Online Appendix

Primary sources on paediatric bipolar disorder (PBD) referred to in the paper

Reference	Origin	Purpose	Design	Major Findings
Clinical Description				
Clinical Features				
Geller et al. (1995)	USA	Original proposal for ultradian cycling ("narrow phenotype") as a basis for diagnosing PBD	Cross-sectional study of 9 children (age ≤ 12 years) and 17 adolescents (age ≥ 13 years) with proposed PBD	• 80.8% of youths studied showed evidence of what the authors considered to be frequent brief episodes of mania/hypomania • The mean age of onset of episodes was in childhood (8.5 years) • "Mixed states", hyperactivity, suicidality, and psychotic phenomena were common across patients • There were no clear differences between children and adolescents
Wozniak et al. (1995)	USA	Original proposal for chronic irritability ("broad phenotype") as a basis for diagnosing PBD	Cross-sectional study comparing 43 children (age ≤ 12 years) with proposed PBD, 164 children with ADHD, and 84 children without ADHD	• Mania, as defined by the researchers, was relatively common in their sample (16% of consecutively referred patients to a paediatric psychiatric clinic for a psychopharmacological opinion) • 70% of children with mania had an onset of mania at age ≤ 5 years • All but one child diagnosed with PBD (98%) also had ADHD
Van Meter et al. (2016)	USA	Determine the prevalence of different manic symptoms associated with PBD	Systematic review of studies reporting the prevalence of different types of manic symptoms in PBD	• There was large heterogeneity in the particular symptoms associated with mania in PBD both between and within the 20 studies identified • There were no clear predictors of this variability
Galanter et al. (2012)	USA	Clarify the criteria used to diagnose PBD	Systematic review of the instruments and criteria used in the diagnosis of PBD	• There was large variability in criteria across six instruments, including how DSM criteria for bipolar disorder are conceptualised, whether symptoms need to differ from a child's baseline, requirements for features to co-occur, and general administration and scoring

Ryles et al. (2017)	UK	Compare the frequency and severity of manic symptoms reported by children, adolescents, and adults diagnosed with bipolar disorder	Systematic review of studies that compared the frequency or severity of manic symptoms in children, adolescents, and adults diagnosed with bipolar disorder and presenting with first episode mania	• Across nine studies, findings tentatively suggested that irritability is more prominent for onset in childhood; activity is more prominent in adolescence; and pressure of speech is more prominent in adults • No studies directly compared children and adults • There were other significant limitations: there was geographic bias as most studies were from the USA; methods were heterogeneous; and studies generally failed to consider comorbidities
Inter-Rater Reliability				
Regier et al. (2013)	USA	DSM 5 field trials: Assess the inter-rater reliability of DSM diagnostic criteria	Experimental: Independent evaluation of patients using DSM 5 diagnostic criteria	• Unable to obtain an accurate estimate for bipolar disorder type I/II inter-rater reliability in children given large variability (95% CI around estimate > 0.5; intraclass kappa 0.52, 95% CI 0.13-0.80) • Poor reliability of disruptive mood dysregulation disorder (DMDD) diagnosis (intraclass kappa 0.25, 95% CI 0.15-0.36) • In adults, bipolar disorder type I diagnosis had moderate reliability (intraclass kappa 0.56, 95% CI 0.45-0.67); unable to obtain an accurate estimate for bipolar disorder type II given large variability
Larios et al. (2018a, 2018b)	USA	Assess expert agreement on symptoms and diagnosis of PBD	Experimental: 12 written clinical histories rated by 12 PBD experts from the Pediatric Bipolar Biobank Consortium	• Poor agreement on hypomania (ICC 0.10) and bipolar disorder not otherwise specified (interclass correlations, ICC, 0.09), both with large variability (95% CI -0.01-0.47 and -0.02-0.50 respectively) • What authors term “fair” agreement on mania (ICC 0.41), though with very large variability (95% CI 0.19-0.76) • Poor/fair agreement on individual symptoms (ICC 0.29 to 0.69), with large variability across symptoms • Poor agreement on clinical impairment (ICC 0.23) with large variability (95% CI 0.09-0.60)

