



Using SSRIs in Children & Youth

Katharina Manassis, MD, FRCPC

Professor Emerita, Dept. of Psychiatry, University of Toronto



Disclaimer

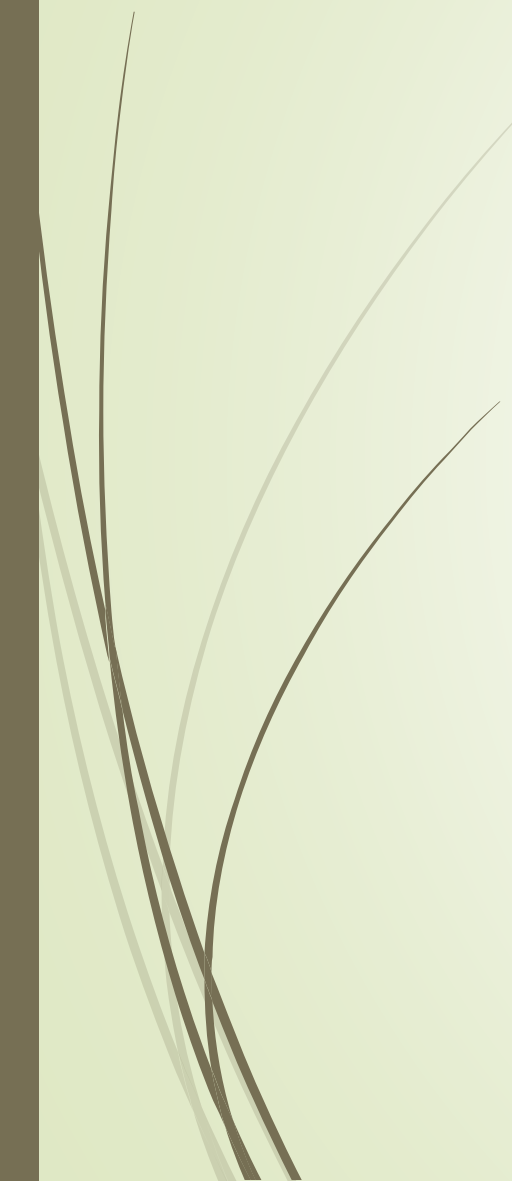
- Everything I am about to tell you is OFF-LABEL!

Conflicts

- I get book royalties from Routledge, Guilford, and Barron's
- I have done unrestricted talks for Shire & Janssen



Outline

- ▶ A brief history of SSRI use in North America
 - ▶ Key evidence by disorder
 - ▶ Use of SSRIs in kids—explaining it to families step by step
 - ▶ Your clinical challenges
- 



History



- ▶ Fluoxetine (Prozac) came on the market in 1990
- ▶ Prescribing in children lags about 5 years from adults (i.e., about 20 years experience in kids)
- ▶ There are 5 compounds in regular use now for anxiety, depression, and OCD (in order of arrival): fluoxetine, fluvoxamine, sertraline, paroxetine, and citalopram (escitalopram: active isomere)
- ▶ 2000-2005: reports of suicidal ideation linked to SSRIs especially age <18, and prescribing decreases (interestingly, with *increases* in suicidality in some countries linked to this change)
- ▶ 2006-2010: meta-analyses suggest some increased risk (about 4% vs. 2% baseline) especially in the initial weeks, sometimes linked to behavioral activation; highest risk in depressed (vs. anxious) populations (Bridge et al., 2007)



Today



- ▶ Several multi-site trials showing benefit alone or on combination with CBT
- ▶ Most physicians prescribe with careful monitoring in the early weeks despite warnings in the CPS and lack of Health Canada approval
- ▶ Monitoring sometimes has to occur via telephone/email reports as few have time for weekly appointments
- ▶ Families often need extensive discussion because of the warnings in the CPS and the lack of Health Canada approval; also some cultural preference for “natural” remedies and “chemicals” only as a last resort
- ▶ Given the 25 year history, sometimes other family members have experience with SSRIs which can increase/decrease reluctance



Key evidence by disorder: Anxiety

- RUPP Anxiety Trial: Fluvoxamine > placebo for non-OCD anxiety (moderate to severe)
- CAMS Trial: Sertraline + CBT > Sertraline OR CBT > Placebo for non-OCD anxiety (moderate to severe)
- Multiple smaller trials for all the other SSRIs for non-OCD anxiety
- Younger children and mildly affected children may respond to CBT/parent intervention alone
- Introverts respond best!



