Part 3: Key Question Posting Document for Psychosocial and Pharmacologic Interventions for Disruptive Behavior in Children and Adolescents

Background

Approximately 8% to 10% of children under the age of 5 years have significant mental health conditions[1] with some presenting as or including disruptive behaviors. According to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), disruptive behavior disorders (DBDs) affect more boys than girls and include oppositional defiant disorder, conduct disorder and intermittent explosive disorder.[2] Common to these disorders are violations of other's rights and/or problems with authority figures. To meet diagnostic criteria, these behaviors must cause impairments in the child's or adolescent's functioning at home, at school, or with peers. The cause(s) of disruptive behavior disorders in children and adolescents are not well understood but risk factors include genetic, environmental and experiential factors such as parental psychopathology and/or substance use, low socioeconomic status, harsh discipline, and exposure to violence and ACEs (adverse childhood experiences), among others.[3-6] Having multiple risk factors is associated with increased likelihood of DBDs.[3,6,7]

Rather than a mostly inward focus, such as with depression and anxiety, persons with disruptive behavior disorders manifest their distress outwardly towards others.[2] DBD behaviors may be destructive (e.g., assault, fire-setting) or less destructive (e.g., arguing with authority figures, temper tantrums).[8] Individuals with oppositional defiant disorder (about 3.3% of the population[9]) are often angry, argumentative, and can be spiteful or vindictive. Individuals with conduct disorder, which affects between 1.5% and 3.4% of the population,[9] are often violently cruel to people and animals and may lie, steal or destroy property. Individuals with intermittent explosive disorder, which cannot be diagnosed before the age of 6 years and has a lifetime prevalence of 7%,[10] may be impulsive with intermittent anger outbursts out of proportion to the inciting event. [11] Individuals may also meet criteria for more than one mental health disorder (e.g., 16%-20% of persons with conduct disorder also have comorbid attention-deficit/hyperactivity disorder [ADHD],[12] and 90% of persons with oppositional defiant disorder will develop another mental illness in their lifetime[13]).

Around 30% of individuals with oppositional defiant disorder progress to a diagnosis of conduct disorder.[8] At least 40% of children with conduct disorder at age 8 engage in criminal behavior in adolescence, such as assault, theft, and vandalism.[14] These children often drop out of school, have few friends, engage in substance use, and are often ill-prepared to participate effectively in mainstream society as an adult.[15] About 40% of those with conduct disorder will later meet criteria for antisocial personality disorder.[11]

However, with age and maturity, approximately 70% of children and adolescents with oppositional defiant disorder will outgrow it by age 18.[13] The use of psychosocial interventions[16-18] (considered first-line treatment) and/or pharmacotherapy (e.g., antipsychotics, stimulants, anti-seizure medications)[19-21] may resolve or help resolve disruptive behaviors. It is currently recommended that treatment for DBDs in childhood and adolescence be individualized. In 2015, the Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review on psychosocial and pharmacologic interventions for disruptive behavior disorders in children and adolescents that included 84 studies and found that psychosocial interventions that include a component involving the parent are more effective than interventions that include only the child.[22] The 2016 technical report published by the American Academy of Pediatrics also concludes that family-focused interventions have the greatest evidentiary support.[23] The 2013 National Institute for Health and Care Excellence (NICE) guidelines recommend against routine pharmacotherapy for behavior problems in children and young people, but suggests that risperidone (an antipsychotic) be considered in severely aggressive youth who have not responded to psychosocial interventions.[24] The 2015 Canadian guidelines recommend treating aggressive behaviors in children with comorbid ADHD with ADHD medications first and, if additional pharmacotherapy is needed, to consider risperidone but recommended against the use of quetiapine, haloperidol, lithium, and carbamazepine for aggressive behaviors due to adverse effects of these medications and poor-quality evidence supporting their use.[25]

