Oppositional defiant disorder

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Abstract

Oppositional defiant disorder (ODD) is a disruptive behaviour disorder involving an ongoing pattern of angry/irritable mood, argumentative/defiant behaviour, and vindictiveness. Onset is typically before 8 years of age, although ODD can be diagnosed in both children and adults. This disorder is associated with substantial social and economic burden, and childhood ODD is one of the most common precursors of other mental health problems that can arise across the lifespan. The population prevalence of ODD is ~3 to 5%. A higher prevalence in males than females has been reported, particularly prior to adolescence. No single risk factor accounts for ODD. The development of this disorder seems to arise from the interaction of genetic and environmental factors, and mechanisms embedded in social relationships are understood to contribute to its maintenance. The treatment of ODD is often successful, and relatively brief parenting interventions produce large sized treatment effects in early childhood. Accordingly, ODD represents an important focus for research, practice, and policy concerning early intervention and prevention in mental health.

[H1] Introduction

Oppositional defiant disorder (ODD) is characterised by an ongoing pattern of angry and irritable mood, argumentative and defiant behaviour, and vindictiveness. This disorder can be diagnosed at any age between early childhood and adulthood although onset is typically before 8 years of age. Research into ODD has focused largely on early-to-middle childhood (ages 2-11 years), and it is among the most common mental health disorders during these periods [1].

The social and economic burden of ODD is substantial and includes long-term costs arising from clinical service use and criminal offences, as well as indirect costs such as due to lost productivity of caregivers and individuals with ODD later in life [2,3]. Moreover, childhood ODD is one of the most common precursors of other mental health problems throughout the lifespan [4]. Treatment of ODD is often successful; evidence-based interventions for ODD and other disruptive behaviour problems typically produce moderate sized treatment effects, whereas relatively brief parenting interventions in early childhood produce large effects [5]. Accordingly, ODD should be a key priority for research, practice and policy concerning early intervention and prevention in mental health.

ODD seems to form part of a broader externalising spectrum with conduct disorder (CD), attention-deficit/hyperactivity disorder (ADHD), substance use disorder and antisocial personality disorder [6,7]. These disorders are often comorbid, which is thought to arise from shared genetic factors [8] or due to common liabilities (such as trait impulsivity; a tendency to act without thinking or consideration of the consequences of one's actions [7]). [8,9].

ODD has been relatively under-researched compared with these other disorders for several reasons. One reason is the historical tendency for researchers to combine ODD and CD into a single construct, which was consistent with the diagnostic definitions of ODD in the Diagnostic and Statistical Manual of Mental disorders (DSM) and the International

Classification of Diseases (ICD) until their most recent revisions. Other reasons for the comparative lack of research into ODD include a tendency to regard ODD as a disorder limited to early childhood, assumptions that ODD has a singular external cause (such as dysfunctional parenting), and a lack of recognition by funding agencies [10]. Moreover, dimensional measurements based on grouping these related disorders is common in child and adolescent research, with scales often combining ODD and CD symptoms into a single measure of 'conduct problems'. Owing to these factors, data on ODD specifically are limited.

Despite the limited research into ODD, studies have demonstrated that it is a unique and highly heterogeneous disorder. In DSM-5-TR this heterogeneity is reflected by the organisation of symptoms into three dimensions (angry/irritable mood; argumentative/defiant behaviour; and vindictiveness) that have been proposed to vary in terms of development, comorbidity profiles and prognosis [11]. Other multidimensional models of ODD symptoms have been proposed, which include one dimension of affective (chronic irritability) symptoms but vary in the specification of either one or two behavioural (defiant/headstrong or hurtful/vindictive) components [12,13]. Of note, ICD-11 criteria for ODD include specifiers for subtypes of ODD presenting with limited or typical prosocial emotions (also known as callous-unemotional traits), and/or with or without chronic irritability and anger [14].

This Primer provides an overview of diagnosis, aetiology and pathophysiology, and the effectiveness of intervention and prevention programmes for ODD. Moreover, this Primer discusses the prevalence of ODD, its effect on child health and development, and the social, educational and occupational outcomes associated with this disorder. Key challenges and directions for future research are also addressed.

[H1] Epidemiology

[H2] Prevalence

The prevalence of ODD is typically estimated as aa cross-sectional prevalence at a given point in time. In clinical samples, the prevalence of ODD among children and adolescents tends to be high. One systematic review reported estimates of 28-65% from multiple studies of clinical samples[15], with higher rates being reported in clinics specializing in treatment of behavioural problems or of ADHD specifically. The prevalence of ODD among adolescents in juvenile justice settings is estimated at 43% [16], 55% [17] or 10.7–30.5%, depending on age and gender [18].

Prevalence estimates in representative community samples are substantially lower than in samples from clinical and justice settings A worldwide meta-analysis of 25 studies estimated the prevalence of ODD of 3.3% between 5 and 18 years of age [19]. Similarly, a meta-analysis of 10 studies from eight countries estimated a prevalence of 3.9% between 1 and 7 years of age[20]. Most studies of the prevalence of ODD are from Europe and North America; however, some nationally representative studies from non-Western countries are available. These have provided concordant findings, with prevalence estimates of 3.6% in China [21], and 3.9% in Iran [22]. Variability across individual studies seems to be explained by methodological rather than regional differences [19,20]. Thus, the true population prevalence of ODD seems to be around 3 to 5%.

Whether the prevalence of ODD varies with age is unclear [19,23].Evidence for a declining prevalence into adolescence might be limited only to studies in which diagnosis of ODD was not given when CD criteria were also met[24]. Researchers who employed this restriction were following a DSM IV diagnostic rule that was eliminated in DSM 5. Additionally, few studies have examined ODD in those >18 years of age, with no studies providing high-quality estimates of point prevalence. In a non-representative study of north-eastern US college students, one study found prevalence estimates of 3.4% and 4.1%, consistent with those from youth samples [25].

Estimates of cumulative lifetime prevalence of ODD tend to be higher than estimates of point prevalence. For example, one study found a lifetime prevalence of 10.2% in a representative sample of US adults[26]. A similar lifetime prevalence estimate was reported for adolescents between 13 and 18 years of age [27], although this study considered ODD present if symptoms were identified by either a parent or child, likely inflating the estimate compared with studies using a single informant. By contrast, cumulative lifetime prevalence among adults in Northern Ireland was estimated at 2.7%[28]. Of note, that study employed the aforementioned DSM IV prohibition against ODD when CD was present. Ultimately, cumulative lifetime estimates are ambiguous regarding the cross-sectional point prevalence in adulthood, as it is not clear whether the disorder occurred in childhood and/or later in life.

[H3] Gender and Developmental Differences in Prevalence Rates

Among community samples, one study noted that a male-to-female ratio of about 1.7:1 in the prevalence of ODD in childhood diminished in adolescence[15]. However, a worldwide meta-analysis of 19 studies between 6 to 13 years found a ratio of 1.6:1 for boys relative to girls, with no difference across ages [23]. Other studies have demonstrated no gender difference among youths in China [21] or a 1.4:1 ratio of boys relative to girls among youths in Iran [22]. In adults, no difference was found in the prevalence of ODD between men and women among US college students [25] or in lifetime prevalence in a US representative sample (11.2% for men and 9.2% for women)[26].

Similar gender and developmental effects may be evident when ODD is measured dimensionally. In a representative US sample of children aged between 5 and 12 which examined either dimensional scores or ODD symptom counts, no significant difference was found in mean score or symptom count by age. However, a significant but modest difference was demonstrated in symptom scores between boys and girls (a mean of 1.2 symptoms and

151 1.0 symptoms, respectively) [29].

152

153 **[H2] Comorbidities**

154 ODD commonly co-occurs with depression, anxiety, ADHD and CD [15,22]. ODD was
155 previously considered as inherently subsumed under CD or as an integral part of a
156 developmental pathway to CD; however, more recent data has refuted this thinking. For
157 example, in a community sample of children and adolescents aged 9 to 16 years, only 9.2%
158 of those who developed CD also had a history of ODD [30]. It may be that ODD is not a
159 precursor to CD without co-occurring CD symptoms [31] or psychopathy traits [32].

160 Similarly, cross-sectional comorbidity data fails support a distinct linkage between
161 ODD and CD. For instance, in a national population survey, 11.5% of youth with ODD also
162 met criteria for CD; higher rates of co-occurrence between ODD and ADHD (28.9%),
163 separation anxiety (20.3%), generalized anxiety (14.9%) and depressive disorder (13.9%)
164 were found [22]. Co-occurring ODD was identified as central in attenuating multiple observed
165 comorbidities between other disorders [33]. This role of ODD in the comorbidity of emotional
166 and behavioural disorders may be due to its distinct dimensional symptoms of chronic
167 irritability and oppositional behaviour [13,34], as these symptoms differentially predict
168 emotional versus behavioural disorders [35]. Behavioural genetics analyses using twin studies
169 have suggested that unique genetic factors explain part of the link between chronic irritability
170 and affective disorders or oppositional behaviour and behavioural disorders, along with a
171 substantial amount of common genetic factors shared across ODD dimensions and other
172 disorders[12,36] .

173

174 **[H1] Mechanisms/pathophysiology**

175 **[H2] Genetic influences on ODD**

Heritability estimates of 0.34-0.73 have been reported for ODD or ODD symptoms[7,9,37-39], indicating that the heritability of ODD is moderate to high. Non-shared environmental influences accounted for most of the remaining variance (0.30-0.41), with minimal shared environmental influences on ODD [9]. The genetic liability of ODD, CD, inattentive ADHD and generalised anxiety disorder (GAD) symptoms overlaps substantially, with genetic correlations all >0.5 [7]. In studies examining the genetics of psychopathology trans-diagnostically, ODD loaded highly onto a higher order externalising genetic factor (0.53) and moderately onto a general psychopathology factor (0.32), with modest genetic influences unique to ODD (0.15) [7]. Similarly, another study found that ODD loaded highly onto a general externalising behaviour factor (0.50), along with CD and ADHD, whilst genetic influences unique to ODD were minimal (0.05) [38]. These data suggest the genetic underpinnings of ODD are largely shared with other externalising disorders or a higher-order psychopathology factor which increases risk for mental disorders in general.