Key evidence by disorder: Depression

- ▶ TADS: Fluoxetine + CBT OR Fluoxetine alone > CBT OR Placebo for adolescent depression
- ▶ The monotherapies “catch up” by 6 months
- ▶ 1 full year of SSRI is better than a shorter course
- ▶ TORDIA (lack of response to one SSRI in depression): switch to another SSRI +CBT OR switch to venlafaxine + CBT > medication switches without CBT
- ▶ Multiple smaller trials for fluoxetine & 1 for citalopram for teen depression
- ▶ Venlafaxine XR is less activating than SSRIs so may be worth considering in depression with ADHD (75mg increments)



Key evidence by disorder: OCD

- ▶ POTS: Sertraline + CBT > Sertraline OR CBT > Placebo for OCD
- ▶ Smaller trials for other SSRIs
- ▶ POTS Jr: Younger children (5-8) may respond to CBT alone
- ▶ Augmentation with atypical antipsychotics (e.g., Abilify) is sometimes used, as SSRIs often result in only modest symptom reduction (30% YBOCS reduction = 'response')

- ▶ In all disorders, non-response to 2 SSRI's suggests a) optimizing CBT & other psychosocial interventions; b) trying SNRI or augmentation
- ▶ IMPACT study at CAMH (age 13+) can tell you what will or won't be tolerated based on liver enzyme genes



Evidence in other conditions

- ▶ Black & Uhde (smallish trial): Prozac > placebo for Selective Mutism
- ▶ Oerbeck et al.: Younger children with selective mutism (<7) often respond to CBT alone; only 33% do once they are 7+
- ▶ PTSD—several small trials; not very convincing; SSRIs may augment CBT effects so worth considering if debilitating symptoms
- ▶ Anxiety in ASD: small, open trials for citalopram & buspirone (anecdotally, I've had several young ones with 'transition tantrums' on fluoxetine)
- ▶ School avoidance: small trials suggest that combining medication and behavioral/cognitive behavioral treatment is best
- ▶ Better evidence for stimulants in ADHD + Anxiety (high risk activation)



Overall

- ▶ Combination treatments seem to work best
- ▶ CBT reduces relapse risk when medication stopped, and may be sufficient in some mildly affected or young children
- ▶ When increasing dose, anxiety typically responds first, then depression, and OCD last & partial response (so sometimes augment with atypicals in OCD)
- ▶ Behavioral activation is more common in children than adults across disorders and across specific medications (theoretically highest for fluoxetine & paroxetine; least for fluvoxamine but every child is different)
- ▶ Note: tricyclics have been shown NOT to work in depressed youth, so stick to SSRIs or venlafaxine

Talking to families

- What the medication does
- Why it is needed
- Why this particular medication
- What to expect (risks & benefits)
- How we will monitor
- What are the alternatives





What the medication does

- ▶ It increases the level of a brain chemical called serotonin that is important for regulating mood and controlling anxiety
- ▶ Nature recycles serotonin quite quickly
- ▶ The medication interferes with the recycling process, so that the person's serotonin stays active in the brain longer
- ▶ As the serotonin stays active longer, the person becomes less anxious and less depressed
- ▶ This process takes time, so the medication does not work right away
- ▶ It needs to be taken daily for several weeks (2 – 6 weeks) to get the benefit, once the dosage is right
- ▶ Curious adolescents sometimes like a more detailed drawing of synapse etc.



Why it is needed

- ▶ We only give these medications to people whose anxiety problems, mood problems, or OCD are interfering regularly in their lives
- ▶ For children, this usually means daily or almost daily impairment in school, at home (including sleep/eating problems), or socially
- ▶ Children can also fall behind their peers in development if they are impaired in one of these areas for a long time, which can leave them vulnerable to other mental health problems later (e.g., depression)
- ▶ We always look at a balance of possible risks versus possible benefits, both for medication and also for not medicating
- ▶ In my judgment, the possible benefits of medication outweigh the possible risks at this point in your child's life
- ▶ You will probably be told at the pharmacy that this is "off label" in children



Why this particular medication

- ▶ Fluoxetine: Best evidence for depression and also selective mutism; comes in a minty sweet liquid for kids who can't swallow pills; long half-life means you can create intermediate doses easily by adjusting how much is taken per week; no withdrawal reaction if you miss a dose so be careful
- ▶ Fluvoxamine: Least activating of the SSRIs, good evidence for anxiety
- ▶ Sertraline: Best evidence for OCD & good evidence for anxiety, not very activating, can tell if dose gets too high (loose stools)
- ▶ Citalopram: Some evidence for depression, most weight-neutral, least effect on glycemic index, fewest interactions with other medications, arrhythmia risk at doses >40mg (which are sometimes needed in OCD)
- ▶ Escitalopram: teens like it, but difficult to finely titrate dose in kids
- ▶ Paroxetine: short half-life (bid dose & withdrawal risk) so I avoid it
- ▶ "Family history of response": no real evidence for this, but it may augment placebo effect



The SSRI 'Spectra'

