a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA

BC Children's Hospital

Celecoxib versus placebo as an adjunct to treatment-as-usual in children and youth with obsessive-compulsive disorder: A single-site randomized quadruple-blind phase II study

The **A**djunctive **CE**lecoxib in childhood-onset **OCD** (ACE-OCD) study

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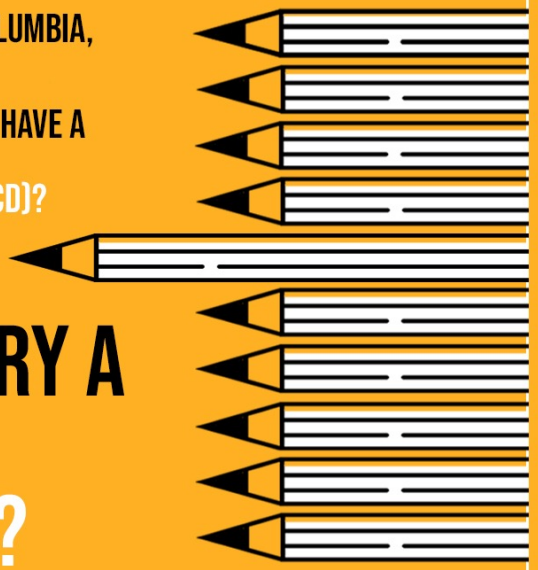
DO YOU LIVE IN BRITISH COLUMBIA, CANADA?

DOES YOUR CHILD OR TEEN HAVE A DIAGNOSIS OF OBSESSIVE-COMPULSIVE DISORDER (OCD)?

DO YOU WANT TO TRY A DIFFERENT APPROACH?



Contact us regarding a clinical trial of the non-steroidal anti-inflammatory celecoxib as an **add-on to usual treatment** in children and youth ages 7-18 years.

The Principle Investigator for this study is Dr. Evelyn Stewart, director of the Provincial OCD Program at BC Children's Hospital.

UBC BC Children's Hospital

Visit our website by scanning the QR code or contact us by email at aceocd@bcchr.ca or by phone at 604-875-2000 ext. 3068

