Regional Academic Summit

Dr. Jessica Smith

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Speaker Disclosure

- No conflicts of interest
- I have received honoraria from Knight Therapeutics for doing menopause presentations for primary care providers.
- I do not have any relationships with any organizations that involve funded grants, clinical trials, advisory boards or drug/device patents.
- I do not have any other relationships or investments that have the potential to influence the content of this presentation.

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Objectives

By the end of this session, participants should be able to:

- Start ASA in patients at risk- don't miss the window of benefit!
- Identify medications that pose fetal risks and switch to safer alternatives.
- Educate patients on medication and lifestyle strategies for common pregnancy concerns.

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What is the primary consideration with medication safety in pregnancy?

- Risk/fear of congenital anomalies
- Baseline population risk of congenital anomalies is **2-4%** (chromosomal, genetic and structural)
  *This is why we need a Nuchal Translucency (NT) US even if patient declines genetic screening!
- Congenital heart defects > Limb defects > Chromosomal anomalies > GU > Neuro
- Key modifiers of baseline risk: advanced maternal age (AMA), consanguinity, pregestational and gestational DM, maternal obesity, environmental exposures

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ASA for Prevention of Preeclampsia

- ASPRE Trial from 2017- ASA 150mg PO taken nightly at bedtime starting at 11-14wks GA reduced the incidence of preterm preeclampsia by 62% (did not reduce term preeclampsia)

- SOGC 2022 Hypertensive Disorders of Pregnancy Guideline does not reach consensus on the optimal dose of ASA for our at-risk patients: 81mg PO qHS vs 162mg PO qHS

- Small risks of ante/intrapartum bleeding and increased postpartum bleeding, and the very rare (0.06%) absolute increased risk of neonatal IC hemorrhage after birth can be mitigated by having our patients stop ASA at 36 wks GA

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ASA for Prevention of Preeclampsia

- **SOGC Recommendation:**

For any patient identified as being at elevated risk of preeclampsia, need to strongly recommend starting ASA 81mg or
ASA 162mg PO qHS **prior** to 16wks GA (after 11 wks), until 36wks GA

This is often, unfortunately, the #1 thing that gets missed prior to referral to OB care, especially in patients without a PCP!

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ASA for Prevention of Preeclampsia

Box 2. Clinical risk factors for preeclampsia that can be identified in early pregnancy[a]

	High risk factors (any 1)	Moderate-risk factors (2 or more)
Pregnancy history	Prior preeclampsia	• Prior placental abruption • Prior stillbirth • Prior FGR
Demographics	Pre-pregnancy BMI >30 kg/m^2	Maternal age >40 y
Pre-existing medical conditions	• Chronic hypertension • Pre-gestational diabetes mellitus • Chronic kidney disease[b] • Systemic lupus erythematosus/antiphospholipid antibody syndrome[b]	
Current pregnancy	Assisted reproductive therapy	• Nulliparity • Multifetal pregnancy

Reproduced with permission from Magee LA, Brown MA, Hall DR, et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. Pregnancy Hypertens. 2021;27:148-69.[134] Source: modified from Bartsch et al.[47]

[a]Women are considered to be at increased risk of preeclampsia if they have at least 1 high-risk factor, or at least 2 moderate-risk factors.

[b]Listed as high-risk (rather than moderate risk as in Bartsch *et al*[47]).

BMI: body mass index; FGR: fetal growth rate.

SOGC Guideline No. 426: Hypertensive Disorders of Pregnancy: Diagnosis, Prediction, Prevention and Management, 2022

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ACEi & ARB

- Well-established teratogenic and fetotoxic effects, especially with exposure in T2 and T3, due to interference with kidney development and function
- RAS-inhibitor fetopathy:
  - Renal dysgenesis and neonatal renal failure
  - Oligohydramnios (which leads to pulmonary hypoplasia, skeletal deformations)
  - Skull hypoplasia
  - IUGR, risk of fetal or neonatal death