Activation

Paroxetine > Fluoxetine > Citalopram > Sertraline > Fluvoxamine

Half-Life

Fluoxetine > Citalopram & Sertraline & Fluvoxamine > Paroxetine

(5 days)

(about 24 hours)

(< 24 hours; CR longer)

What to expect (for child)

- ▶ You will take it daily with food, either at breakfast or dinner time
- ▶ It may upset your stomach the first few days, but that goes away
- ▶ Tell your parents if you feel unusually restless, can't sleep, or have any unusual thoughts
- ▶ The medication will take a few weeks to work, so be patient
- ▶ We'll start with a little bit, and I will see you every few weeks until we get the dose right





What to expect (parents)

- ▶ I give the same explanation as for the child, but also indicate:
 1. Need to call/email if insomnia, extreme restlessness, or suicidal thoughts (emphasizing that 96% of the time it's not an issue);
 2. Use ER if any safety concerns
 3. Headaches, rashes, weight gain (usually modest) are less common but possible
 4. In teens, there may be effects on sexual function

Feel free to call or email if you observe any changes you're not sure about.

Anxious kids are often suggestible, which is why I don't always mention all the side effects to the child.



How we will monitor

- ▶ We will do a baseline of your child's most distressing/impairing symptoms (frequency, intensity, duration, ability to manage/carry on—let's quantify!)
- ▶ We will get baseline from both child and parent, and teacher too if symptoms occur at school
- ▶ Some children report more verbally; others on questionnaire (MASC, CDI, YBOCS)
- ▶ Change is often gradual (like watching grass grow) and the people around the child may notice it first; good days & bad days are the norm, with good ones becoming more frequent over time
- ▶ We “start low and go slow” with dosage to minimize the risk of side effects
- ▶ Because 6 weeks is a long time to wait, I often adjust dose every 3 weeks (might go slightly high, but at least the child doesn't suffer for months)



Dosages



- ▶ Fluoxetine, citalopram, and paroxetine all go in 5-10mg increments; fluvoxamine and sertraline go in 25mg increments; escitalopram in 5mg; can reduce the size of the increment if history of adverse reactions (e.g., alternating 10mg/20mg fluoxetine capsules to create 15mg)
- ▶ Beware of accidental liquid Prozac overdose (4mg/mL, so 10mL=40mg)
- ▶ Starting dose is lower the smaller the child, but the final dose may be in the adult range (rapid metabolism, high volume of distribution) and there is no exact formula by body weight
- ▶ Some slow metabolizers respond at low doses; more common in Asians
- ▶ Preschoolers: 6mg of liquid fluoxetine, increase in 2mg increments
- ▶ School age: 10mg of fluoxetine or 25mg of sertraline to start
- ▶ Adolescents: 20mg fluoxetine or 50mg sertraline to start



NO thanks!

- ▶ What are you most concerned about? (explore & discuss: e.g., deciding based on one negative reaction in a close friend/relative vs. a large trial)
- ▶ Would you like to talk to your spouse about this (or come back with your spouse)?
- ▶ Would you like some more information?
- ▶ Let's think about the long term with/without using medication
- ▶ I don't have to write a prescription today—take some time to think about it and let's follow up in a few weeks
- ▶ We could try other interventions for a month or so, and then revisit the question of medication
- ▶ Take my card—you can always call back if things change



Will my child be on this forever, and what will that do to him/her?

- ▶ We never say 'forever' because there are new treatments being developed all the time, and some children do get better at using coping strategies with CBT and/or maturation
- ▶ Evidence suggests that depressed teens need to be on at least a year, and usually anxious kids do better with this too as it allows time to build confidence; OCD treatment is often longer term but up to 50% do come off medication eventually
- ▶ We will monitor at least every 6 months and determine if a dosage increase is needed (usually for growth) or if your child is doing well enough to decrease the dose and see how he/she handles this; gradual decreases (e.g. monthly) will ensure that the child is on the minimum needed
- ▶ I rarely taper children in the summer, as September is usually stressful
- ▶ Amotivation is the only long-term side effect documented, and it responds to dosage reduction or discontinuing medication



What are the alternatives?

- ▶ The best evidence is for CBT, although the benefits are limited in depression if medication is not also used
- ▶ There is some evidence for regular aerobic activity in preventing depression and regulating mood & anxiety symptoms (endorphin effect; 4x/week)
- ▶ Regular sleep patterns are helpful (review good sleep hygiene), and some also benefit from melatonin for this
- ▶ Avoiding caffeine (to reduce anxiety) and avoiding alcohol & street drugs helps
- ▶ There is no special diet that has been proven to work in any of these conditions
- ▶ When it comes to natural supplements: caveat emptor
- ▶ Do not mix St. John's Wort with SSRIs as the interaction can be dangerous (serotonin syndrome)



What are your clinical challenges?