In childhood and adolescence, DBDs are the most common reason for childhood referral to mental health services.[26] However, some studies suggest that disparities exist in the diagnosis and treatment of DBDs due to such factors as gender, race/ethnicity and SES. For example, several studies using "real-world" samples have found Black children more likely to be diagnosed with oppositional defiant disorder than White children and White children more likely to be diagnosed with ADHD than Black children.[27-29] These differences in diagnostic practices may have long-term consequences, related to the negative associations with having a DBD as opposed to less-stigmatized diagnoses (e.g., adjustment disorder, autism, ADHD), that disproportionally affect minority children.[30]

Key decisional dilemmas for this review include determining the most effective treatments (while weighing benefits and harms) for DBDs that include various psychosocial interventions, pharmacotherapy, or a combination of the two; determining if any patient, clinical, treatment characteristics or treatment history impact the benefits and harms of treatment; and determining the presence and extent of disparities in the diagnosis and treatment of DBDs.

This systematic review is an update of the 2015 AHRQ review with the additional investigation on how any potential harms of various therapies may differ based on patient, clinical, and treatment characteristics, as well as patient treatment history. Preliminary searches identified multiple clinical trials,[31,32] systematic reviews[33,34] and meta-analyses[35,36] published

since the 2015 AHRQ review on treatments for DBDs. However, most new studies focused on single psychosocial interventions with less evidence for combined psychosocial interventions with pharmacotherapy or pharmacotherapy alone, which is consistent with the findings from the AHRQ review. Updating the evidence in these areas will facilitate decision making around the primary decisional dilemmas and will help inform an update of guidelines on this topic.

Controversies and challenges with this review include: (1) not all children who exhibit disruptive behaviors that would meet criteria for DBD are diagnosed with a DBD and may be missed in searches; (2) children and adolescents with DBDs often have other mental or behavioral health co-occurring conditions (e.g., ADHD, mood disorders, autism, below average intelligence) that may predispose to disruptive behaviors, making it difficult to parse out the effects of treatment on DBDs;[37-40] (3) disparities in diagnosis of DBD based on race, socioeconomic status (SES), or other factors;[41-43] (4) few randomized trials for some interventions;[25] (5) concern for publication bias and small study effects in meta-analyses of psychological interventions;[44,45] (6) concern that benefits of psychosocial interventions are limited to the short-term;[44] and (7) heterogeneity of treatment effects.[44]

Draft Key and Contextual Questions

Key Question 1. In children under 18 years of age diagnosed with disruptive behaviors, are psychosocial interventions more effective for improving short-term and long-term psychosocial outcomes compared to no treatment or other psychosocial interventions?

Key Question 2. In children under 18 years of age diagnosed with disruptive behaviors, are pharmacologic interventions including alpha-agonists, anticonvulsants, beta-blockers, central nervous system stimulants, first-generation antipsychotics, second-generation (atypical) antipsychotics, and selective serotonin reuptake inhibitors more effective for improving short-term and long-term psychosocial outcomes compared to placebo or other pharmacologic interventions?

Key Question 3. In children under 18 years of age diagnosed with disruptive behaviors, what is the relative effectiveness of psychosocial interventions compared with pharmacologic interventions for improving short-term and long-term psychosocial outcomes?

Key Question 4. In children under 18 years of age diagnosed with disruptive behaviors, are combined psychosocial and pharmacologic interventions more effective for improving short-term and long-term psychosocial outcomes compared to individual interventions?

Key Question 5. What are the harms associated with treating children under 18 years of age for disruptive behaviors with either psychosocial, pharmacologic interventions or combined interventions?

Key Question 6:

Key Question 6a. Do interventions for disruptive behaviors vary in effectiveness and harms based on patient characteristics, including sex, age, racial/ethnic minority, developmental status or delays, family history of disruptive behavior disorders or other mental health disorders, prenatal use of alcohol and drugs (specifically methamphetamine), history of trauma or Adverse Childhood Experiences (ACEs), parental ACEs, access to social supports (neighborhood assets, family social support, worship community, etc.), personal and family beliefs about mental health (e.g. stigma around mental health), socioeconomic status or other social determinants of health?