Interestingly, behavioural genetic analysis of ODD symptoms within a multidimensional framework has shown that the defiant subdimension overlaps heavily with the genetic influences on CD, ADHD, and substance use disorders, whereas the irritable subdimension overlaps with depression and anxiety [12,40]. This finding may explain why ODD increases risk for both externalising and internalising disorders [12,13,41], unlike CD, which specifically increases risk for externalising disorders[4,30].

Despite the relatively consistent picture from behavioural genetic studies, evidence regarding the molecular genetics of ODD is limited, with few candidate gene studies available [42] and only one genome-wide association study published to date, in children with ADHD [43]. Although this study suggested the involvement of genes involved in neurite outgrowth (and thus brain development), none of the findings achieved genome-wide significance. By contrast, and supporting the bifactor model described above, epigenetic

findings suggest the irritable and defiant subdimensions of ODD have different aetiologies, with one epigenome-wide study reporting epigenetic changes in genes involved in neurotransmitter and cell signalling in ODD and its defiant subdimension [44]. The irritable subdimension was not associated with epigenetic changes.

[H2] Environmental influences on ODD

No single environmental risk factor accounts for the development of ODD. Most research on environmental aetiological factors has investigated broader classes of psychopathology such as externalising disorders or conduct problems, which are not specific for ODD. One exception is a New Zealand birth cohort study (N = 926) that demonstrated multiple environmental risk factors, including maternal smoking during pregnancy, parental maladaptive behaviour, exposure to abuse and interparental violence, socioeconomic adversity, and adolescent affiliation with deviant peers, predicted ODD symptom count at age 14-16 years [45]. Similarly, the US-based National Comorbidity Survey (N=5,877; 15-54 years) demonstrated that exposure to parental divorce, family violence and physical abuse are associated with an increased lifetime risk of disruptive behaviour disorders (including ODD and CD) [46]. Of note, neither study found that the effects were specific or unique to ODD after controlling for other mental health problems.

Adverse childhood family experiences are a common antecedent to ODD and have a central role in coercion theory, a key model of the development of aggressive and antisocial behaviour in general, and is highly pertinent to the development and treatment of ODD [47]. This theory states that ODD emerges as a result of interactions within the family whereby caregivers inadvertently reinforce children's difficult behaviours, which then elicit negative caregiver reactions, and continue to do so, until the interaction is discontinued when one of the dyad 'wins' (FIG. 2). These coercive cycles can be initiated when the child reacts angrily

to a caregiver's request, evoking caregiver anger, which intensifies as the cycle escalates [48]. Over time, the adverse effects of these cycles on the parent-child relationship, including attachment processes, can further maintain and amplify both coercion and conduct problems [49] (FIG. 3). Thus, children learn a pattern of relating within the family which influences their interactions with those outside the family, such as peers and teachers. When coercive interactions dominate within the family, child conduct problems are more likely to emerge and may stabilise throughout development. In relation to ODD, the frequency and severity of anger outbursts, noncompliance, and controlling interpersonal behaviour may increase over time through these mechanisms[50].

There is compelling evidence that harsh, negative and controlling parenting are important risk factors for ODD, although oppositional behaviours also elicit more coercive or harsh parenting from caregivers [51,52]. One study investigated the relationship between positive and negative parenting and child psychopathology, and found that punitive discipline was common across disorders, although low parental warmth and involvement were uniquely related to ODD[53]. However, some of these effects could reflect passive gene-environment correlations, whereby the effects are due to shared genetics rather than parenting. Thus, although family interaction patterns likely partly reflect common genetic variance, they also concurrently drive and are driven by the child's ODD, such that self-maintaining/escalating loops of coercion emerge. Owing to the strong evidence of the positive effects of reducing coercive parent-child interchanges in early intervention and prevention programs, this risk factor is considered the most well-established modifiable causal factor for ODD [54].

Both genetic and environmental risk factors for ODD tend to co-occur in disadvantaged communities. Studies using genetically-informed designs to examine the association between socioeconomic risk and ODD have not been conducted, although other studies have evaluated the effect of changes in socioeconomic status on subsequent risk of

developing ODD. In a natural experiment in which income levels were raised across an entire US community, ODD and CD symptoms declined among children in families raised out of poverty [55]. Of note, such effects were not seen for other disorders, such as depression and anxiety, supporting a social causation model of ODD. In addition, ODD and CD symptoms were much higher in children from persistently poor families versus families who were never in poverty. Similarly, another study demonstrated that ODD was related to lower socioeconomic status compared with other psychiatric disorders, and ODD with comorbid CD was associated with even lower SES[56]. Youths with ODD reported greater family dysfunction (conflict and lower cohesion) than children with other disorders, although the direction of effects is unclear. The effect of socioeconomic disadvantage as a risk factor for childhood mental health problems, including ODD, are in part mediated by associated deterioration in parent-child relationships [57].

[H2] Neuroendocrinology and psychophysiology

Several studies have investigated the stress response system (the hypothalamic-pituitary-adrenal axis) in ODD. These studies have demonstrated an association between ODD and lower cortisol levels at rest (basal cortisol) [58] and blunted cortisol responses to psychological stress [59,60]. Interestingly, cortisol hyporeactivity to stress predicts a weaker treatment response to parent management training in youths with ODD [61]. Similar findings were obtained for reductions in aggression following parent management training in individuals with ODD or CD[62]. Of note, these studies used all-male or predominantly male samples, so it is unclear whether ODD in females is associated with low basal cortisol or hyporeactivity to stress. Related to this issue, a study with a mixed-sex sample reported higher basal cortisol levels in girls with ODD compared with control girls, with lower basal cortisol levels in boys with ODD compared with controls [63], and another study investigating

long-term cortisol secretion via hair samples found higher cortisol levels in girls with ODD and co-occurring ADHD compared with control girls [64]. An important question is whether these alterations are driven by ADHD comorbidity, owing to meta-analytic evidence of lower cortisol levels in ADHD[65] . The few studies to directly compare ODD, ADHD and comorbid ODD and DHD found that cortisol hyporeactivity was specific to those with ODD[60,66]. These data have been interpreted as evidence for hypoarousal in ODD, although alternatively, the hypothalamic-pituitary-adrenal axis may have become desensitised by repeated stress exposure.

In terms of autonomic functioning, a meta-analysis found that youths with conduct problems (including ODD) showed lower resting heart rate and skin conductance levels, and lower skin conductance levels during task performance, further supporting hypoarousal in ODD [67]. By contrast, those with conduct problems showed greater cardiovascular reactivity than controls, which does not support a role of hypoarousal. Another study reported lower eyeblink responses to aversive stimuli in youth with ODD or CD than controls [68], indicating reduced defensive motivational responses (interpreted as evidence of 'fearlessness'). Youth with ODD or CD also showed reduced facial mimicry when viewing dynamic facial expressions, in addition to weaker facial muscle responses and less congruent facial emotional responses to empathy-inducing videos [69,70], with some evidence of more pronounced empathic deficits in children with co-occurring callous-unemotional traits [71]. These data suggest that empathy deficits in ODD/CD can be seen even at the level of motor activity; youth with ODD/CD do not seem to spontaneously 'mirror' the emotions of others, in the way that most typically developing children do. Such evidence regarding atypical emotion processing has also informed emerging work on novel interventions for children with conduct problems and callous-unemotional traits (see Outlook, below).

[H2] Neuropsychological studies of ODD

ODD has been linked to deficits in reinforcement learning, emotion processing and social cognition [72]. In particular, deficits in learning from punishment have been reported in ODD, as demonstrated in, for example, tasks whereby participants have to learn to withhold a response to avoid losing points or money or inhibit previously rewarded responses that now lead to punishment [73,74]. Studies using decision-making tasks have reported that youth with ODD are hypersensitive and show increased autonomic responses to rewards, in addition to insensitivity to punishment [75,76]. ODD is also associated with difficulties in recognising negative facial expressions, especially anger [77], although in this study the ODD group was less impaired than the CD group, who showed marked recognition deficits across emotions. Research comparing youth with ODD and comorbid ADHD versus ADHD alone showed that emotion recognition deficits were specific to the ODD with ADHD group [78], suggesting ADHD comorbidity does not account for these deficits.

ODD is also associated with executive function or response inhibition deficits [79,80]. However, one study found no evidence of general executive dysfunction, but strong evidence for motivational inhibitory problems in children with ODD[74], and a meta-analysis of studies using the Stop-Signal Task (which assesses ability to inhibit a response once it has been initiated) found no reliable support for response inhibition problems in ODD [81]. The extent to which these ODD-related difficulties are independent of ADHD is unclear, although one study observed impaired inhibitory control in a pure ODD or CD group (without comorbid ADHD) [82]. The ODD/CD group also made more risky choices in a decision-making task, showed poorer sustained attention on a continuous performance task, and greater reaction time variability across tasks than controls. These data suggest that ODD is associated with executive dysfunction and inhibitory control or self-regulation deficits even in the absence of comorbid ADHD, in line with the study on facial emotion recognition described above.

