotional and impulsive-irresponsible	[261]

[a] short form available

Figure 1. Features of psychopathy operationalised by the Hare Psychopathy Checklist – Revised.

The most widely accepted and used conceptualisation of psychopathy in the scientific and clinical community is based on the construct operationalised by the Hare Psychopathy Checklist – Revised[9] (PCL-R). Based on the PCL-R, psychopathy is underpinned by two correlated dimensions of interpersonal and affective features (Factor 1) and a chronic antisocial lifestyle (Factor 2). More recently, Hare (2003)[9] proposed a four-facet model in which the original Factor 1 is parsed into interpersonal style (*Facet 1*) and affective experience (*Facet 2*), and Factor 2 is parsed into lifestyle (*Facet 3*) and antisocial (*Facet 4*) manifestations. Note that for diagnostic purposes, the presence of these traits cannot be scored without reference to the formal criteria contained in the published manuals[9]. Two behaviours that are common in people with psychopathy (promiscuous sexual behaviour and many short-term marital relationships) contribute to the total score but do not load on any factors. PCL-R 2nd Edition. Reprinted with permission from the copyright holder, Multi-Health Systems Inc.

Figure 2. The association between psychopathy and other psychiatric disorders and maladaptive outcomes.

Psychopathy can co-occur with antisocial personality disorder (ASPD), and narcissistic personality disorder. Some symptoms of narcissistic personality disorder (such as grandiose sense of self-worth, exploiting others for personal gain and lack of empathy) conceptually overlap with some interpersonal/affective features of psychopathy[31]. Other conditions commonly comorbid with psychopathy involve problems with behavioural disinhibition, such as attention-deficit/hyperactivity disorder, borderline personality disorder, and substance use

disorders, which tend to be most strongly related to the chronic antisocial lifestyle symptoms of psychopathy. When different psychopathy symptom dimensions are studied separately, the direction of the association with internalizing symptoms varies; internalizing problems are modestly, positively correlated with the lifestyle/antisocial facets of psychopathy, whereas the interpersonal/affective facets tend to be associated with lower levels of trait anxiety. ASPD and criminal recidivism are weakly associated with interpersonal/affective traits, but are more strongly related to lifestyle/antisocial traits[262-264]. The interpersonal facet is most strongly related to instrumental violence[210], whereas the affective facet is most robustly associated with treatment drop out[265].

Figure 3. Dispositional and environmental risk factors for psychopathy.

Multiple dispositional and environmental risk factors for psychopathy operate across the lifespan; their hypothesized associations over time, many of which are yet to be empirically tested, are depicted in this figure. The nature and importance of these risk factors vary depending on the developmental stage. For example, genetic influences on fearless temperament may contribute to the risk for early behavioural problems, whereas genetic influences on low empathy could increase risk of engaging in bullying during adolescence. The importance of environmental risk factors also varies by developmental stage, with low parental warmth contributing to risk behaviours during childhood and ineffective parental monitoring becoming more important during adolescence. Many of the dispositional factors also contribute to generation of environmental risk (gene-environment correlation), as well as to susceptibility to environmental risk (gene-environment interactions). The challenge for the field is to use innovative study designs to improve the understanding of the gene-environment

interactions in the development of psychopathy. Figure 3 adapted with permission from Ref[116].

Figure 4. Brain abnormalities in psychopathy and children and young people at risk of psychopathy.