Chronic HTN, ACEis & ARBs

- Unclear if increased risk of congenital anomalies from exposure to ACEi or ARB in T1 once you adjust for confounders such as HTN and DM
- **HTN itself is teratogenic**- similar adverse effects from untreated HTN.
- Can keep patients on ACEi and ARB medications if they are well-controlled and/or for renal protection (if CKD) if they are trying to conceive, as long as we switch them to other agents once pregnancy is confirmed
- Otherwise, switch to a pregnancy-safe alternative and stabilize BP ahead of conception!
- Safe antihypertensives: Labetalol, Nifedipine, Methyldopa

SSRIs and SNRIs

- Depression and anxiety present a large disease burden in women, including pregnant patients
- Both remain under-diagnosed and especially under-treated for fear of adverse fetal outcomes, often a patient decision
  ***Perception of teratogenicity is much higher than true risk!**
- Un/under-treated depression in pregnancy carries many risks:
  - Miscarriage, Prematurity, Low birth weight, NICU admission
  - GHTN and preeclampsia
  - Operative Delivery, Postpartum hemorrhage
  - Increased risk of **PP depression-** can be life-threatening!

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SSRIs and SNRIs

- Large meta-analysis found no significant increase in major congenital anomalies and congenital heart defects with T1 SSRI exposure when the comparator was patients with a psychiatric diagnosis
- Antidepressants are similar in efficacy and side effect profiles
- Monotherapy at lowest effective dose is ideal

- First Line: Escitalopram, Citalopram, Fluoxetine, ***Sertraline**(*lowest passage into breast milk)
- Second line: Duloxetine, Venlafaxine, Fluvoxamine, Mirtazapine, Buproprion
- Third line: Quetiapine, Trazadone, ***Paroxetine**(*theoretically highest risk of anomalies and of PNAS- poor neonatal adaptation syndrome)

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SSRIs and SNRIs

Check out the amazing resources on **AskMasi.com**

-screening tools, decision flow chart, treatment algorithm charts ☺

First-Line Treatment Options for Depression, Generalized Anxiety Disorder, PTSD, OCD				
Medication	**sertraline* (Zoloft)**	**fluoxetine (Prozac)**	**citalopram (Celexa)**	**escitalopram (Cipralex)**
Starting dose	25 mg qAM (if sedating, change to qHS)	10 mg qAM	10 mg qAM	5 mg qAM
Titration Schedule	titrate by 25 mg, q 4-7 days as tolerated	titrate by 10 mg, q 4-7 days as tolerated	titrate by 10 mg, q 4-7 days as tolerated	titrate by 5 mg, q 4-7 days as tolerated
Usual target dose	200 mg	40 mg	40 mg	20 mg
Therepeutic range***	100-200 mg	40-60 mg	20-40 mg	10-20 mg
Maximum dose***	250 mg	80 mg	60 mg**	30 mg**
Individualized approach to titration	Slower titration (e.g., every 10-14 days) may be needed for patients who are antidepressant naïve or with significant anxiety about using medications. Starting at lower doses and titrating more frequently by smaller increments (compared to usual prescribing guidelines) minimizes side effects and can facilitate better adherence.			
*Lowest degree of passage into breast milk compared to other first-line antidepressants. **Side effects include QTc prolongation: Obtain baseline ECG at 40 mg citalopram/20 mg escitalopram; titrate by 10 mg citalopram/5 mg escitalopram q week and repeat ECG with each increase. Target QTC <460ms in women. ***Anxiety disorders generally require higher treatment doses. Dilutional effects may warrant higher doses in 3rd trimester.			Notes on domperidone: QTc-prolonging; monitor ECG if co-administering with antidepressant Abrupt discontinuation can precipitate psychiatric symptoms	

Phone Service



613-800-0188

Monday - Friday
9:00am - 4:00pm

Watch a short video about our phone service

1:20

If you have a question about managing your pregnant or postpartum patient's mental health concern, please call us.

Everyone who phones will speak with an Ask Masi team member and can be provided with resources and referral information for programs in the community.

Psychiatry Consult

Physicians and nurse practitioners can speak with a perinatal psychiatrist about a specific patient in real-time.
The perinatal psychiatrist will provide coaching and consultation on screening, assessing, diagnosing, and starting treatment for your patient.

You must have your patient's consent to share their information with us.
Prescribers can bill OHIP for this consultation call (Billing code K730).