[H2] Brain structure and function in ODD

Reduced grey matter volume has been observed in brain regions involved in social and emotional functioning in youth with ODD or CD, for example, the insula, amygdala, inferior frontal gyrus and dorsomedial prefrontal cortex (FIG. 4). A meta-analysis of structural MRI studies revealed lower grey matter volume in the amygdala, insula and frontal gyrus in children with ODD or CD [83]. To our knowledge, only one study [84] has attempted to disentangle the brain structural alterations associated with ODD versus CD. This study found reduced cortical thickness in the ventromedial prefrontal and orbitofrontal cortices in youth with ODD, but reduced thickness in the medial prefrontal, dorsal anterior cingulate and superior frontal cortices in CD, suggesting greater problems in social cognition and self or emotion regulation in ODD than in CD. Both groups showed lower volumes of the insula and inferior frontal gyrus, which are implicated in empathy, threat processing and cognitive control/emotion regulation. Of note, this study had a very small sample (n=22 for the DBD group overall) and therefore requires replication.

Another study using diffusion tensor imaging investigated white-matter microstructure in individuals with DBDs (ODD or CD) compared with individuals with comorbid DBD and ADHD and healthy controls [85]. This study observed lower fractional anisotropy and increased diffusivity in multiple white-matter tracts in those with DBD and comorbid ADHD compared with controls and those with DBD only suggesting reduced microstructural integrity in the former group, whereas the DBD only and control groups did not differ. In line with this finding, another study found no differences in white-matter microstructure between healthy controls and youths with ODD or CD and callous-unemotional traits (although this study had a small sample size) [86]. Other studies in this area have focused on CD, with no consistent findings in terms of the location or direction of

effects; however, the uncinate fasciculus (which connects the amygdala and orbitofrontal cortex and is implicated in emotion regulation) has been identified as altered in several studies [83,87].

Few functional MRI studies have investigated brain responses in youths with ODD or in mixed ODD or CD groups. One series of studies focusing on psychopathic or callous-unemotional traits demonstrated reduced amygdala responses to fearful facial expressions in youths with DBDs (mostly ODD)[88], and lower amygdala responses to empathy-inducing stimuli (hands or feet in painful situations)[89]. Youth with DBDs also showed lower amygdala responses when performing a morality-based implicit association test and reduced functional connectivity between the amygdala and several brain regions (the anterior cingulate cortex, orbitofrontal cortex and superior temporal cortex) [90]. Another study investigating reward processing using the Monetary Incentive Delay task reported heightened ventral striatal responses to reward feedback in youths with externalising disorders (mostly ODD) [91]. A similar study reported reduced ventral striatal responses to reward feedback in youths with persistent DBD compared with youths with desisting DBD and healthy controls, and greater amygdala responses to loss feedback in the persistent DBD group versus the other two groups [92].

A meta-analysis of functional MRI studies of ODD or CD distinguished between those assessing ‘hot’ and ‘cool’ executive functions (EFs) based on whether the executive function tasks involved a motivational, emotional component or not [83]. This analysis revealed lower amygdala, striatal and fusiform gyrus activity in youth with ODD or CD when they performed ‘hot’ executive function tasks compared with controls (FIG. 5) [83], independent of comorbid ADHD. By contrast, the precuneus, anterior cingulate and insula, were underactive in children with ODD or CD compared with controls when performing ‘cool’ executive function tasks (FIG. 5). One fMRI study evaluating ‘cool’ executive functions assessed the

neural correlates of response inhibition in boys with ODD using the Stop-Signal Task[93]. This study found lower right inferior frontal gyrus activation during Stop trials (those requiring response inhibition), but increased left inferior and superior frontal gyri activation, in boys with ODD compared with controls[93]. The authors interpreted these findings as evidence that response inhibition problems are less extensive in ODD than in CD or ADHD (where widespread inferior parietal and dorsolateral prefrontal cortex under-activation has been reported [94,95]).

Overall, data from psychophysiological, neurocognitive, and functional neuroimaging studies of ODD are broadly consistent in demonstrating heightened reward and reduced punishment sensitivity in this disorder. ODD is also associated with social cognitive difficulties which are particularly marked for social punishment signals (such as angry faces), and reduced activity and altered structure in brain regions involved in emotion processing, emotion regulation and response inhibition such as the amygdala, ventromedial prefrontal cortex and inferior frontal gyrus.

[H1] Diagnosis, screening and prevention

[H2] Clinical diagnosis

ODD has been included in diagnostic classification systems since the DSM-III [96], including the most recent editions of both major psychiatric classification systems, DSM-5-TR [11] and ICD-11 [14] (Box 1). However, as ODD symptoms commonly occur in typically developing children and are frequently co-morbid with other disorders, concerns have been raised as to whether ODD classifies as a disorder or if it is a normative pattern of behavior that is only problematic when accompanied by another disorder [97]. Contrary to these concerns, the presence of ODD symptoms is highly predictive of a range of psychiatric outcomes (for example, behaviour problems, anxiety and depression), and this risk is at least

partially independent of comorbid conditions [35,97,98].

The symptoms used in the diagnostic classification of ODD have not greatly changed over the past few decades. However, these symptoms are now known to form several distinct clusters whereby the angry–irritable mood symptoms form a separate factor from the defiant-headstrong behaviour symptoms [98]. Although these symptom clusters are highly correlated and both predict later CD symptoms, they are differentially associated with other comorbid conditions and predict different outcomes [35]. Namely, the angry-irritable dimension is most strongly related to symptoms of anxiety and depression (both concurrently and over time), whereas the defiant-headstrong dimension is more strongly related to CD and ADHD [96]. The relationship between the spiteful or vindictive symptom and other ODD symptoms is less clear. Importantly, the spiteful or vindictive symptom has a stronger association with symptoms of CD and callous-unemotional traits than the other ODD symptoms [99].

[H2] Key approaches to diagnosis

Diagnostic criteria for ODD specify how to distinguish normative versus problematic levels of ODD symptoms. First, the DSM-5-TR criteria specifies that the child must show at least 4 of the 8 symptoms to meet the criteria for ODD. Second, both the ICD-11 and the DSM-5-TR criteria specify that the symptoms must lead to distress in the individual or cause impairment in their social context. Third, both diagnostic systems also specify that the symptoms must be outside the normative range in terms of persistency and frequency for the individual's developmental level, gender and culture. In the DSM-5-TR, except for the spiteful and vindictive symptom, behaviours are considered symptomatic if they occur at least once per week for 6 months in children ≥5 years or if they occur on most days for 6 months in children <5 years. These were informed by research showing that it is not unusual for preschool children to show temper tantrums on a weekly basis [100] but only about 10% of

426 preschool children show daily tantrums [101].

427 Another important consideration in the diagnosis of ODD is that a child only needs to
428 show symptoms in one setting to receive the diagnosis. However, diagnostic criteria for ODD
429 include a specifier for severity based on the number of settings in which the symptoms occur
430 (Box 1). These severity criteria are based on research suggesting that ODD is predictive of
431 later adjustment problems, even when limited to the home context; however, the disorder
432 seems to be more severe and impairing when symptoms also occur outside the home [98].

433 Although these diagnostic considerations are fairly consistent across DSM-5-TR and
434 ICD-11 criteria of ODD, the use of specifiers is different between the two classification
435 approaches. Namely, the only specifier included in the DSM-5-TR is for severity, whereas
436 the ICD-11 does not include this specifier but includes the specifiers of 'with limited
437 prosocial emotions (LPE)', 'with chronic irritability-anger', and 'without chronic irritability-
438 anger'.

439 The with LPE specifier is given when a person with ODD also shows several callous-
440 unemotional traits. This specifier is very similar to the LPE specifier for CD in the DSM-5-
441 TR, although one additional criterion for this specifier is included in ICD-11 only
442 (insensitivity to punishment). ICD-11 includes the LPE specifier for ODD based on research
443 findings that elevated callous-unemotional traits designate a clinically and aetiologically
444 important subgroup of children with conduct problems, typically defined using symptoms of
445 both ODD and CD [102]. Indeed, children with symptoms of ODD and/or CD and elevated
446 callous-unemotional traits have more severe and stable behavioural problems that are not
447 captured well by other indices of severity, such as number of conduct problems, co-morbid
448 diagnoses, and age of onset of conduct problems [103]. Furthermore, elevated callous-
449 unemotional traits seem to designate an aetiologically distinct group of children and
450 adolescents with severe behaviour problems who have distinct emotional deficits underlying

their conduct problems [104]. The DSM-5 limited the use of the LPE specifier to those with severe CD symptoms until more research examined any potentially detrimental labelling effects of using this specifier.

Two other specifiers are included for the diagnosis of ODD in ICD-11 for those 'with chronic irritability-anger', or 'without chronic irritability -anger'. To obtain the specifier 'with chronic irritability-anger', all criteria for ODD must be met and the person's prevailing and persistent irritable mood or anger is atypical for individuals of comparable age, developmental level, gender and sociocultural context; out of proportion in intensity to any provocation; and characteristic of the individual nearly every day. Those individuals who meet criteria for ODD but who don't show this persistent angry and irritable mood are given the specifier 'without chronic irritability-anger'. These specifiers were included in the ICD-11 because the presence of chronic irritability and anger predicts impairment and risk for anxiety and depression [35]. By contrast, chronic irritability and anger is considered a separate disorder in the DSM-5, called Disruptive Mood Dysregulation Disorder (DMDD). The decision to separate the two disorders in DSM-5 was made to convey that the mood disturbance that is core to DMDD. However, the ICD-11 committee included this as a specifier for ODD because most individuals with DMDD also meet criteria for ODD, the specifier shows limited validity in predicting clinical outcomes beyond ODD symptoms, and the specifier does not indicate the need for different treatments from those used routinely with ODD [105].

[H2] Screening.