Rates of Diagnosis				
Moreno et al. (2007)	USA	Examine rates of bipolar disorder diagnoses made by US outpatient physicians over time	Retrospective cross-sectional study: Compared rates of bipolar diagnosis between 1994-1995 and 2002-2003 in youths (0-19 years) and adults (≥ 20 years) using National Ambulatory Medical Care Survey	• Diagnoses of bipolar disorder in youths increased dramatically from 25 to 1003 visits per 100 000 population from 1994-1995 to 2002-2003 • Diagnoses of bipolar disorder in adults also increased from 905 to 1659 visits per 100 000 population over this period • Youths diagnosed with bipolar disorder were more likely to have co-morbid ADHD diagnosis (32.2%) than adults similarly diagnosed (3.0%) • Most youths (91.6%) and adults (86.4%) diagnosed with bipolar disorder received psychotropic medication
Blader and Carlson (2007)	USA	Examine rates of bipolar disorder diagnoses in US inpatients over time	Retrospective cross-sectional study: Population-adjusted rates of hospital discharges with bipolar diagnosis from 1996 to 2004 in children (5-13 years), adolescents (14-18 years) and adults (≥ 19 years) in National Hospital Discharge Survey	• Hospital discharges of children with a primary diagnosis of bipolar disorder increased 439% between 1996 and 2004 • For adolescents, bipolar disorder related discharges increased 297% • For adults, bipolar disorder related discharges increased 56%
International Comparisons				
Dubicka et al. (2008)	UK/USA	Compare clinicians from USA and UK in diagnosing prepubertal mania	Experimental: 5 vignettes of prepubertal children (4 ambiguous, 1 classical mania) presented to 73 clinicians from UK and 85 clinicians from USA	• USA clinicians were more likely to diagnose mania in ambiguous cases • UK clinicians were more likely to diagnose pervasive developmental disorders and adjustment disorders in ambiguous cases • There was no difference between USA and UK clinicians in diagnosing cases of classical mania
James et al. (2014)	UK/USA	Compare hospital discharge rates of PBD between USA and England	Cross-sectional: Compared hospital discharge rates of PBD, other child psychiatric	• PBD discharge rates were 72.1x higher in the USA compared to England • After controlling for differences in length of stay, PBD discharge rates

			diagnoses, and adult bipolar disorder between US and England over 2000-2010	remained 12.5x higher in USA compared to England • For all other child psychiatric diagnoses, discharge rates were 3.9x higher in the USA compared to England • For adult bipolar disorder, discharge rates were 7.2x higher in USA
Clacey et al. (2015)	UK	Compare hospital discharge rates for PBD and other diagnoses across countries	Cross-sectional: Compared hospital discharge rates across 5 countries (USA, England, Germany, Australia, and New Zealand) using national datasets for youths (< 20 years) and adults (20-64 years)	• Bipolar disorder discharge rates were much higher in the USA compared to other countries (age < 20 years, discharge rates/100 000 population: USA 95.6, Australia 11.7, New Zealand 6.3, Germany 1.5, England 0.9) • Most marked divergence in discharge rates for ages 5-9 years (USA 27.0, Australia 0.1, New Zealand 0.2, Germany 0.0, England 0.0) • For adults aged > 20 years, bipolar disorder discharge rates were still higher in the USA, though more comparable (USA 150.6, Australia 135.5, Zealand 76.0, Germany 136.1, England 29.8) • Borderline personality disorder discharge rates were lower in the USA compared to other countries for both youths and adults
Douglas and Scott (2014)	UK	Determine the prevalence of mood disorders in community studies of prepubertal children (aged ≤ 12 years)	Systematic review and meta-analysis of observational studies assessing prevalence of mood disorders in community samples of prepubertal children	• Across five studies, assessing > 5000 children in total, only one case with a probable diagnosis of mania was identified • This yielded an estimated prevalence of < 0.02% for bipolar disorder in children aged ≤ 12 years
Van Meter et al. (2011)	USA	Determine the prevalence of PBD in community samples and assess whether countries differ	Systematic review and meta-analysis studies reporting prevalence of bipolar disorder in childhood and adolescence (age ≤ 21 years)	• Mean prevalence of PBD was 1.8% (95% CI 1.1-3.0%) over 11 studies • There were no differences in findings between US and non-US studies • Analyses were limited by the fact that children were grouped together with adolescents and the diverse criteria for bipolar disorder used across studies (see Parry et al., 2018)