https://www.bcchr.ca/POP/our-research/ace-ocd

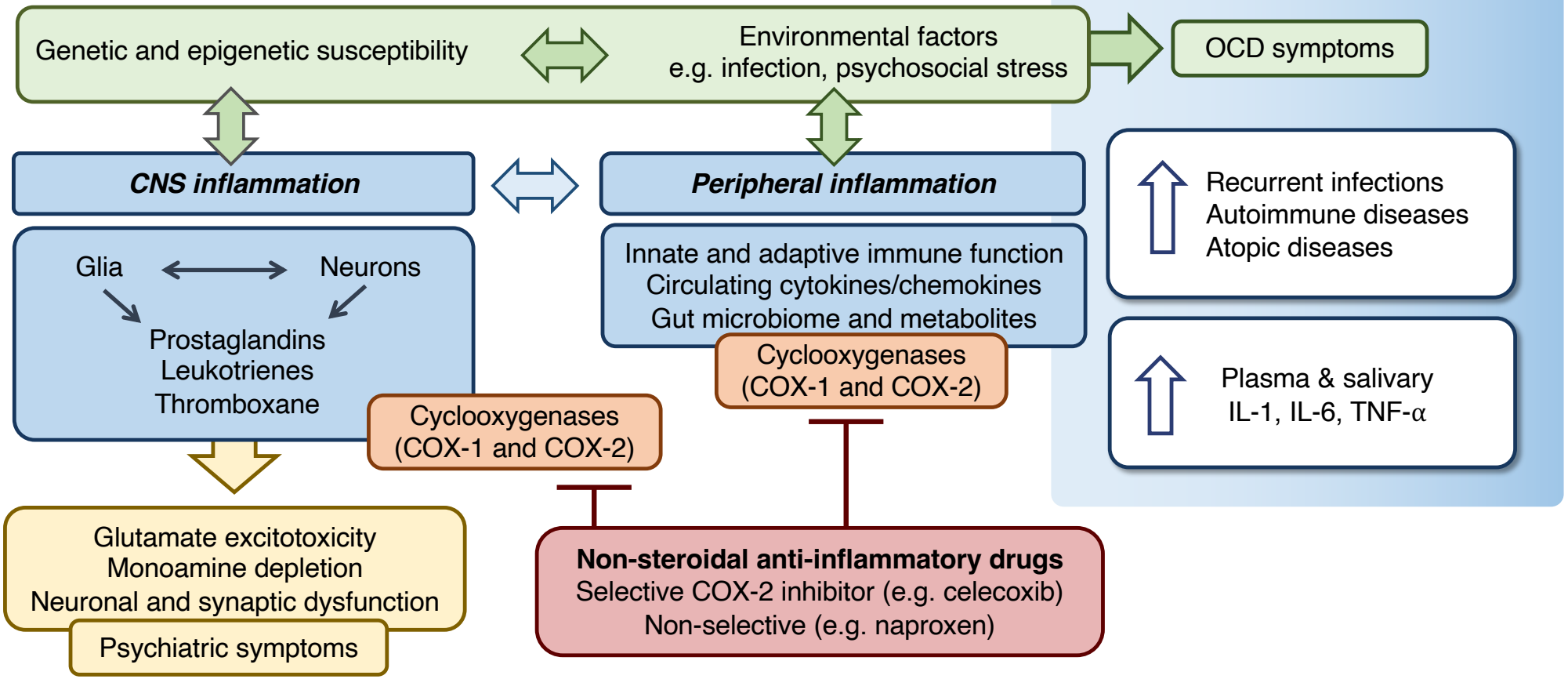
Objectives

1. **What is already known about OCD and inflammation?**
   To describe existing evidence informing the use of non-steroidal anti-inflammatory drugs (NSAIDs) in adults and children with OCD.

2. **Why are we doing this study?**
   To understand the rationale for evaluating the efficacy of adjunctive celecoxib in childhood-onset OCD, not restricted to PANS/PANDAS.

3. **What does the study involve?**
   To appreciate the objectives and design of the ACE-OCD study.

Inflammation in obsessive-compulsive disorder: Role of cyclooxygenase (COX) enzymes



Westwell-Roper, C. & Stewart, S. E. *Front Psych* **11**, 264 (2020)
Westwell-Roper, C. *et al. J Child Adolesc Psychopharmacol* 29:615 (2019).
Westwell-Roper, C *et al. J Psychosom Res* 2022. In press. https://doi.org/10.1016/j.jpsychores.2022.110743

Why celecoxib?

	Dosage	*Preparation*	*Consideration*
(1) Ibuprofen	10 mg/kg every 6–8 hours (maximum 600 mg/dose)	Tablet, chewable, capsules, or liquid.	Requires frequent dosing to maintain continuous anti-inflammatory action. Available OTC. Liquid and chewable preparations taste better than naproxen.
(2) Naproxen	10 mg/kg every 12 hours (maximum 500 mg/dose)	Tablets, capsules, or liquid.	Naproxen is a potent long-acting NSAID that only requires twice daily dosing. Generally tolerated by children. Liquid formulation available as prescription (250 mg/5 mL) but the taste is often intolerable.
(3) Sulindac	2–4 mg/kg·day every 12 hours; maximum 6 mg/kg·day; do not exceed 400 mg/day	Tablets; can be compounded into a suspension.	Sulindac is equal in potency to naproxen and is also long acting. It may have fewer GI side effects.
(4) Celecoxib	10–25 kg: 50 mg twice a day >25 kg: 100 mg twice a day	Capsules; can be compounded into a suspension.	Fewer GI side effects. Less potent than naproxen and sulindac but helpful if patient develops gastritis symptoms on other NSAIDs.

- Specific profile of enzyme inhibition with celecoxib may be beneficial
- Efficacy as adjunct in RCT for adult OCD and other psychiatric disorders
- Most RCT evidence across psychiatric disorders

