

THERAPEUTICS INITIATIVE

Evidence Based Drug Therapy

Stimulants for ADHD in children: Revisited

This Letter reviews our previous publications and research on this topic and explores whether our publications have led to a change in prescribing of stimulants to children in BC. Despite concerns, stimulant drug treatment of childhood attention-deficit/hyperactivity disorder (ADHD) has increased worldwide over the last two decades.¹ The optimal management of this behavioral condition remains unknown and this is reflected in the wide variation of stimulant treatment by country, jurisdiction, income, race and ethnicity.^{1,2}

Children are particularly vulnerable to harms of long-term drug therapies and there should be a higher level of evidence of effectiveness to justify their use.

In May 2008 we published Letter #69 summarizing the evidence for using Central Nervous System (CNS) stimulants (methylphenidate, dextroamphetamine and mixed amphetamine salts) to treat ADHD in children.³ We concluded that CNS stimulants:

- improve teacher and parent ratings of hyperactive/impulsive disruptive behaviour;
- do not improve children's ratings of anxiety nor measures of academic achievement;
- do not change the incidence of delinquency or substance abuse at 3 years;
- decrease height and weight at 3 years;
- have not been studied for their long-term effects on standardized exams, quality of life, school completion, employment, longevity and future health.

We concluded that *"better benefit and harm evidence is necessary before long-term stimulant treatment in children can be recommended."* Cochrane systematic reviews of methylphenidate in 2015⁴ and amphetamines in 2016⁵ support our findings and conclusions.

In the March 2009 Letter #73 entitled "Atomoxetine for ADHD in Children and Adolescents" we recommended: *"Without long-term RCTs showing that atomoxetine improves educational achievement, school completion, employment and future health and in view of the risk of serious harm, use of atomoxetine should be limited to exceptional cases intolerant to other ADHD drugs."*⁶

British Columbia birth month study

We undertook a study of the utilization of stimulant drugs by BC children 6 to 12 years of age between December 1st 1997 and November 30th 2008. This study found that boys were 41% more likely and girls 77% more likely to be prescribed a stimulant medication if they were born between September and December than if they were born in January.⁷ Because of school enrolment rules, children born in January are the oldest and those born in December are the youngest in their class. We suggested that poor and disruptive behaviour among the youngest children in a classroom might be driving rates of ADHD diagnosis and treatment. This strongly suggests that teachers, parents and physicians are medicalizing a social rather than a medical problem. The study received global media attention and was reported in many media outlets both in Canada and abroad including Time Magazine, The Globe and Mail, and ABC News.⁸⁻¹⁰

TI birth month study on stimulant prescribing replicated in other countries

- Elder et al¹¹ found that the youngest children in fifth and eighth grades in the US are nearly twice as likely as their older classmates to be prescribed ADHD medications.
- Evans et al¹² found that US children born just after the school enrollment cutoff date had a significantly lower incidence of ADHD diagnosis and treatment than those children born before the cutoff date. They estimated that "roughly 20 percent of the 2.5 million children (in the US) who use ADHD stimulants have been misdiagnosed."



- An Icelandic study¹³ found that the relative age of children affects academic performance as well as a child's risk of being prescribed stimulants for ADHD.
- A Dutch study¹⁴ found that relatively younger students were more than two times as likely to be prescribed methylphenidate as their older classmates. That study also found that most Dutch physicians and teachers were not aware of an association between birth month and ADHD medication use.
- A German study¹⁵ found "robust evidence for school-entry age related misdiagnosis in Germany."

Has stimulant prescribing to children in British Columbia changed between 2000 and 2017?

Given the strong evidence for the birth month effect, we expected to see a reduction in prescribing of CNS stimulants to children in BC after 2012.

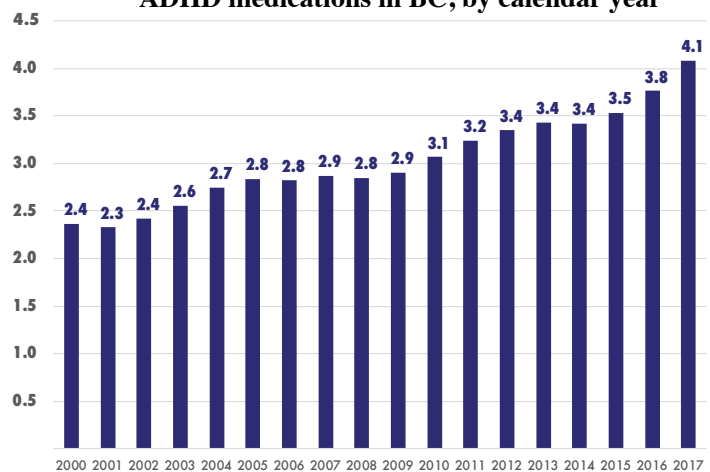
The Figure shows that the use of ADHD drugs in BC children between the ages of 6 to 12 grew between 2002 and 2005, remained steady for several years, then began to climb again in 2010. Over that 17 year period, the percent of BC children 6 to 12 years old receiving ADHD drugs increased from 2.4 to 4.1.

We were unable to find evidence that our 2012 BC birth month study findings had any impact on the overall rate of stimulant drug prescribing in BC children. Moreover, the recent increase in stimulant prescribing to BC children remains unexplained and is in need of further study.

Conclusions

- Whether the benefits of long-term CNS stimulants for ADHD in children outweigh the harms remains unknown.
- **There is convincing evidence that a proportion of boys and girls treated with stimulants in BC and around the world are simply the youngest in their class.**
- There is insufficient evidence to know whether our publications or research findings had an impact on the overall rate of stimulant drug prescribing in BC children.
- The recent increase in CNS stimulant prescribing in BC is unexplained and concerning.

Figure: Percent of 6-12 year old children receiving ADHD medications in BC, by calendar year



ERRATUM: We have removed cyclosporine eye drops (Restasis) from Table 2 in Therapeutics Letter 108 (September-October 2017). The Prescribe article referred to Ikervis, a 0.1% cyclosporine solution. Restasis is a 0.05% cyclosporine solution.

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