Van Meter et al. (2019)	USA	Determine the prevalence of PBD in community samples and assess whether countries differ	Systematic review and meta-analysis studies prevalence of bipolar disorder in childhood and adolescence (age ≤ 21 years; update of authors' 2011 meta-analysis)	• Mean prevalence of PBD was 3.9% (95% CI 2.6-5.8%) over 19 studies • There were no differences in findings between US and non-US studies • Analyses were limited by the fact that children were grouped together with adolescents and the diverse criteria for bipolar disorder used across studies (see Parry et al., 2021)
Parry et al. (2018)	Australia	Determine the prevalence of PBD in community samples and assess whether countries differ	Re-examination of Van Meter et al. (2011) systematic review and meta-analysis	• The author identified limitations in Van Meter et al. (2011): almost all studies focused on adolescence (up to age 21 years), rather than childhood; studies used heterogeneous methodologies and diagnostic criteria, making statistical meta-analysis problematic • When restricting focus to children (rather than adolescents), very few were diagnosed with PBD • Studies from the USA had slightly higher rates of PBD in children than studies from other countries
Parry et al. (2021)	Australia	Determine the prevalence of PBD in community samples and assess whether countries differ	Re-examination of Van Meter et al. (2019) systematic review and meta-analysis	• The authors noted similar limitations in Van Meter et al. (2019) as those in Van Meter et al. (2011) • When restricting focus to children (rather than adolescents), very few were diagnosed with PBD • Studies from the USA had slightly higher rates of PBD in children than studies from other countries
Parry et al. (2019b)	Australia	Compare attitudes towards PBD between researchers in the USA and researchers from the rest of the world	Bibliographic analysis of articles that cited seminal papers on PBD: citing papers were categorised by country and whether they were supportive or not of the PBD construct	• Most articles on PBD (79%) were published by authors from the USA • Most articles from the USA (83%) supported the PBD construct • Most articles from other countries (60%) were critical of the PBD construct and supported the notion that bipolar disorder was rare prior to mid-adolescence

Delimitation				
Frías et al. (2015)	Spain	Determine rates of comorbidities in youths diagnosed with PBD	Systematic review of studies reporting comorbidities in youths (age 4-18 years) diagnosed with PBD	• ADHD had a mean prevalence of 48% in children and adolescents with PBD, though with large heterogeneity (range 4-98%) and with significantly higher rates in children than adolescents (odds ratio 2.8) • Across samples, 19% had a pervasive developmental disorder (range 11-30%), 31% had a disruptive behaviour disorder (range 7-75%), 54% had an anxiety disorder (range 41-80%), and 31% had a substance use disorder (range 16-48%)
Evans et al. (2021)	USA	Assess experts' accuracy at diagnosing conditions involving irritability in children	Experimental (parallel group): 196 clinicians provided diagnoses for 5 vignettes using either DSM V, ICD 10, or ICD 11 criteria	• Clinicians showed poor/moderate accuracy at diagnosing the bipolar disorder type II vignette: 38.1% accuracy using DSM-V, 66.7% accuracy using ICD-10, and 64.7% using ICD-11 criteria • Clinicians using ICD criteria were more accurate in distinguishing chronic irritability from episodic bipolar disorder irritability than those using DSM V criteria
Duffy (2012)	Canada	Examine the relationship between childhood ADHD and subsequent development of bipolar disorder	Systematic review of prospective longitudinal studies of children at high risk of bipolar disorder	• Childhood ADHD was not a reliable predictor for the development of bipolar disorder across the nine identified studies • Subjective concerns of inattention, alongside anxiety and depressive symptoms, were reported by some patients during the early stages of developing bipolar disorder
Parry (2012, 2021)	Australia	Examine the contribution of attachment and trauma to PBD	Systematic review of research on PBD examining attachment, abuse, maltreatment, PTSD, and trauma	• Only 15 articles contained the term "attachment" and only three considered this as a significant theme; none had it as a primary focus • 64 articles contained at least one term relating to abuse; for PBD proponents, abuse was often referred to in a dismissive fashion (e.g., reporting implausibly low rates, suggesting trauma arose from mania) • Overall, the PBD literature appeared to neglect attachment and trauma

