Most medication trials specifically exclude children with ID/IDD, as opposed to including them and reporting any differential responses based on the presence and severity of ID/IDD. Although a medication's effects may be influenced by medical and neurological disorders associated with ID, there continues to be no clear evidence that ID/IDD itself changes the mechanism of action of psychotropic medications. Children with ID/IDD may be more sensitive to side effects of medication and thus conservative dosing is generally recommended; although this may reflect shifts in dose-response as opposed to changes in the mechanism of action of a medication. In selecting a medication, clinicians should consider the evidence base for psychopharmacology in youth with ID/IDD and consult the literature on children with typical development when there is a lack of evidence for guidance.

Irritability and Aggression

Multiple studies in youth with ID/IDD have shown risperidone to improve symptoms of irritability and aggression as well as additional problem behaviors associated with conduct disorder (CD) and oppositional defiant disorder (ODD).[70-72,74[rct]] The positive findings usually started within 2 weeks of initiation and were sustained in 2 open-label, 48-week extension studies.[73,75[ob]] In the risperidone studies, the most common side effects were headache and somnolence. The extrapyramidal symptom profile of the medication group was comparable to placebo, and no changes were detected on electrocardiography. However, the medication group experienced more weight gain and had asymptomatic increases in prolactin. Descriptions of concurrent behavioral therapy were limited to whether it was allowed[70,71] or not allowed[71] for the duration of the study. Although these studies indicate that risperidone can improve irritability, aggression, and other behaviors associated with behavior disorders in children and adolescents with ID/IDD, because of its side effect profile risperidone is best considered after assessments of whether potential contributors to irritability and aggression could be addressed by nonpharmacological means.

Hyperactivity and Inattention

Stimulants. Guidelines on the pharmacologic management of ADHD for children with typical development recommend methylphenidate (MPH) as the first line agent[86]; however, most medication trials of methylphenidate exclude children with ID/IDD. Two RCTs of MPH in children with ID/IDD have been performed (N = 122[77]; N = 24[76]), the larger of which found methylphenidate to be effective in about 40% of children with ID/IDD and an *ICD-10* diagnosis of hyperkinetic disorder, with an effect size of 0.39 to 0.52.[74[rct]] This effect size is consistent with that in the other RCT in youths with ID[76[rct]], but is lower than the effect size reported in studies of typically developing children (eg, the Multimodal Treatment of Attention Deficit Hyperactivity Disorder Study (MTA), which reported an effect size of 0.8−0.9).[87[rct]] The adverse effects experienced by children with ID/IDD in these RCTs were similar to those observed in children with typical development with ADHD, primarily appetite suppression and sleep problems.[76,77,] The study by Simonoff *et al.*[77] did not find the efficacy of MPH to be moderated by level of ID, the presence or absence of autistic symptoms, or the severity of ADHD symptoms. These studies suggest that despite a lower effect size in children with ID versus children with typical development, MPH can be considered in children with ADHD and ID/IDD regardless of severity of ID/IDD or ADHD or presence of ASD.

Atypical Antipsychotics. Two large RCTs of risperidone that targeted irritability and aggression in children with ID/IDD and disruptive behavior disorders (DBDs) also reported improvements in hyperactivity as a secondary outcome.[72,74[rct]] These trials permitted children with co-occurring ADHD to continue their stimulant medication. A post hoc analysis combining these studies and selecting the patients with ADHD (in addition to ID and DBD) suggested that the addition of risperidone to a stimulant resulted in better control of hyperactivity than was achieved with stimulant treatment alone, without causing an increase in adverse events.[78[rct]] In a comparison study of risperidone and MPH for treatment of ADHD in children 6 to 16 years of age, Filho *et al.*[79[rct]] found both medications to reduce inattention and hyperactivity, in addition to ODD symptoms, with more pronounced effects for risperidone. Despite the potential efficacy of risperidone for the treatment of ADHD, due to risperidone's side effect profile, MPH remains the first-line agent.

Other Agents. A single study reported improvement in ADHD symptoms in children with ID/IDD taking an α-2 agonist, clonidine.[80[rct]] It is reasonable to assume that other α-2 agonists, such as guanfacine, could be similarly efficacious, although there are no trials of guanfacine in more than 10 children with ID/IDD. Potential side effects with α-2 agonists of depression, sleep disturbance, sedation, cardiac disturbances, and cognitive dulling should be taken into consideration.[1]

Anxiety and Depression. There have been no new studies since 1999 on pharmacologic treatment of anxiety or depressive disorders in children with ID/IDD, and the