A| Functional MRI (fMRI) studies examining brain response to emotional stimuli (mostly emotional faces expressing fear or stimuli depicting pain in others) have demonstrated that adults with psychopathy and children and young people (CYP) at risk of psychopathy are characterized by reduced responses within a set of cortical (such as the ventromedial prefrontal and insular cortices) and subcortical (such as the amygdala and striatum) regions. In terms of reinforcement-based decision-making, fMRI studies have reported reduced neural responsiveness to reward within the striatum and ventromedial prefrontal cortex (both in adults and CYP) as well as a relative failure to reduce activity within the ventromedial prefrontal and/or the posterior cingulate cortex (in adults only) following unanticipated punishment. Both adults with psychopathy and CYP at risk of psychopathy are compromised in at least some forms of moral judgments and, relative to individuals without psychopathy, exhibit reduced response in associated regions, such as the ventromedial, rostromedial and dorsomedial frontal cortices, anterior insula cortex, striatum, and amygdala. **B|** Structural neuroimaging studies of grey matter have shown that adults with psychopathy are characterized by abnormalities across the four lobes, mostly in the form of *reduced* volume across all four lobes of the brain and cortical thickness in the frontal and temporal lobes. Evidence in CYP at risk of psychopathy suggests that CU traits are negatively related to grey matter volume and thickness in the amygdala, insular and temporal cortices, but positively associated with volume of the striatum. **C|** In terms of white matter tracts, both adults with

psychopathy and CYP at risk of psychopathy have been found to exhibit microstructural changes within the uncinate fasciculus, corpus callosum, dorsal cingulum and anterior thalamic radiation. However, the microstructural changes are in opposite directions to in adults.

Figure 5. Quality of life and psychopathy.

Psychopathy is devastating for individuals and society owing to its association with diverse negative outcomes across the lifespan, including mental and physical health problems, legal and institutional problems, social and family impairments, educational and employment problems, as well as consequences of reckless and irresponsible behaviour. Figure 5 adapted with permission from Ref[116].

Box 1. Psychopathy, ASPD, dissocial personality disorder and sociopathy.

Antisocial personality disorder (ASPD) and psychopathy are often considered synonymous, possibly as the Diagnostic and Statistical Manual of Mental Disorders (DSM)[266] diagnostic criteria for ASPD consist of a subset of the symptoms of psychopathy; ~37.5% of the interpersonal/affective and ~60% of the lifestyle/antisocial features included in the Psychopathy Checklist-Revised (PCL-R) are included in ASPD diagnostic criteria[267]. However, although psychopathy and ASPD are moderately correlated[13] and both disorders include a life-long pattern of antisocial behaviour, they are distinct[268,269]. Indeed, the diagnostic criteria for ASPD mostly focus on a severe and chronic pattern of antisocial and criminal behaviour, whereas psychopathy is mostly operationalized based on personality features with an emphasis on emotional impairments and interpersonal features (Fig. 1). Consequently, about 80-90% of individuals with a diagnosis of psychopathy would meet

criteria for a diagnosis of ASPD, whereas only about 25-40% of those with a diagnosis of ASPD would meet criteria for psychopathy[13,270]. In the community, the prevalence of psychopathy is thought to be ~1%[10,29] whereas the prevalence of ASPD is estimated at ~ 4% for ASPD[7]. Moreover, studies that have directly compared ASPD and psychopathy suggest that they are characterized by distinct emotional disturbances[271,272], as well as structural[273] and functional[80] brain abnormalities.

Dissocial Personality Disorder (DPD) within the ICD-11[138] is the 'equivalent' of the DSM diagnosis of ASPD, but its core features are closer to psychopathy. Indeed, disregard for the rights and feelings of others, including both self-centeredness and lack of empathy, are part of the diagnostic criteria for DPD, but may not all be present in a given individual at a given time. However, there is almost no research focussing specifically on DPD.

The definition of sociopathy has varied over time[274,275]. Although the descriptions have included behaviours and features that overlap with psychopathy (such as antisocial and aggressive behaviour, impulsivity, extreme self-centeredness and lack of empathy), no comprehensively validated and widely used assessment tools for sociopathy exist. Although the term 'sociopath' is still occasionally used it is not currently a focus of active, systematic scientific research at multiple levels of analysis.

Box 2. Children and young people (CYP) at risk of psychopathy.