Key Question 6b. Do interventions for disruptive behaviors vary in effectiveness and harms based on clinical characteristics or manifestations of the disorder, including specific disruptive behavior or specific disruptive behavior disorder (e.g., oppositional defiant disorder, conduct disorder), co-occurring behavioral disorders (e.g., attention deficit hyperactivity disorder or substance abuse), related personality traits and symptom clusters, presence of non-behavioral or psychiatric comorbidities, age of onset, and duration?

Key Question 6c. Do interventions for disruptive behaviors vary in effectiveness and harms based on treatment history of the patient?

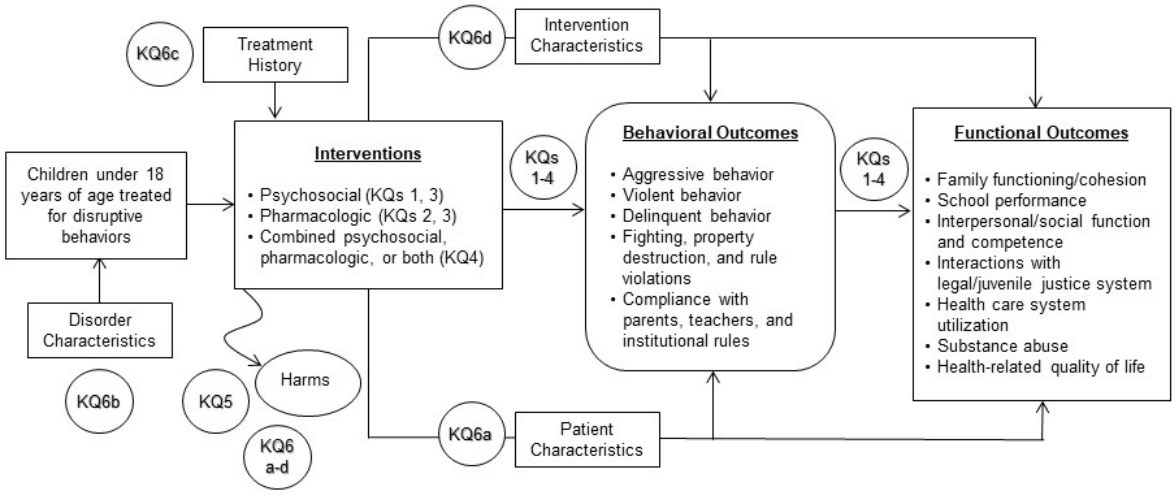
Key Question 6d. Do interventions for disruptive behaviors vary in effectiveness and harms based on characteristics of treatment, including setting, duration, delivery, timing, and dose?

Contextual Question 1. What are the disparities in the diagnosis of disruptive behavior disorders (based on characteristics such as gender, race/ethnicity, socioeconomic status, other social determinants of health, or other factors) in children and adolescents?

Contextual Question 2. What are the disparities in the treatment of disruptive behaviors or disruptive behavior disorders (based on characteristics such as gender, race/ethnicity, socioeconomic status, other social determinants of health, or other factors) in children and adolescents?

Draft Analytic Framework

Figure 1. Draft Analytic Framework for Psychosocial and Pharmacologic Interventions for Disruptive Behavior in Children and Adolescents[a]



The analytic framework illustrates how the populations, interventions, and outcomes relate to the Key Questions (KQ) in the review.

[a] Outcomes vary by KQ and are specified in Table 1.