Screening for ODD early in childhood is important to prevent the associated poor mental health outcomes later in life [106]. Screening is typically carried out through several publicly and commercially available behavior rating scales that can be completed by parents

and teachers. Obtaining information from both parents and teachers is important as the number of contexts in which the child shows these behaviors is an important indicator of severity. Obtaining information from one parent is typically sufficient for screening purposes, as long as the parent is involved in the care of the child on a regular basis. Children with high scores upon screening can be further assessed with more time-consuming and expensive assessment procedures (such as clinical interviews and behavioral observations) to determine if they meet full diagnostic criteria for ODD and are in need of clinical intervention [107].

Screening measures can vary by availability, length and how well their content corresponds to the diagnostic criteria. Two examples of commercially-available rating scales are the Achenbach System of Empirically Based Assessment (ASEBA) [108] and the Behavioral Assessment System for Children, 3rd Edition (BASC-3) [109]. These scales are helpful for screening for ODD as they provide T-scores based on large representative samples of children, allowing the determination of whether the child's behaviors are more severe than expected. Normative data for the ASEBA are available for various countries. Notably, the items on both scales do not correspond directly to DSM or ICD ODD criteria. Also, items related to the irritable-angry and defiant-headstrong behavioral dimensions of ODD are included with items related to physical aggression on Aggressive Behavior subscales or with other conduct problems associated with CD. This structure is not necessarily a limitation when these scales are used for screening, given that detecting early aggression and broader types of conduct problems is important for evaluating the severity of the behavior; however, it is an important consideration when these scales are used for diagnostic purposes, as high scores on these items may be due to ODD symptoms, aggressive behaviour or other antisocial behaviors (such as lying and stealing). The main limitation of using these scales for screening is that they are quite long as they assess a range of emotional and social difficulties, and behaviour problems.

The Strengths and Difficulties Questionnaire (SDQ) is briefer and is publicly available. The SDQ comprises 25 items, is widely used in research, and is available as both parent-report and teacher-report versions[110]. Similar to the ASEBA and BASC-3, the SDQ assesses a range of emotional and social problems. The 5-item conduct problems subscale of the SDQ includes four items assessing ODD symptoms and one item assessing fighting and bullying. As the SDQ is widely used in research around the world, many translations are available and various normative samples exist that can be used to create cut-off scores for different countries. However, of note, that the SDQ is not publicly available for computerized use and the few items on the scale often lead to problems with internal reliability.

Other screening measures were developed that directly correspond to the DSM criteria, such as the publicly available DBD Rating Scale [111,112] and the commercially sold Child Symptom Inventory–4 (CSI-4) [113]. The DBD Rating scale consists of 42 items, which includes the 8 ODD symptoms, and the symptoms of CD and ADHD. By contrast, the CSI covers a large number of diagnoses, which makes it quite long and, as a result, limits its use as a screening tool. These scales have strong sensitivity and specificity for screening for ODD. For example, the positive predictive power of parent ratings on the DBD was >0.90 for clinical diagnoses based on structured diagnostic interviews in a sample of 151 5-10 year olds[114]and 185 7-11 years olds[115]. However, screening measures that correspond to the DSM criteria typically do not provide norm-referenced scores [116] .

Moreover, the commercially available parent-report Eyberg Child Behavior Inventory (ECBI) and teacher-report Sutter-Eyberg Student Behavior Inventory-Revised (SESBI-R) [117] only assess conduct problems. The 36 ECBI items and 38 SESBI-R items are also unique compared with other screening measures by assessing whether the informant considers each behaviour is a problem (Problem scale) that is indicative of impairment, as well as the frequency of the behaviour (Intensity scale).

526

527 **[H2] Prevention**

528 Prevention programs offer a proactive public health solution to avoid or delay the
529 transition from ODD symptoms that are subthreshold or within normal limits to those that
530 meet diagnostic thresholds, thereby limiting the long-term consequences of ODD. Preventing
531 the occurrence of ODD is more effective and cost-effective than treating the disorder after its
532 onset, as the latter requires an adequate workforce of trained professionals providing more
533 intensive and costly treatments [54]. This cost is one of several barriers resulting in only 25-
534 30% of children with DBDs accessing mental health services in North America, the UK and
535 Australia [118-120].

536 Three levels of prevention programs are available for ODD: primary or universal
537 programs (delivered to the general population to provide support before problems occur),
538 selective programs (administered to individuals at higher risk of ODD owing to individual or
539 contextual risk factors), and indicated or targeted prevention programs (delivered to children
540 with subclinical levels of symptoms who are at very high risk of ODD). Universal and
541 selective programs only produce small or negligible effect sizes, whereas targeted prevention
542 programs produce medium effect sizes [121-123]. Another advantage of targeted programs is that
543 they economize on scarce prevention resources by intervening with a limited number of
544 children who are at highest risk of progressing to ODD.

545 Prevention programs range in duration (1 month to 10 years) and can be delivered in
546 home, preschool, school or other community settings. These programs have a small but
547 significant positive effect (d_{tot}=.17-.25) on preventing behavioral symptoms at least 6 months
548 after the program ends [124,125]. Of note, effect sizes are comparable between meta-analyses
549 including all three types of prevention programs and those excluding universal preventions
550 (*d*tot= 0.28 [120] versus 0.25 [121]).

The most effective prevention programs follow three principles, which are shared with the most effective treatments [5,126]. First, they target family-based risk factors (particularly parenting quality), and actively involve adults responsible for the child's day-to-day socialisation. Second, they are informed by established aetiological models of conduct problems; for example, behavioural parent training involves strengthening parenting by teaching parents specific skills and techniques (such as differential attention, positive reinforcement, antecedent control and firm consistent discipline; For review see[122]) to change the negative cycles that emerge between parents and children with behaviour problems [127]. Third, they are often delivered in early childhood when the behaviour is most malleable. Moreover, studies of the developmental trajectories of children with the most severe and chronic courses of antisocial behaviour have found that their problems begin in early childhood [128,129].

Several prevention programs target children at school. Delivering indicated prevention programs in schools is most likely to reach young children with the most persistent and pervasive conduct problems who have the greatest risk of later maladjustment. A meta-analysis of only school-based universal, selective and targeted prevention studies found that they had a small but significant beneficial average effect on problem behaviours (d = 0.15) [127]. School-based programs that address classroom behaviour management, child social and emotional skills training, and multicomponent programs appear most promising. For example, the Fast Track Project is an example of a comprehensive multicomponent prevention, which involved multiple levels (universal and indicated components to at-risk children) of long-term program delivery (over 10 years from ages 6 to 16 years old)) to students in 55 schools across four diverse American communities. Children randomly assigned to the Fast Track intervention were less likely to be diagnosed with ODD, CD and ADHD after the first three intervention years compared with the no-intervention control

condition. Among the highest risk group of children, 33% of the Fast Track intervention group were diagnosed with ODD by 14-15 years old compared with 52% of the control group [130].

[H1] Management

[H2] Behavioural interventions

Behavioural interventions focused on parenting skills, teacher-classroom management, and child cognitive-behavioural skills have shown promise in reducing oppositional behaviour across a range of age groups [131](FIG. 6). Of these, parenting interventions have the strongest supporting evidence and are recommended as the primary approach[131-133]. Of note, one potential limitation of the available treatment literature is that most studies focus on conduct problem or DBD outcomes more broadly, rather than specifically ODD symptoms or diagnoses. However, meta-analyses have demonstrated comparable effect sizes for treatment outcome measures that assess symptoms of CD (aggression/serious rule violations) versus ODD (oppositionality/noncompliance) [5]). Psychopharmacological approaches are not recommended for ODD[131].

[H2] Psychosocial interventions in early to middle childhood.

[H3] Parenting interventions. The most robust and extensive evidence base is for parenting interventions, and consequently they are recommended by many clinical guidelines, including NICE [131] and WHO [132]. Parenting interventions for ODD are skills-based programs, often comprising 8-16 sessions, and are effective when delivered in both group or individual formats in the home or clinic. Many interventions focus on early-middle childhood (ages 2-9), but similar approaches seem effective in late childhood and adolescence. Many ‘brands’ of parenting program are available but most share common core principles and elements

601 based on social learning theory [134]. Examples of effective programs that have been tested in
602 multiple RCTs include Triple P, Incredible Years, Parent Child Interaction Therapy (PCIT),
603 Parent Management Training - Oregon Model, and Helping the Noncompliant Child, and in
604 LMICs, Parenting for Lifelong Health.

605 Effective parenting programs typically begin with enhancing parent-child
606 relationships by increasing parental warmth, child-centred play and positive reinforcement of
607 desirable child behaviour. These are followed by positive discipline-focused components
608 during which parents are helped to set clear, realistic rules and expectations for their child, to
609 provide effective instructions, and, where needed, to apply calm, consistent, non-violent
610 consequences to set limits on oppositional behaviours. Improvements in positive parenting
611 seems to be an important mechanism of change in ODD outcomes[135] .

612 Systematic reviews of parenting interventions have revealed the efficacy of these
613 approaches [126,131,133]. For example, one review identified 278 RCTs of social learning theory-
614 based parenting programs in children aged 2-9 years, in >30 countries across all regions of
615 the world (with 90% of the trials conducted in high-income countries). Around 200 of these
616 trials assessed a relevant ODD or conduct problem outcome (in most cases a continuous
617 measure of ODD-related symptoms) and found an overall small effect size (d = 0.38, 95% CI
618 0.44-0.31), with moderate certainty of evidence in support of these interventions [136].
619 However, of note, improvements were greater for trials for children with high levels of
620 oppositional problems, with moderate effect sizes (d = 0.46-0.53) found in indicated
621 prevention and treatment studies, and smaller effects (d = 0.28) in universal and selective
622 prevention studies. Most trials report outcomes based on parent-reported checklists of ODD
623 outcomes. However, one review investigated whether similar findings are found when
624 outcomes are reported from individuals who are less directly involved in the intervention.
625 This review [133] found higher effect sizes for blinded direct observational assessments (d =

626 0.64) and for independent interviewers (d = 0.72), compared with parent reports (d = .45),
627 suggesting that parents involved in these interventions are not biased when reporting
628 outcomes. However, effects on ODD-type symptoms do not seem to generalise well to the
629 classroom, with teacher-reports producing lower effects (d = 0.08)[133].