Please note, Ask Masi is a provider consultation service, not a referral service.

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SSRIs and SNRIs

- KEY POINTS:
  - We **MUST** counsel on the importance of treating anxiety/depression and treat any patient who is willing (counselling +/- medication)!
  - If stable on an agent- **CONTINUE!**
  - If did well on an agent in the past- **RESTART!**
  - If not yet on anything and counselling not adequate and/or accessible, **START** patient on the safest med and up-titrate their dose to effect (often needs to increase with progressing trimesters and continue during lactation)

Preconception Counselling

- If you have a medically-complex patient who requires advice/optimization prior to trying to conceive, please feel free to:
  - Send them our way for a preconception consult to help optimize medications + counsel on physical and mental health
  - Send to Maternal-Fetal Medicine/High Risk Obstetrics in London if very complex (or we can refer on if needed)
  - Request that their **managing specialist dedicates an appointment to preconception counselling!**

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Hyperemesis Tips

- Counsel on lifestyle measures first
- Diclectin as first step: safe to take up to 8+ tabs/day
- If above is insufficient, best strategy= **POLYPHARMACY!** ☺

ADD:

- Dimenhydrinate 50mg PO or PR suppository q4-6h PRN
- Metoclopramide standing or PRN- 10mg PO q8h
- Antacid- OTC → H2 receptor antagonists →PPI!
  Reassure patient that these are completely safe!
- *Save Ondansetron refractory cases- still some controversy over risk of congenital malformations in T1 (paucity of data, no strong studies)

References

- SOGC Guideline No. 456: Prenatal Screening for Fetal Chromosomal Anomalies, 2024
- SOGC Guideline No. 426: Hypertensive Disorders of Pregnancy: Diagnosis, Prediction, Prevention and Management, 2022
- Research Letter: Optimal Timing and Aspirin Dose for the Prevention of Preeclampsia, *J Obstet Gynaecol Can 2022;44(11):1131-1132*
- MotheRisk Rounds; Use of Antidepressants in Pregnancy: Focus on Maternal Health, *J Obstet Gynaecol Can 2015;37(1):56–63*
- *AskMasi.com:* Clinical Toolkit
- SOGC Guideline No. 339: The Management of Nausea and Vomiting in Pregnancy, 2016

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EXTRA SLIDES

Folic Acid

- Folate-sensitive congenital anomalies: NTD, certain congenital heart and GU tract anomalies, orofacial clefts, limb reduction anomalies

- People trying to conceive should be on folic acid for 2-3 months prior to conception, and for at least 4-6 weeks postpartum (and ideally the entire duration of breast feeding)
  *needs to be taken with B12
  B12 and iron are standard in all prenatal vitamins

Folic Acid Risk Categories

Box 1. Identified risk factors for fetal neural tube defects or for low-folate status in pregnancy[12-14,50-54]

Personal or family history risk	• Neural tube defects:
	  ◦ Maternal or paternal family affected
	  ◦ Previous affected fetus for either parent
	  ◦ Affected child, sibling, or second-degree relative

Maternal medical or surgical existing conditions	• Medications: antiepileptic or other folate-inhibiting medications • Gastrointestinal conditions: malabsorption or inflammatory bowel disease; Crohn disease; active celiac disease; gastric bypass surgery; advanced liver disease • Diabetes: pre-gestational diabetes (type 1 or 2) • Maternal obesity: body mass index >30 kg/m^2 or pre-pregnancy weight ≥ 80 kg • Renal: kidney dialysis
Sociocultural maternal factors	• Low socio-economic or demographic status • For immigrant women, limited access to health care, and language or knowledge barriers • Poor adherence to oral medication (previous use of multivitamins during pregnancy) • Smoking • Alcohol use disorder • Non-prescription drug use or abuse • Poor or restricted diet (e.g., gluten-free)

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Folic Acid Dosing

Table 3. Evidence-based pre-conception folate and multivitamin supplementation dose[a]