Table 1. Draft PICOTS

PICOTS	Inclusion	Exclusion
Population	**KQs 1-6.** Children under 18 years of age who are being treated for disruptive behavior or a disruptive behavior disorder (KQs 1-6)	- Asymptomatic children - At-risk children - Treatment of disruptive behavior secondary to other conditions (e.g., substance abuse, developmental delay, intellectual disability, pediatric bipolar disorder) - In the case of ADHD, exclude studies of ADHD-related disruptive behaviors but included studies of non–ADHD-related disruptive behaviors in populations of children with ADHD if the children were identified as also having another DBD
Interventions	**KQs 1, 3-6.** Psychosocial interventions including: behavior management training - social skills training - cognitive behavioral therapy - functional behavioral interventions - parent training - dialectical training - psychotherapy - contingency management methods	- Preventive interventions for at-risk populations - Preventive interventions for caregiver health - Specialized diet or dietary supplements - Allied health interventions (e.g., speech, occupational, physical therapy)

	- motivational interviewing - equine-assisted psychotherapy **KQs 2-6.** Pharmacologic interventions that are FDA approved medications used on or off label, including the following class of drugs: - alpha-agonists - anticonvulsants - second-generation (i.e., atypical) antipsychotics - beta-adrenergic blocking agents (i.e., beta-blockers) - central nervous system stimulants - first-generation antipsychotics - selective serotonin reuptake inhibitors - mood stabilizers - antihistamines **KQs 4-6.** Combined psychosocial and pharmacologic interventions included for KQs 1-3.	- CAM interventions (e.g., acupuncture, herbal remedies) - Exercise programs - Massage, chiropractic care - Horse-back riding - Invasive medical interventions (e.g., surgery, deep brain stimulation)
Comparators	- Alternative psychosocial or pharmacologic interventions - Inactive treatment, including waitlist control, other active treatments, and placebo	No comparison group, excluded interventions
Outcomes	**KQs 1-4, 6.** Behavioral outcomes: - Aggressive behavior - Violent behavior - Delinquent behavior - Fighting, property destruction, and rule violations - Compliance with parents, teachers, and institutional rules - Affective or mood elements of DBD - Patient-reported outcomes, especially around trauma, PTSD, etc. **KQs 1-4, 6.** Functional outcomes: - Family functioning/cohesion - School performance/attendance - Interpersonal/social function and competence/need for special accommodations - Interactions with legal/juvenile justice systems - Health care system utilization - Substance abuse - Logistical family outcomes (days of work lost, etc.) - Health related quality of life **KQ 5.** Adverse effects/harms: - Metabolic effects: weight gain, hyperglycemia and diabetes, hyperlipidemia - Extrapyramidal effects: parkinsonism, acute dystonia, akathisia, tardive dyskinesia - Cardiac adverse effects: prolonged QT/arrhythmias, hypotension, cardiomyopathy - Prolactin-related effects - Neutropenia as a potential adverse effect of atypical antipsychotics. - Allergic reaction - Sleep disruption - Sudden death - Suicide - Over-medication or inappropriate medication	

	- Negative effects on family dynamics - Stigma - Harms/barriers to utilization of care related to psychosocial interventions (e.g., time investment, limited access to trained providers, and lower acceptability based on a misperception that family-focused psychosocial interventions carry implicit judgements about the quality of their parenting). - Other harms, as reported	
Timing	**KQs 1-6.** Any length of follow-up	
Setting	**KQs 1-6.** Clinical setting, including medical or psychosocial care that is delivered to individuals by clinical professionals, as well as individually focused programs to which clinicians refer their patients; may include classroom settings when intervention is directed to treat disruptive behavior(s) in a specific child (not the whole class) as part of that child's treatment plan	Exclude school wide or system wide settings (e.g., juvenile justice system) wherein interventions are targeted more widely
Study Design	Randomized controlled trials, nonrandomized controlled trials, and observational studies. Published in English on or after 1994.	Published before 1994

Abbreviations

ACE	Adverse Childhood Experiences
ADHD	Attention Deficit Hyperactivity Disorder
AHRQ	Agency for Healthcare Research and Quality
CAM	Complementary and Alternative Medicine
CQ	Contextual Question
DBD	Disruptive Behavior Disorder
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th edition
FDA	Food and Drug Administration
KI	Key Informant
KQ	Key Question
SES	Socioeconomic Status
ODD	Oppositional Defiant Disorder
PICOTS	Population, Intervention, Comparator, Outcome, Timing, Setting
PTSD	Posttraumatic Stress Disorder

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