630 Importantly, parenting interventions seem to transport well across contexts and to be
631 effective in low-and-middle-income countries. One systematic review and meta-analysis
632 found 131 randomized trials of parenting interventions in ages 2-17, with 54 trials assessing
633 ODD-related outcomes, with moderate effect sizes (d = 0.59) overall, and larger effects (d =
634 1.03) in indicated prevention and treatment studies. Effects did not vary by age group of the
635 child[137].

636 Longer-term effects of parenting interventions have been assessed only in a few trials
637 and seem to be less robust. Some studies have demonstrated sustained long-term effects (for
638 example, at 2.5-years follow-up [138]) although meta-analyses have reported more mixed
639 results. Some reviews have found small but sustained effects (d = 0.3) at 6-months or longer
640 follow-up [136,139,140], although another review found very small effect sizes (d = 0.1) at follow-
641 ups beyond 6 months [136].

642 Parenting interventions can be conducted by primary care, child and adolescent
643 mental health services, social services, schools, NGOs and other community services.
644 Digitally delivered parenting interventions can also produce comparable effect sizes to in-
645 person interventions [141].

646 Children with more severe oppositional problems tend to benefit most from parenting
647 interventions [142]. Overall, it seems that effects are greater when interventions are targeted at
648 children with early signs of ODD or those with severe symptoms (indicated prevention or
649 treatment) compared with similar interventions aimed at universal or selective prevention [122].
650 Effects seem robust across social groups, with children in disadvantaged families (defined by

651 a range of indicators) benefiting as much as children in other families [143].

652 Interventions in early childhood are often stated to be more effective than
653 interventions in later childhood, although evidence in support of this has been limited[126]. The
654 only large-scale moderator study to test this found no effect of age on conduct problem
655 outcomes in children aged 2-9 years, although cost-effectiveness tended to be higher with
656 increasing age [144,145]. Similarly, child age was not a significant moderator of treatment effects
657 in a meta-analysis of non-pharmacological interventions in youths <18 years, although a
658 trend towards smaller effect sizes in studies involving children aged ≥10 years was reported
659 compared with those <10 years old [146].

660 Another common perception is that parents with depression may not be able to engage
661 in and benefit from group-based parenting programs. However, one large pooled data study
662 found stronger effects on conduct problem outcomes in children with parents (almost all
663 mothers) with depression[142].

664 ***[H3] Teacher-focused interventions***. As the effects of parenting interventions do not
665 generally seem to transfer to the school environment, school-based interventions might be
666 needed for children who are disruptive in school. Several classroom management
667 interventions that focus on enhancing teacher-child relationships and behaviour management
668 have shown promise. For example, a systematic review of the Incredible Years teacher-
669 training program [147], and a subsequent large UK trial of this intervention [148] found beneficial
670 effects on classroom oppositional behaviours in children who were disruptive. Moreover, the
671 Good Behavior Game (a universal, classroom-based behaviour management intervention) has
672 also shown promise in several trials for reducing classroom oppositional behaviour in
673 children showing elevated levels of oppositional behaviour [149]. However, this evidence base
674 is smaller and less robust than for parenting interventions.

675 ***[H3] Child-focused interventions.*** These typically include cognitive behavioural

676 therapy (CBT) and social-problem solving skills to help children identify negative emotional
677 and behavioural triggers to oppositional, aggressive or angry behaviour, and improve social
678 skills and self-regulation. These approaches have been used in early to middle childhood with
679 mixed results [150,151], but seem to be less effective in this age group compared with in older
680 children[126]. Many trials combine child-focused interventions with parenting interventions,
681 with very few showing superior effects compared with parenting interventions only [152]. NICE
682 guidelines [131] recommends the use of child-focused interventions only for ages 9-16.
683
684 **[H2] Psychosocial interventions in late childhood and adolescence.**
685 ***[H3] Parenting interventions.*** Parenting interventions seem effective across all ages.
686 Parenting interventions aimed at late childhood are similar to interventions for younger
687 children, with many services delivering interventions to groups of parents with children aged
688 3-10 years. This approach is possible as most interventions are flexible to the differing needs
689 of families, based on developmental stage, family context and severity of problems.
690 In adolescence, similar social learning principles underpin parenting interventions, but the
691 focus often shifts towards improving parent-adolescent communication and negotiation skills,
692 and parent monitoring of the child's activities, particularly risky behaviours, outside the
693 home. Parenting interventions for adolescents show beneficial effects on ODD-related
694 outcomes, with one review demonstrating similar effects (d= 0.38) to those found in younger
695 children[133]. Although, of note, >95% of studies included in this review were from high-
696 income countries. One analysis of studies from LMICs, demonstrated beneficial effects of
697 interventions for adolescents (d= 0.80), with no significant difference to effects in younger
698 children, although with high heterogeneity between trials[137]]. The interventions in low-
699 income and middle-income regions were largely based on social learning theory, for example,
700 Familias Unidas in Ecuador, and Familias Fuertes in Honduras, with other trials carried out in

Iran, China, Kurdistan and Rwanda. Relevant to youth who might be diagnosable with ODD, the small number of trials in LMICs focusing on treatment or indicated prevention for children with elevated conduct/ oppositional problems, tended to show higher effect sizes, compared to selective prevention or universal programmes.

Many interventions target adolescents with CD or involvement with offending, rather than ODD specifically. These interventions are often multimodal programs with both child-focused and family-focused components. Few well-known evidence-based interventions are available for adolescents with oppositional and conduct problems, who are not also referred for offending [146].

[H3] Youth-focused and multimodal interventions. Youth-focused interventions typically include cognitive-behavioural and social skills training programs targeting self-regulation, anger and aggression. Some adolescent-focused programs have been rated as 'possibly' efficacious (such as cognitive mediation) or having evidence only from weak, uncontrolled designs (such as aggression replacement training), suggesting that these can only be tentatively recommended, and that further work is needed to identify effective and superfluous components[153]. Other reviews have reported very few effective youth-focused treatments[140,152,154]. Indeed, one review [153] rated only two adolescent programs as 'well established'; both programs were aimed at youths with CD or offending and were highly intensive multimodal interventions (Multisystemic Therapy and Multidimensional Treatment Foster Care).

Coping Power is a child-focused group-based CBT intervention for aggressive and disruptive behaviour, and has shown promising effects in late childhood [155,156]. The unique contribution of Coping Power to ODD outcomes is not clear, as most studies have evaluated this program in combination with parenting interventions. However, a Swedish study of 8-12-year-olds diagnosed with ODD found that adding Coping Power to parent training yielded further

beneficial effects on ODD symptoms in children with the highest levels of ODD at study start[157]. However, no added benefit of Coping Power was demonstrated across the whole sample of children with ODD, compared with parenting alone. A study of aggressive 9-10-year-old boys in schools in Pakistan compared Coping Power and no intervention, and demonstrated beneficial effects on both teacher-reported and parent-reported aggression with Coping Power compared with no intervention[158].

Information for professionals and parents about evidence-based programs can be found in resources such as those produced by the American Academy of Child and Adolescent Psychiatry[159], and by the Clearinghouse, Blueprints for Health Youth Development[160].

[H2] Psychopharmacological interventions

Pharmacological interventions are not recommended for children and adolescents with ODD. Th evidence-base for pharmacological intervention is very limited and is often based on atypical groups of children, for example, those hospitalised for extreme aggression. Trials of antipsychotics such as risperidone have also revealed harmful adverse effects [54] such as weight gain, and potential development of movement disorders.

However, NICE guidelines recommend stimulants for reducing oppositional behaviour in children with ADHD, although parenting interventions should be the first line of treatment[131] .

[H2] Ineffective or harmful interventions

Several interventions do not seem effective or have more limited evidence for oppositional problems. These interventions are not recommended in clinical guidelines (such as NICE [131]) and include play therapy and individual non-directive counselling,

751 psychodynamic psychotherapy [153], and dietary interventions.

752

753 **[H1] Quality of life**

754 ODD is associated with increased lifelong risk of psychopathology, social and health
755 problems, which is only partly mitigated by successful treatment and/or desistance of ODD
756 symptoms. Moreover, youths with ODD have greater impairment across multiple life
757 domains than youths with other psychiatric disorders[56]. ODD was also related to social
758 impairment across settings, such as the family (parents and siblings), school and with peers.
759 Similarly, ODD is part of the developmental history of a wide range of disorders in (young)
760 adulthood, and patterns of comorbidity seem to vary based on subdimensions of ODD
761 symptoms [4 99].

762 Conduct problems are associated with substantial long-term costs. Indeed, one study
763 estimated that youths with conduct problems cost society 3.5 times as much to raise to
764 adulthood as youths without conduct problems [161]. Increased costs were associated with
765 crime, extra educational provision, foster and residential care, state benefits and health care.

766 The first study of long-term academic and occupational effects of childhood ODD in
767 adults[162] compared outcomes in the Victorian Healthy Youth Survey in Canada . This study
768 reported that ODD symptoms in adolescence (12-17 years) predicted lower occupational
769 prestige, lower academic attainment (in males), higher debt (in females), greater financial
770 strain, delays in receiving medical attention, and greater perceived workplace stress in
771 adulthood (22-29 years). Moreover, increased ODD symptoms, particularly limited
772 perseverance and compliance, contributed to poorer academic outcomes by the final follow-
773 up, and higher perceived personal conflict in the workplace for females. Similarly, another
774 study found that ODD symptoms in boys predicted poorer quality romantic relationships,
775 paternal relationships and peer functioning at age 24[163]. These associations remained

776 significant when controlling for parent-reported psychopathology [163].