Geller et al. (2000)	USA	Examine psychosocial functioning in PBD, including relationships with parenting and previous experiences of abuse	Cross-sectional study comparing 93 children diagnosed with PBD (mean age 10.9 years), 81 diagnosed with ADHD, and 94 controls	• Children diagnosed with PBD had lower levels of maternal warmth and greater tension with both parents than controls and children diagnosed with ADHD • < 1% of children with PBD reported to have a history of sexual abuse, though 43% showed hypersexuality, which the authors interpreted to suggest that hypersexuality was a manifestation of mania • Parry (2021) argued that this prevalence of abuse is implausible given rates in both the general population (19% of females and 7% of males in meta-analyses) and other samples of PBD
Carlson et al. (2009)	USA	Determine the underlying diagnoses for children presenting with severe anger outbursts	Cross-sectional study of 130 different children aged 5-12 (mean 9.7 years) from 151 consecutive hospital admissions	• 55% of the children were admitted for rages • One-third of children with rages had been given a diagnosis of bipolar disorder prior to their admission • Only 9% of children with rages were given that diagnosis after careful observation during the study
Follow-Up Studies				
Broad Phenotype				
Althoff et al. (2010)	USA	Examine adult outcomes of childhood emotional dysregulation	Prospective 14 year longitudinal study of 2076 children recruited from random community sample (mean age at baseline 9.9 years)	• Emotional dysregulation in childhood was associated with anxiety disorders, major depression, disruptive behaviour disorders, drug abuse, and suicidality at 14 year follow-up • Emotional dysregulation in childhood was not associated with bipolar disorder at 14 year follow-up
Brotman et al. (2006)	USA	Examine the longitudinal course of severe mood dysregulation in children	Prospective 15 year longitudinal study of 1420 children at risk of mental health service use (mean baseline age 11.7 years)	• Severe mood dysregulation was present in 3.3% of children recruited • Severe mood dysregulation predicted adult depressive disorders • Bipolar disorder was vary rare in follow-up samples (only one child later met criteria for bipolar disorder type II; none met criteria for bipolar type I or bipolar disorder not otherwise specified)