The impulsive and irresponsible lifestyle facets of psychopathy capture behaviours similar to symptoms of ADHD and are highly correlated with conduct problems[276]. By contrast, callous-unemotional (CU) traits **[G]** constitute the core affective facets of adult psychopathy[5,277]. They are less highly correlated with conduct problems in CYP than the

impulsive and irresponsible lifestyle facet[276] and, most importantly, CU traits characterize a subgroup of children and young people (CYP) with conduct problems who seem to have a stronger genetic predisposition to their antisocial behaviour that is independent of the severity of conduct problems[278] or ADHD[279], and who show emotional and neurocognitive correlates comparable to those seen in adults with psychopathy. Based on these data, CU traits seems to designate a clinically and potentially aetiologically important subgroup of antisocial CYP that share features with psychopathy in adults[16,140].

In addition, there is substantial evidence that high levels of CU traits designate a subgroup of antisocial CYP characterized by severe and stable conduct problems, delinquency, and aggressive and violent behaviours, and which can critically be instrumental (goal-directed) in nature[16]. Further, antisocial CYP with high levels of CU traits remain more impaired after treatment than antisocial CYP with low levels of CU traits. Crucially, there are prospective longitudinal data showing that antisocial CYP with high levels of CU traits are most at risk for psychopathy in early in adulthood[141,280,281].

Accordingly, CU traits are included in diagnostic criteria[138] under the form of the specifier 'With Limited Prosocial Emotions' for the diagnoses of conduct disorder (CD) in the DSM-5[7] and ICD-11[138], and oppositional defiant disorder (ODD) in ICD-11. Of note, CU traits are the only facet of psychopathy to be included in these diagnostic systems. Other facets of psychopathy continue to be represented by the impulsive-hyperactive symptoms of ADHD and in the deceitfulness or theft symptoms of CD.

There are two important things of note with the CU specifier. First, the DSM-5 allows for the specifier only for the diagnosis of CD. However, there is evidence that CU traits may predict impairment (such as conduct, emotional and hyperactivity problems and crime) in the absence of conduct problems severe enough to warrant a diagnosis of CD[282,283] which led the ICD-11 to allow for its use with the diagnosis of ODD. Further, the ability of CU traits on

their own to designate subgroups of CYP with ADHD who have different emotional correlates (emotion dysregulation for ADHD with low CU traits versus low emotional arousal for ADHD with high CU traits) has also been supported by some emerging research[284]. Further research is needed to determine if CU traits are an important specifier for other diagnoses, in addition to CD. Second, the symptoms indexing CU traits in diagnostic systems were selected based on research showing the best indicators of the construct from items on ratings scales across various samples[285]. Testing how these criteria are being assessed in many clinical settings is still important, to determine if they still capture the construct in ways that define a clinically and aetiologically important subgroup of CYP who are at risk for future psychopathy. In addition, it is important to conduct longitudinal research investigating whether the addition of impulsive and interpersonal facet items that are not covered by ADHD and CD symptom criteria, add to the prediction of not just antisocial behaviour and related outcomes (such as substance abuse[286]), but also adult psychopathy.

Box 3. Methodological considerations in neuroimaging studies.

Several methodological considerations with neuroimaging studies, likely affect the interpretation of their results and generalizability (for more detailed discussions, see[234,287-289]). Those methodological considerations include the nature and size of the sample and control group, the PCL-R cut-off score to identify those with psychopathy, and the potential influence of demographical and clinical factors.

In terms of the nature of samples, study participants drawn from clinical and forensic settings are likely to present higher levels of psychopathic traits than those recruited in the community, which may translate into differences in neuroimaging results across studies. In

addition, many neuroimaging studies have included small samples resulting in low statistical power[290] and replications in this field have been rare. Crucially, it must also be noted that the nature and the size of the sample are not independent from each other (a problem referred to as confounding moderators in meta-analytic work[291]). Studies focusing on clinical and forensic samples are more likely to have a small sample size (but see[115]), compared with studies from the community (such as the ABCD study), some of which have included hundreds of participants. Somewhat related, there is substantial variability between studies in the PCL-R score used to classify individuals with psychopathy (ranging from15-31).