777 Taken together, this research paints a picture of declining health, academic,
778 occupational, and relational capital that particularly affects males with ODD compared with
779 their peers. The effects of ODD can persist into adulthood, impairing functioning and
780 predicting health and social problems across a variety of domains. Moreover, these effects are
781 not restricted to the children themselves; stress, social function and health in peers, parents,
782 teachers and other caregivers are affected by the quality of their relationships, and a true
783 picture of the effects of ODD should factor in the child's intimate relationships and social
784 networks. Little research into these effects has been conducted, but it is clear that child ODD
785 negatively affects parental mental health [164].

786 Of note, individual differences in outcomes and quality of life vary greatly among
787 children with ODD. The effects described here are therefore not inevitable, particularly when
788 the disorder desists. Moreover, evidence-based treatment for ODD is associated with reliable
789 reductions in ODD symptoms [126] and improvements in economic and social conditions [165].
790 Accordingly, there is grounds for much optimism when families access, and engage with,
791 appropriate support.

792

793 **[H1] Outlook**

794 **[H2] Raising awareness**

795 ODD is often undetected, underdiagnosed, and untreated compared with other
796 common child and adolescent disorders. Moreover, research into ODD remains underfunded
797 in many parts of the world [166,167]. Despite the high prevalence and burden associated with
798 child conduct problems, neither ODD nor CD were named in reports on mental health
799 funding from the US and UK, such as The Anatomy of NIMH Funding or UK Mental Health
800 Research Funding, respectively. Research into parenting interventions is also underfunded

[168]. This under-funding may in part reflect poor recognition of these problems as mental health disorders.

As ODD often precedes the more severe problems of CD and other psychiatric disorders, it is arguably one of the highest priorities for expenditure on mental health research and infrastructure concerned with early intervention and prevention. Although ODD is not included in the WHO Global Burden of Disease Study, CD was included and was found to be the leading cause of burden among all mental disorders in children aged 0–14 years [169]. Notwithstanding the need for greater research into ODD and its associated burden, there is strong support for treating this disorder as a major public health issue. Research and clinical services for children with ODD and their families should be properly resourced and funded accordingly.

[H2] Mechanisms/pathophysiology

Ongoing research is needed to understand the pathophysiology of ODD and its subtypes, and the mechanisms underlying heterogeneous risk pathways and comorbid disorders among children with ODD. This research should include studies evaluating the pathophysiology of risk pathways that are associated with specific subdimensions of ODD, for example, the angry or irritable mood subdimension and its relationship to chronic irritability, and the vindictiveness subdimension as it relates to developmental trajectories of CU traits. We are not aware of any studies that have investigated whether the subdimensions of ODD show differential associations with neuropsychological performance. Future neuropsychological and neuroimaging studies could also distinguish between the defiant and irritable subdimensions of ODD to examine whether they are differentially associated with neurocognitive or brain dysfunction. A testable hypothesis is that irritability is related to dysfunction in brain circuits underlying emotion regulation whilst defiant behaviour is related

826 to deficits in punishment sensitivity. Longitudinal studies are key to understanding how early
827 brain markers are associated with later mental health disorders involving homotypic
828 continuity (where a disorder predicts itself, or a closely related condition, later in
829 development; e.g., development of CD or ASPD) as well as heterotypic continuity (where a
830 disorder predicts another disorder later in development; e.g., depression or anxiety), among
831 children with ODD.

832 Evidence regarding the molecular genetics of ODD is particularly limited, with
833 available data largely derived from males, similar to studies of the neuroendocrine system in
834 ODD. Accordingly, research with females is needed to better understand sex differences
835 related to such mechanisms [63]. Additionally, functional neuroimaging and
836 neuropsychological studies have largely focussed on emotion processing and decision-
837 making or reward processing and selected their cognitive tasks and regions of interest
838 accordingly, such that 'cool' executive functions and their supporting brain networks have
839 not been systematically investigated [170].

840 Differentiating mechanisms associated with ODD versus CD is a major challenge as
841 many studies and systematic reviews have combined these disorders and their subtypes to
842 form a single disruptive behaviour disorders group [83]. To our knowledge, only one study has
843 attempted to disentangle the structural brain alterations associated with ODD compared with
844 CD, and found alterations common to both disorders as well as disorder-specific changes [84].
845 Moreover, only a handful of functional MRI studies have investigated brain responses in
846 youths with ODD. Further investigation is needed to examine whether ODD and CD are two
847 ends of a spectrum or distinct disorders with partially dissociable neural correlates. As most
848 of the genetic influences on CD are unique to CD whereas genetic risk for ODD is largely
849 shared with other disorders [7], some differentiation may be expected. This differentiation is
850 further complicated by potential age effects, as ODD typically affects younger children and

many of those with ODD will ultimately develop CD [171,172] [30].

[H2] Prevention and Treatment

Only a minority of children and adolescents with ODD and their families receive evidence-based intervention, even in countries with comprehensive health care such as the US [120]. Moreover, individuals who receive evidence-based interventions often do not access this intervention in early-childhood to -middle childhood, when it may be most effective and economical, and has the greatest potential to prevent chronic antisocial behaviour and psychopathology. Common barriers to access include a lack of clinical infrastructure in underserviced and remote communities, factors that affect engagement with traditional services (such as parental mental health disorders and household adversity) [173]. Digital (telehealth or eHealth) parenting interventions have been recommended to overcome such barriers and have produced promising results [174,175]. However, scalable systems for integrating digital intervention with broader services in care pathways for ODD are still needed. Research is also needed to understand the specific challenges associated with digital interventions in diverse cultural contexts and their applicability in low-middle-income countries (e.g., [176]). Other barriers relate to poor mental health literacy among parents, educators, health professionals and policy makers, which can limit early detection and may lead ODD to be dismissed as 'bad behaviour' [177,178]. Erroneous beliefs about causes of ODD can also interfere with help-seeking by contributing to unnecessary stigma towards children with ODD and their parents. Accordingly, initiatives targeting mental health literacy at the population level are needed to facilitate access to early intervention for such children [178].

Understanding how available interventions for ODD can be delivered and adapted to best meet the needs of children with specific symptom profiles and comorbidities is also needed. Some evidence indicates that parenting interventions for ODD may also improve

internalising problems [179]. Less is known about how the specific symptom dimensions of ODD respond to these interventions, or the clinical change processes implicated in distinct dimensions (such as irritability versus argumentative or defiant behaviour). Further research into the processes that account for dimension-specific and transdiagnostic effects would inform the ongoing development and refinement of these interventions.

Moreover, further work is needed to develop interventions for individuals with ODD who do not respond to available evidence-based interventions. Children with ODD or CD and CU traits have been a key focus of existing research, given that this group tends to start treatment with more severe behaviour problems and, despite responding to treatment, still leaves with more severe behaviour problems [180]. Studies suggest that the relatively poor outcomes of youths with conduct problems and elevated CU traits could be enhanced through the integration of emotion-focused components into standard parenting interventions. However, findings have been mixed, and mechanisms of change in this high-risk subgroup remain poorly understood [181-184]. In addition to targeting such subgroups, a worthwhile aim for future research is to test novel clinical strategies among children with ODD who have already not responded to previous interventions. The diverse stakeholders involved in the care of children with ODD will be essential to guiding this work.

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In this highly informative study, two meta-analyses were conducted to identify which components of evidence-based parenting programs for conduct problems most account for program effects, when delivered for the purpose of prevention and treatment respectively.

Gardner, F., et al., Equity effects of parenting interventions for child conduct problems: a pan-European individual participant data meta-analysis. The Lancet Psychiatry, 2019. 6(6): p. 518-527.
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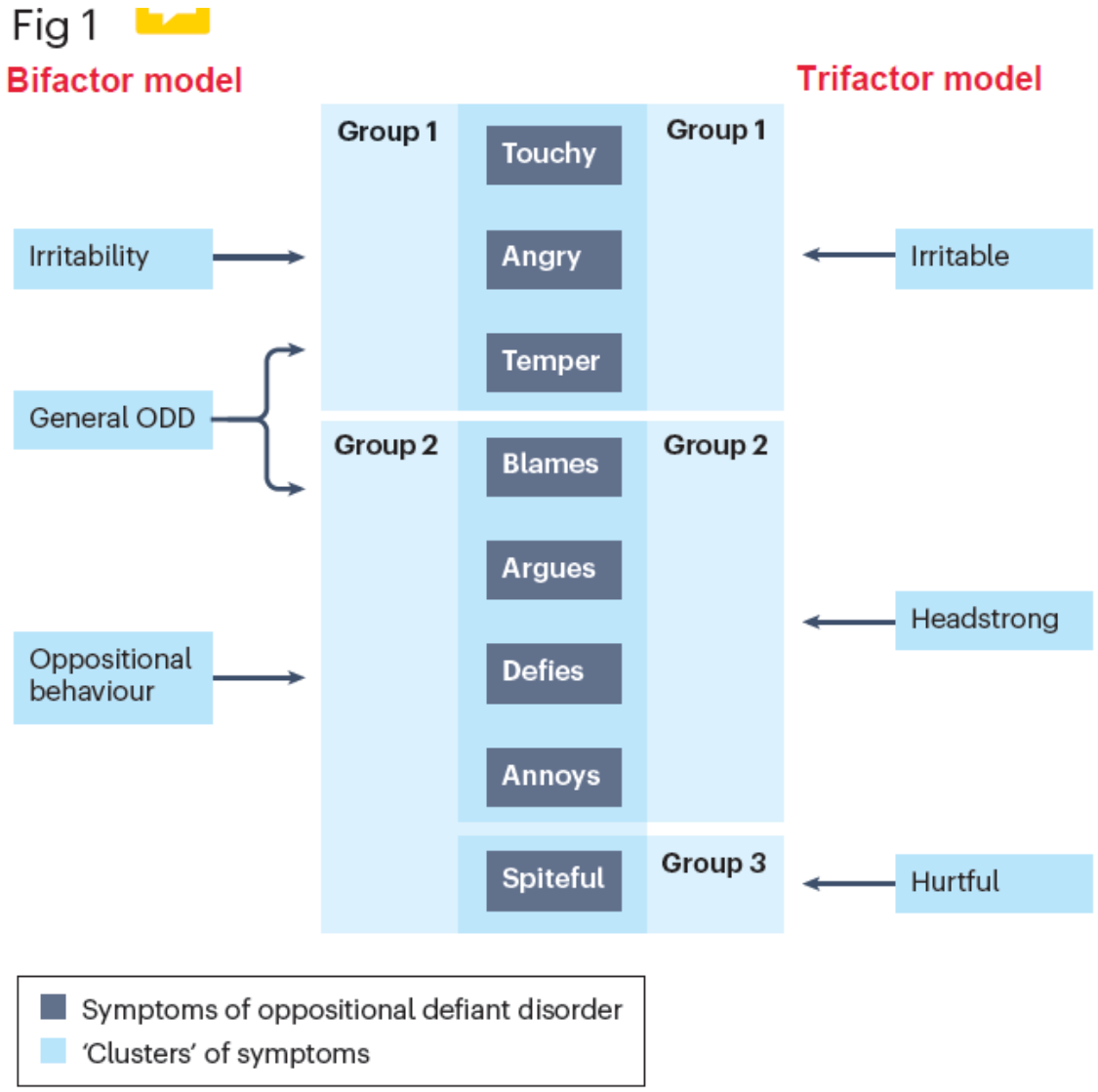