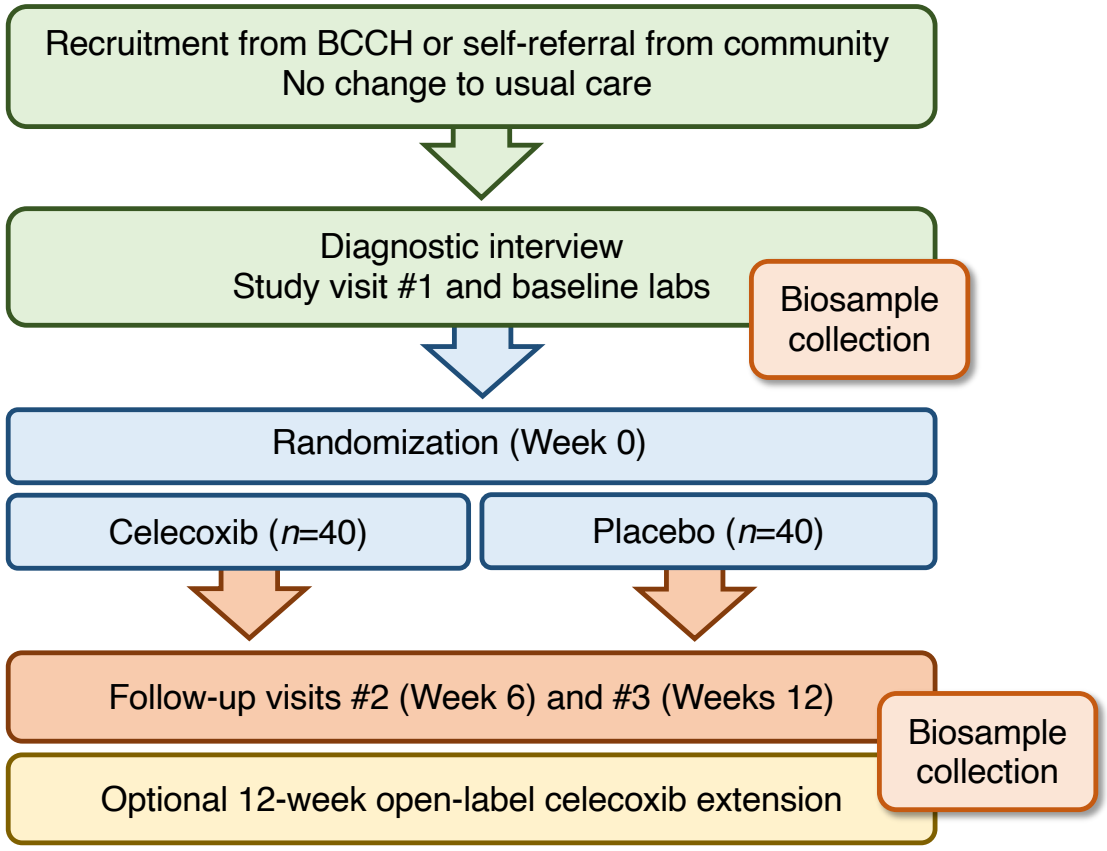
Frankovich *et al.* 2017. *J Child Adolesc Psychopharmacol* 27(7): 574-593.
Sethi, R. *et al. Front Psychiatry* **10,** 605 (2019).

Summary of rationale

- **Cyclooxygenase (COX) enzymes** oxidize arachidonic acid to prostaglandins, which modulate neuronal function and inflammation in the CNS.
- Pre-clinical studies and preliminary data in adults suggest that COX-2 inhibition can modulate **mood and anxiety symptoms** – possibly in specific **subgroups of individuals with OCD.**
- **Clinical practice guidelines** suggest **non-steroidal anti-inflammatory drugs** such as celecoxib as (a) third-line adjunctive therapy in adults with OCD and (b) in children with PANS/PANDAS, but there is limited empiric evidence guiding this approach in children and youth.
- There is good safety data for NSAIDs in children and youth with juvenile idiopathic arthritis, showing maximal response at **12 weeks** of treatment

Study Overview

Primary Objective: To determine the efficacy of the COX-2-selective inhibitor celecoxib as an adjunct to treatment-as-usual in children and youth aged 7-18 with moderate-to-severe OCD.



Key eligibility criteria:

- DSM-5 diagnosis of OCD based on prior clinician assessment and standardized diagnostic interview
- Moderate-to-severe symptoms
- No treatment changes in past 4 weeks or during study period

Primary outcome (12 weeks):
OCD severity (as measured by clinician-administered Children's Yale-Brown Obsessive Compulsive Scale) in the celecoxib compared to placebo arm, adjusted for baseline OCD severity

Secondary and other outcomes:
See Clinicaltrials.gov (NCT04673578)

Secondary Outcomes

1. **OCD severity after 6 weeks** of treatment in the celecoxib compared to placebo arm, adjusted for baseline OCD severity;
2. Difference in the proportion of participants achieving a **clinically meaningful response** (defined as a 25% reduction in the CY-BOCS score or CGI-I of 1 or 2 based on previous meta-analyses) after 6 and 12 weeks of treatment in the celecoxib compared to placebo arm;
3. Difference in the proportion of participants achieving **clinical remission (CY-BOCS≤14)** after 6 and 12 weeks of treatment in the celecoxib compared to placebo arm;
4. Mean **clinical global impression of severity (CGI-S)** after 6 and 12 weeks in the celecoxib compared to placebo arm, adjusted for baseline OCD severity
5. Mean **clinical global impression of improvement (CGI-I)** after 6 and 12 weeks in the celecoxib compared to placebo arm, adjusted for baseline OCD severity;
6. Difference between celecoxib and placebo arms in the proportion of participants reporting **adverse events** that are possibly, probably, or definitely related to the study intervention

Exploratory Outcomes

Associations between the following and primary/secondary outcomes:

1. **Demographic factors:** Age, gender, geographic ancestry
2. **General medical factors:** BMI percentile, comorbidities
3. **OCD-related factors:** Time since diagnosis, baseline treatment, baseline severity
4. Presence/severity of **PANS/PANDAS** symptoms or **tics** at any time point
5. **Participant/parent perspective questionnaire items:** Patient-reported outcome measures, perspectives on virtual study visits
6. Self- and parent-report CY-BOCS and Obsessive Compulsive Inventory – Child Version
7. Participant/clinician **treatment expectancy**