Risk of folic acid–sensitive congenital anomalies	Supplementation with oral folate dose from pre-conception to 12 weeks gestation, mg	Oral vitamin B_{12} dosage, μg	Oral iron dose for routine prenatal care, mg[6,7]	Dietary intake of folate- and choline-rich foods	Maternal folate levels, nmol/L	
					RBC	Serum
HIGH Previous NTD history	4.0	2.6	16-20	yes	>907	>28–30
MODERATE History of another folate-sensitive anomaly	1.0	2.6	16-20	yes	>907	>28–30
MODERATE Complex risk due to medical, surgical, and/or lifestyle factors	1.0	2.6	16-20	yes	>907	>28–30
LOW	0.4	2.6	16-20	yes	>907	>28–30

[a]Without the clinical use of pre-conception maternal folate RBC or serum folate evaluation for determination of the supplementation folic acid dose, but with reference values for pregnant people.

NTD: neural tube defect; RBC: red blood cell.

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NSAIDs in Pregnancy

- ASA is the exception of course- need to clarify this to your patient and explain your rationale!
- We generally issue a blanket statement to patients to avoid all NSAIDs in pregnancy, for simplicity and patient adherence.
- Risks are timing/trimester-dependent, with highest risks after 20wks GA
- If NSAID use is required, non-selective NSAIDs (eg. ibuprofen, naproxen) are preferred over COX-2 selective inhibitors (eg. celecoxib) due to limited safety data.

NSAIDs in Pregnancy

1st Trimester	2nd Trimester <20wks	2nd Trimester >20wks	3rd Trimester	Lactation
Periconception: -increased risk of spontaneous abortion -Evidence of teratogenicity from early exposure is very conflicting across studies	-Short term use (few days) does not appear to pose a fetotoxic risk	-Prolonged use risks fetal renal dysfunction leading to oligohydramnios (associated risks) and possible PDA constriction *If use is required (eg severe pain), should limit to lowest effective dose for max 48 hours. -Ideally monitored by MD, with US monitoring of amniotic fluid level	***STRONGLY CONTRAINDICATED*** -Premature closure of PDA (seen in 25-50% of indomethacin-exposed late 2nd/3rd trimester fetuses) -Persistent pulmonary hypertension of newborn -Oligo from fetal renal impairment -Necrotizing enterocolitis -Intracranial hemorrhage	-Safe! -Low infant exposure in breast milk

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Cold and Sinus Meds

- Pseudoephedrine/phenylephrine/oxymetazoline are associated with increased risk of cardiac, limb, GI (gastroschisis) and ear birth defects with T1 exposure
  -no recommendation for or against in T2/T3
- Dextromethorphan (suppressant)-generally considered safe based on observational data/controlled study
- Guaifenesin (expectorant)– generally acceptable for short-term use, limited data
- Nasal congestion and rhinitis:
  -saline rinses
  -antihistamines (2nd generation preferred: cetirizine, loratadine)
  -intranasal corticosteroids

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ASA for Prevention of Preeclampsia

Table 5. Recommendations for preeclampsia prevention according to clinical risk

Prevention	Women at increased risk[a] of preeclampsia	All other women
Low-dose ASA	Low-dose ASA (81 or 162 mg/d) is recommended (strong, high), to be taken at bedtime (strong, moderate), preferably before 16 weeks (conditonal, moderate), and discontinued by 36 weeks (*conditional, low*)	Low-dose ASA is not recommended (*strong, moderate*)
Calcium	For women with low dietary intake of calcium (< 900 mg/d), oral calcium supplementation of at least 500 mg/d is suggested (*conditional, low*)	Same as for women at increased risk[a] of preeclampsia
Vitamin D	Vitamin D supplementation over and above Health Canada's recommendation for adults is not suggested for preeclampsia prevention (*conditional, moderate*)	Same as for women at increased risk[a] of preeclampsia
Exercise	Exercise is recommended for preeclampsia prevention (*strong, moderate*)	Same as for women at increased risk[a] of preeclampsia
Dietary advice	For women who are overweight or obese, dietary advice (reduced calories and food with a low glycemic index) and exercise are recommended (*conditional, moderate*)	—

[a]Increased risk has been most commonly identified by a personal or family history of an HDP or a chronic medical disease; an abnormal uterine artery Doppler before 24 weeks gestation; or, recently, the FMF algorithm. Some of these risk factors are listed in Box 2.

ASA: acetylsalicylic acid.

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