Figure 1: Bifactor and trifactor models of Oppositional Defiant Disorder

Multidimensional models of oppositional defiant disorder (ODD) – such as the bifactor model based on Burke et al.[13] and the trifactor model based on Stringaris and Goodman[185], - all include one dimension of chronic irritability symptoms. They vary in terms of whether they include one oppositional behaviour dimension or two behavioural dimensions – namely 'defiant/headstrong' and 'vindictive/hurtful' [12,163]. These distinctions likely arise due to methodological differences. For example, comparisons across five large community samples [13] consistently supported a two-dimensional model of ODD and refuted a single dimensional structure, but did not test models with three subdimensions. Studies

making empirical comparisons of one, two and three symptom dimension models have found superiority for two dimensional (such as Refs [30,186]) or three dimensional (such as Refs [187,188]) models (see Ref [35] for a review). However, other studies have found only equivocal support for unidimensional and multidimensional models [189] or have rejected multidimensional symptom structures altogether [190]. Behavioural genetic analysis of multidimensional models have revealed substantial genetic concordance between the defiant behaviour subdimension of ODD and conduct disorder (CD), attention-deficit/hyperactivity disorder (ADHD), and substance use disorders, distinct from genetic linkages between the irritable subdimension with depression and anxiety [12,40]. This may explain the broad connections of ODD with both externalising and internalising disorders [12,13,41], unlike CD, which specifically increases risk for externalising disorders.

Fig 2

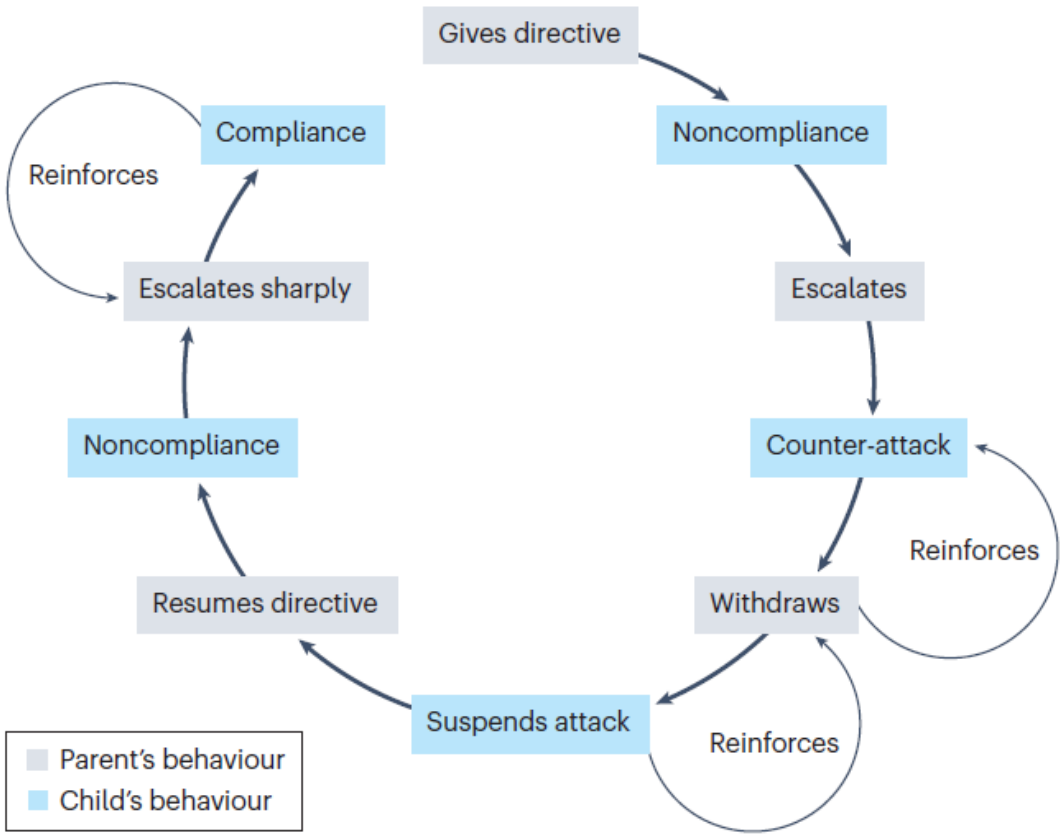


Figure 2: Moment-to-moment reinforcement of parent-child coercion

Figure adapted from Patterson[191], showing coercive cycles in which the contingencies of parent-child interactions reinforce each other's escalation or capitulation, making the interchanges more likely to occur in the future. These self-perpetuating cycles (or 'reinforcement traps') elicit and reinforce harsh and inconsistent discipline practices that allow parents to avoid or escape from escalations in children's aversive behaviour in the short term, but that model coercion and reinforce the child's aversive behaviour in the long term.

Fig 3

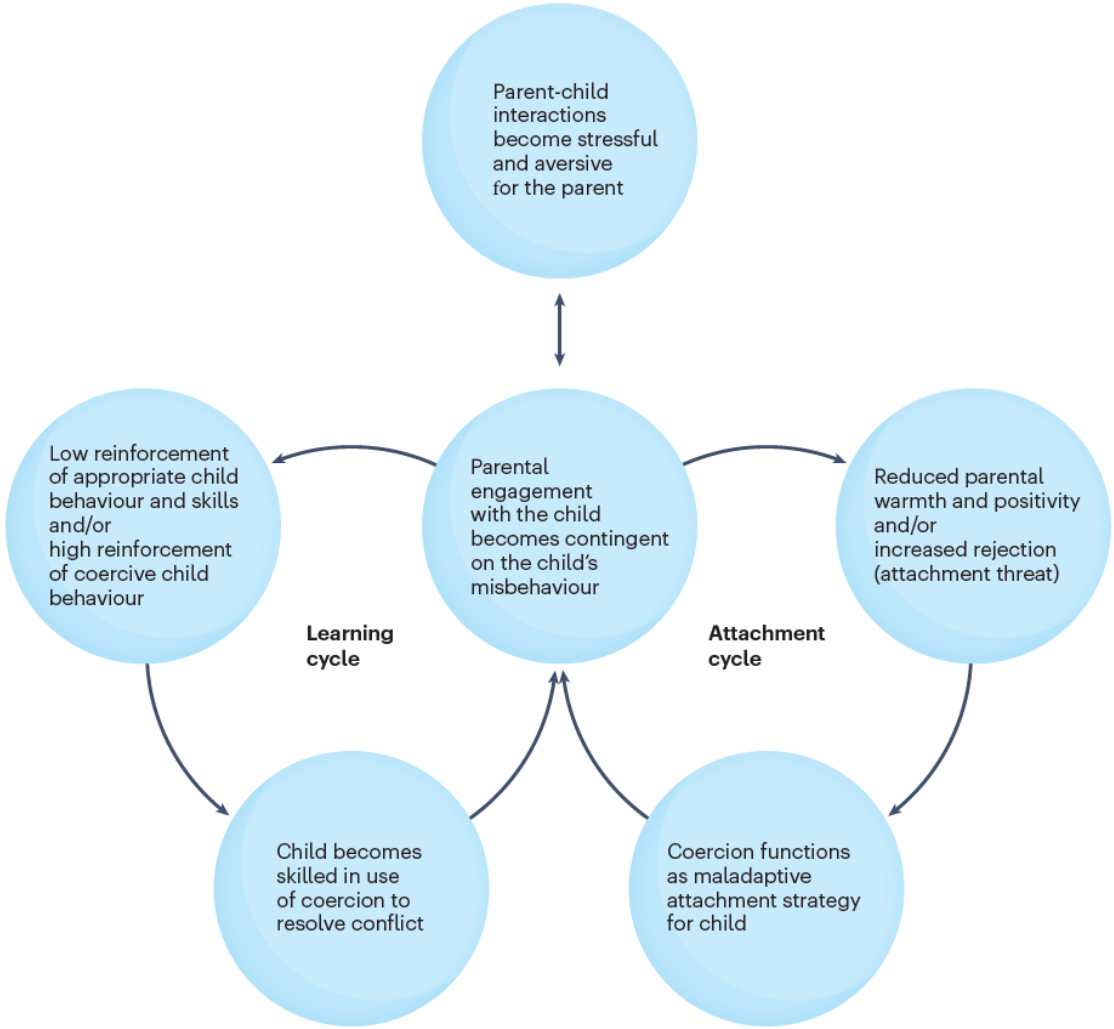


Figure 3: Longer term effects of coercive cycles on the parent-child relationship. Figure adapted from Dadds and Hawes[49]. Cycles of learning and attachment processes contribute synergistically to the breakdown of the parent-child relationship and the maintenance of conduct problems over time. Learning mechanisms (such as modelling and reinforcement) lead the child to become skilled in the use of coercion and, therefore, more difficult to discipline. This child behaviour can also elicit rejecting parental responses that threaten the child's attachment security and result in coercion becoming a maladaptive attachment strategy for the child (for example, a problematic means of regulating proximity, physical contact, and emotional engagement with attachment figure).