Leibenluft et al. (2006)	USA	Examine the longitudinal course of chronic and episodic irritability in children	Prospective nine year longitudinal study of 776 youths recruited from a random community sample (mean baseline age 13.8 years)	• Episodic and chronic irritability remained relatively stable over time, albeit with episodic forms showing a linear increase and chronic forms showing a quadratic trend with a peak in mid-adolescence • Chronic irritability in childhood predicted greater risk of ADHD and ODD at 2 years and depression at 9 years (but not mania) • Episodic irritability was associated with greater risk of generalised anxiety and phobia at 2 years and mania at 2 and 9 years
Stingaris et al. (2009)	USA	Examine the relationship between irritability in early life and adult psychiatric outcomes	Prospective 20 year longitudinal study of 631 youths (further follow-up of Leibenluft et al.'s sample)	• Irritability in early adolescence predicted major depressive disorder, generalised anxiety disorder, and dysthymia – but not bipolar disorder – at the 20 year follow-up
Stringaris et al. (2010)	USA	Compare rates of mania in children with PBD narrow phenotype and children with severe mood dysregulation (broad phenotype)	Prospective 2 year longitudinal study of 93 children with PBD (narrowly defined) and 84 children with severe mood dysregulation (mean baseline age 12.9 and 11.6 years)	• Only 1% of children with severe mood dysregulation were diagnosed with a hypomanic, manic or mixed episode over two years of follow up • By contrast, 62% of children with PBD narrow phenotype were diagnosed with a hypomanic, manic, or mixed episode
Narrow Phenotype				
Cirone et al. (2021)	Italy, USA	Determine the longitudinal outcomes of children and adolescents diagnosed with bipolar disorder	Systematic review of longitudinal studies on bipolar disorder diagnosed in childhood or adolescence	• Early onset bipolar disorder – combining both PBD and bipolar disorder diagnosed in adolescence – appeared to persist, though with significant heterogeneity in the severity of its clinical course • Although the review identified relevant studies on PBD, PBD was not examined separately from bipolar diagnosed in adolescence
Birmaher et al. (2006)	USA	Determine the longitudinal outcomes of children diagnosed with PBD	Prospective two year longitudinal study of 263 youths with PBD (mean age	• 56% of patients had at least one recurrence of mood disturbance • Most recurrences were of depression (57.5%), rather than of mania (13.7%), hypomania (24.2%), or mixed episodes (4.6%)

			13.0 years at baseline; Course and Outcome of Bipolar Youth, COBY, study)	
Birmaher et al. (2009)	USA	Determine the longitudinal outcomes of children diagnosed with PBD	Prospective four year longitudinal study of 413 youths with PBD (part of COBY study)	• 62.5% of participants had at least one recurrence of mood disturbance • Most recurrences were of depression (59.5%), rather than of mania (14.8%), hypomania (20.9%), or mixed episodes (4.8%).
Axelson et al. (2011)	USA	Examine the longitudinal course of subthreshold PBD (bipolar disorder not otherwise specified)	Prospective five year longitudinal study of 140 youths diagnosed with bipolar disorder not otherwise specified (part of COBY study)	• 45% of youths converted to a diagnosis of bipolar disorder I or II • 15-17% had a history of abuse, though this did not predict conversion • Family history of mania or hypomania predicted conversion • Psychosocial treatment was associated with increased conversion rate • Psychotropic medications did not affect conversion rate
Geller et al. (2008)	USA	Determine the longitudinal outcomes of children diagnosed with PBD	Prospective eight year longitudinal study of 115 children diagnosed with PBD (mean age 11.1 at baseline)	• 44% of patients with PBD had a diagnosis of bipolar disorder at eight year follow-up (N.B. ultradian cycling was accepted as a basis for diagnosis across time points, differing somewhat from DSM-IV criteria) • The mean duration of manic episodes at baseline was 2.7 years • Low maternal warmth predicted both relapse of mania and the duration of time that participants were affected by mania or bipolar disorder
Stringaris et al. (2010)	USA	Compare rates of mania in children with PBD narrow phenotype and children with severe mood dysregulation (broad phenotype)	Prospective two year longitudinal study of 93 children with PBD and 84 children with severe mood dysregulation (mean ages 12.9 and 11.6 years at baseline respectively)	• Only 1% of children with severe mood dysregulation were diagnosed with a hypomanic, manic or mixed episode over two years of follow up • By contrast, 62% of children with PBD narrow phenotype were diagnosed with a hypomanic, manic, or mixed episode