The nature of the comparison group has also been inconsistent across studies and complicates the interpretation of the findings. Some studies use prisoners with low psychopathy scores as control group, whereas others studies used healthy controls. These approaches have led to two issues[289]. First, the lack of a healthy comparison group means that it is difficult to identify group difference are distinct from healthy functioning. Second, it is difficult to know whether any group differences are caused by psychopathy or are due to the effects of other variables associated with incarceration, such as length of incarceration and substance misuse.

Finally, demographical factors such as age, sex, and IQ are all associated with brain development and anatomy[292,293]. Psychiatric comorbidities typically associated with psychopathy, such as substance misuse[31], have also been associated with brain abnormalities in some of the same cortical and subcortical regions[294] thought be involved in the pathophysiology of psychopathy, and we know that adults with psychopathy typically have a long history of polysubstance use and CYP at risk for psychopathy begin using substances at a young age. The distribution of those demographic and clinical variables varies across studies and within the same study, and the influence of those variables as well as their potential interactions (for example age and sex) have often not been systematically

investigated across different studies. In addition, it is also worth noting that different pattern of alterations in brain structure and function could reflect the interaction between these demographic and clinical variables as well as main and interacting effects of genetic predispositions and environmental factors[295].

Box 4. CU behaviours in young children.

In the last decade, researchers have extended the study of callous-unemotional (CU) traits to children younger than 5 years by focusing on callous-unemotional-like *behaviours* (such as lack of guilt, low fear and empathy)[218,296]. The term CU behaviours was originally coined to reflect the possibility that these behaviours in very young children might not be stable enough to warrant the status of 'traits'. Empathy and guilt-related behaviours emerge in the first few years of life and a subgroup of persistently aggressive children can already be identified at that stage. These are among the key motivations to extend the study of CU behaviours to young children[297]. These behaviours have been assessed either through standard CU traits measures previously used with CYP or via parent-rated items taken from questionnaires focusing on low empathy and guilt, uncaring behaviour and low emotional responsivity[296]. An emerging body of evidence has accumulated regarding the aetiology, predictive validity, and temperamental precursors of CU behaviours. Although there is evidence that such behaviours at 2 years of age are moderately heritable[298], adoption[52] and twin studies[298] have indicated that heritable risk can be moderated, for example, by warm parenting. Several prospective longitudinal studies have now shown that CU behaviours measured as young as 3 years predict antisocial and proactive aggressive behaviour and CU traits at later ages (up to 10 years). As for temperamental precursors of CU behaviours, the data suggest that "impairments in attending to, recognizing, and responding to interpersonal emotions as early

as infancy may increase risk for CU behaviours" [296]. However, a limitation of the above literature is the lack of follow-up data to determine what proportion of young children will develop conduct problems with stable high levels of CU *traits*, and subsequently the syndrome of psychopathy in adulthood. This will be an important area of future research that has the potential to shed new light on the development of psychopathy and identify key targets for preventative work.

Glossary terms

Reactive aggression. Aggression, underpinned by negative affect, in response to frustration or social provocation.

Social affiliation. The motivation to interact with others.

Aversive conditioning. Learning to associate negative valence with a previously neutral stimulus.

Reinforcement-based decision-making tasks. Tasks where the participant must learn which responses to make to a stimulus to gain reward/avoid punishment

Parent management training. Training that teaches parents social learning techniques and behavioural strategies to increase children's desirable behaviours and decrease their problematic and antisocial behaviours

Contingency management. Rewarding youth for engagement in specified positive behaviour),

Cognitive-behavioural interventions. A family of psychological treatments that aim to alter maladaptive thinking patterns, feelings, and behaviours

Multisystemic therapy. Synergistic interventions that involve the youth, family, school, and community systems

Milieu therapy. Therapeutic communities to treat individual group members through setting norms and boundaries

Callous-unemotional traits. Including a lack of guilt, lack of empathy, lack of concern over poor performance in important activities, and shallow/deficient affect

ToC blurb

Psychopathy is a personality disorder that is characterized by a lack of empathy, guilt, remorse, in addition to grandiosity, arrogance, deceitful and manipulative. This Primer reviews the epidemiology, mechanisms, diagnosis and treatment of psychopathy and describes the effect of this disorder on quality of life and functioning.