Fig 4

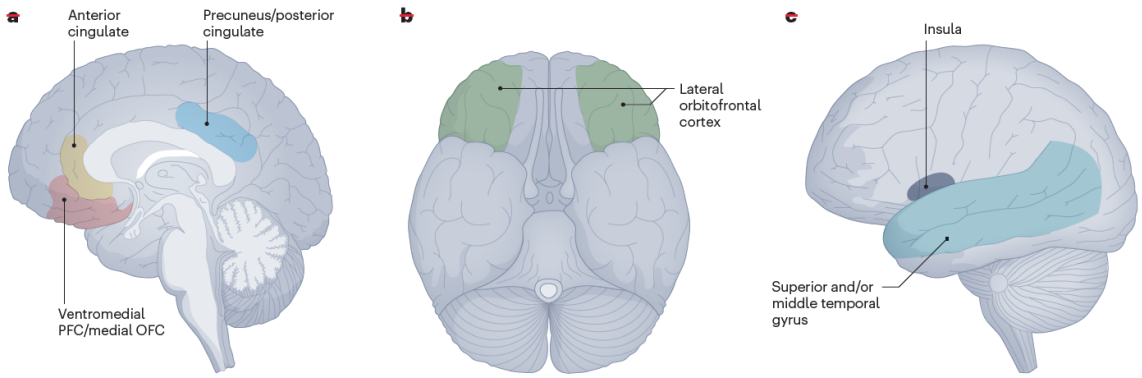


Figure 4: Differences in brain structure in youth with Oppositional Defiant Disorder

Structural MRI studies have reported lower medial and lateral orbitofrontal cortex, inferior parietal cortex, superior frontal gyrus, precuneus, pars triangularis and superior/middle temporal gyrus volume in youths with oppositional defiant disorder (ODD) and comorbid attention-deficit/hyperactivity disorder (ADHD) compared with typically-developing youth[192]). These regions are involved in social cognition, emotion regulation and cognitive control, along with visual and semantic processing. One study attempted to disentangle structural changes associated with ODD compared with conduct disorder (CD) and found that reductions in the medial orbitofrontal and ventromedial prefrontal cortex are specific for ODD, whereas ODD and CD are linked to lower anterior cingulate, insula, superior temporal gyrus, precuneus and posterior cingulate cortical thickness and lower insula, inferior and medial orbitofrontal cortex grey matter volume[84]). The ventromedial prefrontal cortex is strongly implicated in emotion regulation and reward processing. A meta-analysis of structural MRI studies[83]) revealed volume reductions in overlapping regions in youths with ODD or a mixed group of youths with ODD or CD, but effects on cortical thickness appear less robust across studies.

Fig 5

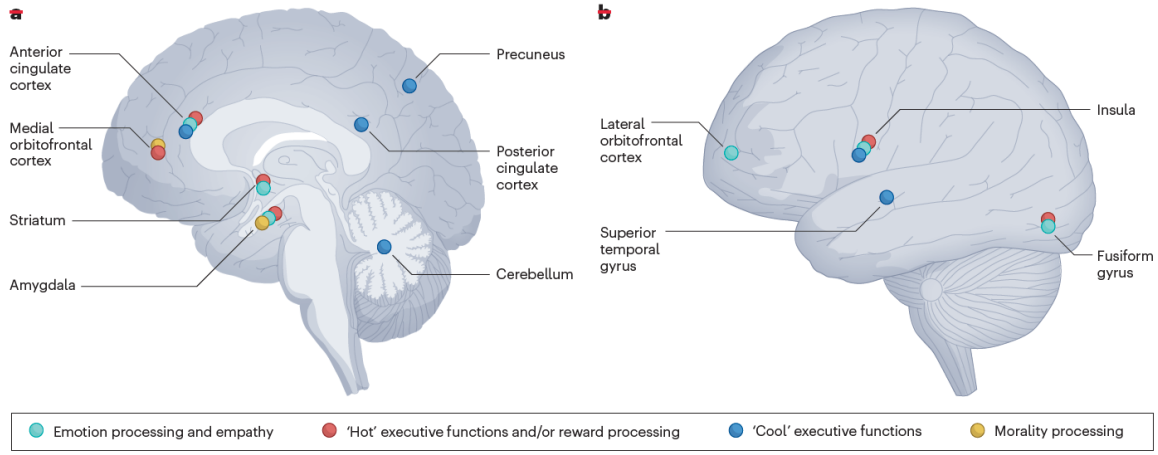
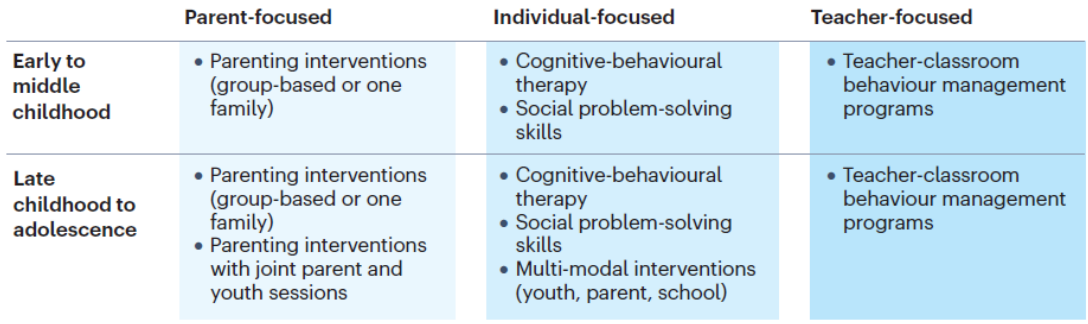


Figure 5: Brain regions which are under-responsive in youth with Oppositional Defiant Disorder

Functional MRI (fMRI) studies of emotion processing and executive functioning have demonstrated lower responses in the amygdala, anterior insula, medial and lateral orbitofrontal cortices, anterior cingulate cortex, striatum, fusiform gyrus and superior temporal gyrus in youth with oppositional defiant disorder (ODD) or mixed cohorts of youth with ODD or conduct disorder (CD). These regions are implicated, respectively, in emotion recognition, empathy and interoception (awareness of one's physiological state), emotion regulation, error processing, and reward processing and learning. The lateral orbitofrontal cortex, superior temporal gyrus and fusiform gyrus are involved in response inhibition, perception of biological motion and face processing, respectively. Each coloured circle indicates that the region was less responsive in youth with ODD in at least one study investigating the specified domain; multiple dots in a given region indicate that the findings for that region are particularly robust or consistent across neurocognitive domains.

Fig 6



	Parent-focused	Individual-focused	Teacher-focused
Early to middle childhood	• Parenting interventions (group-based or one family)	• Cognitive-behavioural therapy • Social problem-solving skills	• Teacher-classroom behaviour management programs
Late childhood to adolescence	• Parenting interventions (group-based or one family) • Parenting interventions with joint parent and youth sessions	• Cognitive-behavioural therapy • Social problem-solving skills • Multi-modal interventions (youth, parent, school)	• Teacher-classroom behaviour management programs

Figure 6: Overview of Management

Parenting interventions based on social learning principles have the most robust and extensive empirical support for management of oppositional defiant disorder (ODD). This focus on parenting remains key across childhood and adolescence, whereas developmental changes during childhood enable older children to participate more actively in treatment and, therefore, older children benefit from individual-focused and teacher-focused components.

Box 1. Summarized DSM-5 diagnostic criteria for Oppositional Defiant Disorder

A pattern of angry/irritable mood, argumentative/defiant behaviour, or vindictiveness lasting for ≥ 6 months, demonstrated by a minimum of four of the following symptoms during interactions with at least one individual who is not a sibling. These behavioural changes must be associated with distress in the individual or other individuals, or negatively affects important areas of functioning. Moreover, the behaviours must not occur exclusively during a psychotic, substance use, depressive, or bipolar disorder. In addition, criteria are not met for disruptive mood dysregulation disorder.

[bH1] Angry/Irritable Mood

- Often loses temper.
- Often touchy or easily annoyed.
- Often angry and resentful.

[H1] Argumentative/Defiant Behaviour

- 4. Often argues with authority figures or, for children and adolescents, with adults.
- 5. Often actively defies or refuses to comply with requests from authority figures or with rules.
- 6. Often deliberately annoys others.
- 7. Often blames others for his or her mistakes or misbehavior.

[H1] Vindictiveness

- 8. Has been spiteful or vindictive at least twice within the past 6 months.

The severity of ODD is determined as follows:

Mild ODD refers to those with symptoms that are confined to only one setting (such as at home, school or work, or with peers).
Moderate ODD refers to those who have some symptoms that occur in at least two settings.
Severe ODD refers to those who have some symptoms that occur in three or more settings.

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Ref [11].