Overall				
Cicero et al. (2009)	USA	Examine the prevalence of bipolar disorder diagnoses over the lifespan	Secondary data analyses conducted on two cross-sectional nationally representative samples in the USA (n = 43 935)	• Diagnoses of bipolar disorders were relatively common in early adulthood (5.5%-6.2% prevalence between ages 18-24 years) • Such diagnoses were significantly less common several years later (3.1%-3.4% prevalence between ages 25–29-year-olds) and became even less common in older age groups • A large age-gradient drop in bipolar disorder diagnoses was evident across the life-span that could not be accounted for by ascertainment biases (e.g., early mortality, incarceration, homelessness).
Family Studies				
Duffy et al. (2011)	Canada	Examine psychopathology in children at high risk of bipolar disorder	Systematic review of cross-sectional and longitudinal studies of high-risk offspring	• Results varied with different methods of family ascertainment and psychiatric assessment • Studies using structured interviews with trained raters reported a broader spectrum of psychopathology and a younger age of onset of mood disorders than studies using either semi-structured interviews by expert clinicians or best estimate diagnostic procedures • The findings suggest that cross-sectional symptom-based diagnostic approaches are at risk of higher false positive diagnosis compared to longitudinal approaches
Duffy et al. (2017, 2020)	Canada/ UK	Examine the outcomes of children at high risk of bipolar disorder	Narrative review of prospective longitudinal studies of high-risk offspring (follows previous systematic review conducted by Duffy, 2011)	• Childhood internalising symptoms and sleep problems – but not neurodevelopmental, cognitive or externalising disorders – predicted subsequent mood disorders in adolescence and early adulthood • Depressive episodes in adolescence usually marked the onset of bipolar disorder

				• Sub-threshold manic symptoms (often episodic) varied in their onset, though typically occurred in later adolescence or adulthood, and predicted subsequent bipolar disorder • Pre-pubertal PBD has not been reported in children of parents with a confirmed bipolar diagnosis in the vast majority of studies
Lau et al. (2018)	Australia	Assess relative risk of psychopathology in high-risk bipolar disorder offspring compared to controls	Systematic review and meta-analysis of prospective cohort and cross-sectional studies	• High-risk bipolar disorder offspring were 9.0x more likely to develop a bipolar-type disorder, 2.4x more likely to develop a non-bipolar disorder affective disorder, and 2.1x more likely to develop an anxiety disorder compared to controls • High-risk offspring had greater risk of ADHD, other behavioural disorders, and substance use disorder compared to controls
Laboratory Studies				
Rich et al. (2007)	USA	Assess the behavioural and psychophysiological correlates of irritability in PBD (narrow phenotype) and DMDD	Experimental: 35 PBD, 21 severe mood dysregulation, and 26 controls compared using affective Posner task and event-related potentials (ERP; mean age PBD 13 years)	• PBD differed from severe mood dysregulation in behavioural (Posner task) and psychophysiological measures (ERP)
Rich et al. (2011)	USA	Assess the behavioural and neural correlates of negative affect in PBD (narrow phenotype) and DMDD	Experimental: 20 PBD, 20 severe mood dysregulation, and 20 controls compared using affective Posner task and magnetoencephalography (mean age PBD 14.9 years)	• PBD differed from severe mood dysregulation in behavioural (Posner task) and psychophysiological measures (magnetoencephalography) • Compared to those with severe mood dysregulation and controls, participants with PBD displayed greater superior frontal gyrus (SFG) activation and decreased insula activation following negative feedback

Kennedy et al. (2015)	USA	Determine the genetics of early-onset bipolar disorder	Systematic review of genetic studies using linkage-analyses, candidate-gene associations, genome-wide association studies, and analyses of copy number variants	• There were no robust positive findings on the genetics of early-onset bipolar disorder regardless of the methodology used
Elias et al. (2017)	Turkey, Italy	Compare cognition in euthymic youths diagnosed with PBD relative to healthy controls	Systematic review and meta-analysis of studies comparing patients with PBD and healthy controls in cognition	• Youths diagnosed with PBD showed impairments in cognition recognition relative to healthy controls
Halac et al. (2021)	Turkey, Italy	Compare social cognition in youths diagnosed with PBD relative to healthy controls	Systematic review and meta-analysis of studies comparing patients with PBD and healthy controls in theory of mind and emotion recognition	• Youths diagnosed with PBD showed impairments in theory of mind and emotion recognition relative to healthy controls
Khafif et al. (2021)	Brazil	Compare emotion regulation deficits in youths diagnosed with PBD relative to healthy controls	Systematic review and meta-analysis of studies comparing patients with PBD and healthy controls in emotion regulation	• Youths diagnosed with PBD showed lower accuracy in emotion regulation tasks relative to healthy controls, but did not differ in response time on the tasks used
Simonetti et al. (2022)	USA, Italy	Examine structural and functional alterations in the amygdala in paediatric bipolar	Systematic review and meta-analysis of neuroimaging structural and functional magnetic resonance imaging (MRI) studies in patients with PBD, youth at high-risk of bipolar, and healthy controls	• Amygdala hyper-reactivity to emotional stimuli was the most commonly reported finding in youths diagnosed with PBD and those at high-risk of bipolar disorder relative to healthy controls • Findings from structural MRI studies were inconsistent