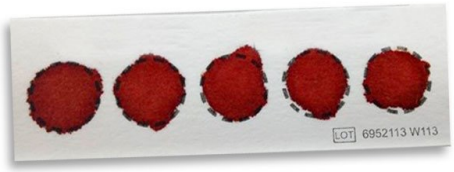
Biosample collection (optional for participants)

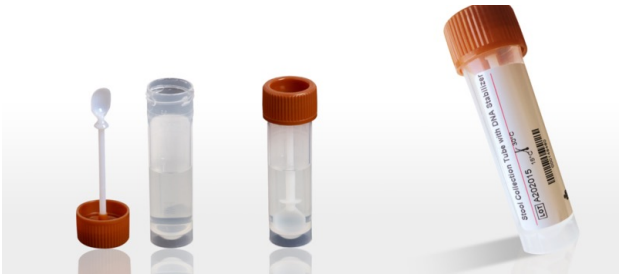
1. Blood
   - Blood spot – cytokines/chemokines
   - Plasma – cytokines/chemokines
   - Buffy coat – functional studies of PBMCs

2. Saliva – inflammatory markers, proteomics

3. Buccal swab – epigenetics

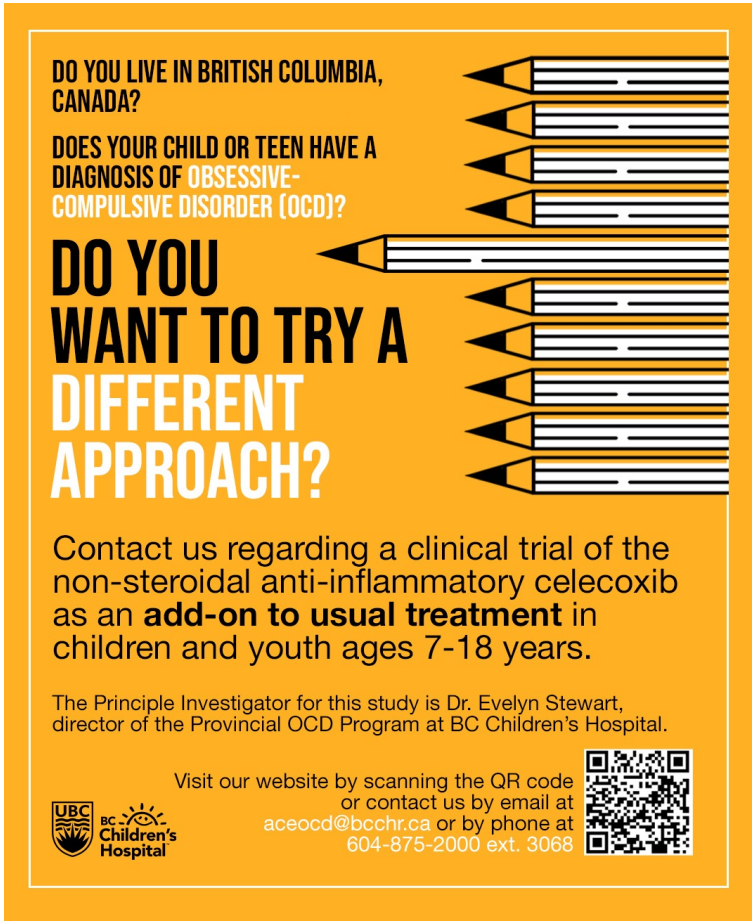
4. Stool – microbiome characterization





Current Status

- The **A**djunctive **CE**lecoxib in childhood-onset **OCD** (ACE-OCD) study will be the first to assess the efficacy and safety of adjunctive anti-inflammatory therapy in pediatric OCD.
- Open-label phase added following patient and family feedback.
- This study is currently open to recruitment (NCT04673578).



Acknowledgements

Stewart Lab
Evelyn Stewart
John Best
Robert Selles
Zainab Naqqash
Boyee Lin
Cynthia Lu
Antony Au
Kashish Dogra

Beasley Lab
Clare Beasley
Li Shao

Investigators/collaborators
Dean Elbe
Susan Baer
Megan MacFadden
Lori Tucker

BCCH CRSU
Peter Subrt
Jennifer Claydon

DSMB
Ran Goldman
Kristin Houghton
Jeffrey Bone
Kyle Williams

Delta Prescriptions Inc.
Michael Milman

BCCH Research Pharmacy
Erin Adams

BCCH Lab and BioBank
Veronica Chow
Vi Nguyen