Treatment and Outcomes				
Duffy et al. (2018)	Canada	Assess the efficacy and tolerability of lithium for the treatment of acute mania in PBD	Systematic review of randomised controlled trials involving lithium	• Lithium was superior to placebo (standardised mean difference, SMD, −0.42, 95% CI −0.88, 0.04) across the four studies identified • Lithium was comparable to sodium divalproex (SMD -0.07, 95% CI -0.31, 0.18) but clearly inferior to risperidone (SMD 0.85, 95% CI 0.56,1.15) for protracted manic/mixed episodes in prepubertal children, particularly those with comorbid ADHD • Lithium was generally well tolerated with no serious adverse events • Findings were limited by the lack of available data, particularly for treatment of classical mania in adolescents (as distinct from PBD phenotypes), and the fact that all studies were conducted in the USA
Yee et al. (2019)	Canada, USA	Assess effectiveness of maintenance pharmacological treatment in PBD	Systematic review of studies examining maintenance pharmacological treatment in PBD	• 3 randomised controlled trials (RCTs) and 13 open trials were identified • Of RCTs, two compared aripiprazole and placebo; one compared lamotrigine as an adjunct to placebo for patients receiving a mood stabiliser or antipsychotic • Grouping these different drugs together, the authors found a lower non-recurrence rate, but no difference in clinical response rate, for the active treatment with high heterogeneity across studies • Common adverse effects included: cognitive dulling (29%), weight gain (28%), nausea/vomiting (25%), increased appetite (21%), headache (21%), tremor (21%), sedation (21%), polyuria (21%), akathisia (20%) • Given the limitations – including the small number of RCTs, poor study quality overall, and high heterogeneity – the authors concluded that the support for maintenance treatment in PBD is inconclusive

Perez Algorta et al. (2018)	UK/USA	Assess parenting stress among caregivers of children with PBD	Cross-sectional: Secondary analyses on baseline data from a longitudinal study of 621 children with PBD and 86 controls recruited from psychiatric clinics	• Children with PBD had more service utilisation, psychiatric diagnoses, mood and anxiety symptoms, and functional impairment, but fewer disruptive behaviour disorders, than controls • Caregivers of children with PBD had greater depressive symptoms, antisocial tendencies, and parenting stress than parents of controls
Vaudreuil et al. (2019)	USA	Assess morbidity of subthreshold paediatric bipolar disorder	Systematic review and meta-analysis of studies examining morbidity of subthreshold paediatric bipolar disorder	• Subthreshold PBD was associated with greater functional impairment; more severe mood symptoms; more disruptive behaviour; higher rates of mood and substance use disorders; and higher rates of suicidal ideation and attempts compared to controls. • There were no differences in the severity of depressive symptoms or rates of comorbid disorders between patients with subthreshold symptoms and those with formal PBD

Note. Full reference details are provided in the main article. ADHD = attention-deficit hyperactivity disorder; CI = confidence interval; DMDD = disruptive mood dysregulation disorder; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Diseases; ODD = oppositional defiant disorder; PBD = paediatric bipolar disorder; SMD = standardised mean difference; UK = United Kingdom; USA = United States of America.