The Management of Inflammatory Bowel Disease *After* Conception

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Conflict of Interest Disclosure

(over the past 24 months)

Commercial or Non-Profit Interest	**Relationship**
CIHR	Salary support award
Takeda, Janssen	Speaker

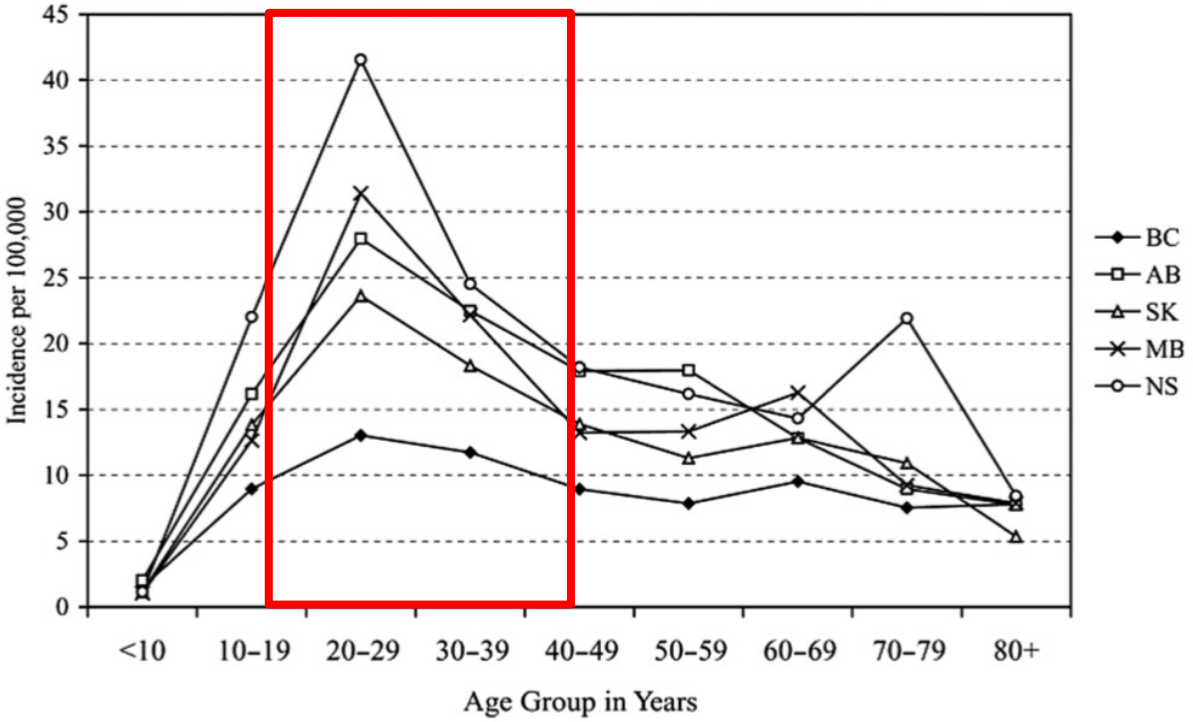
CanMEDS Roles Covered

X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
X	**Communicator** (as *Communicators*, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
	Collaborator (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
X	**Health Advocate** (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
X	**Scholar** (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

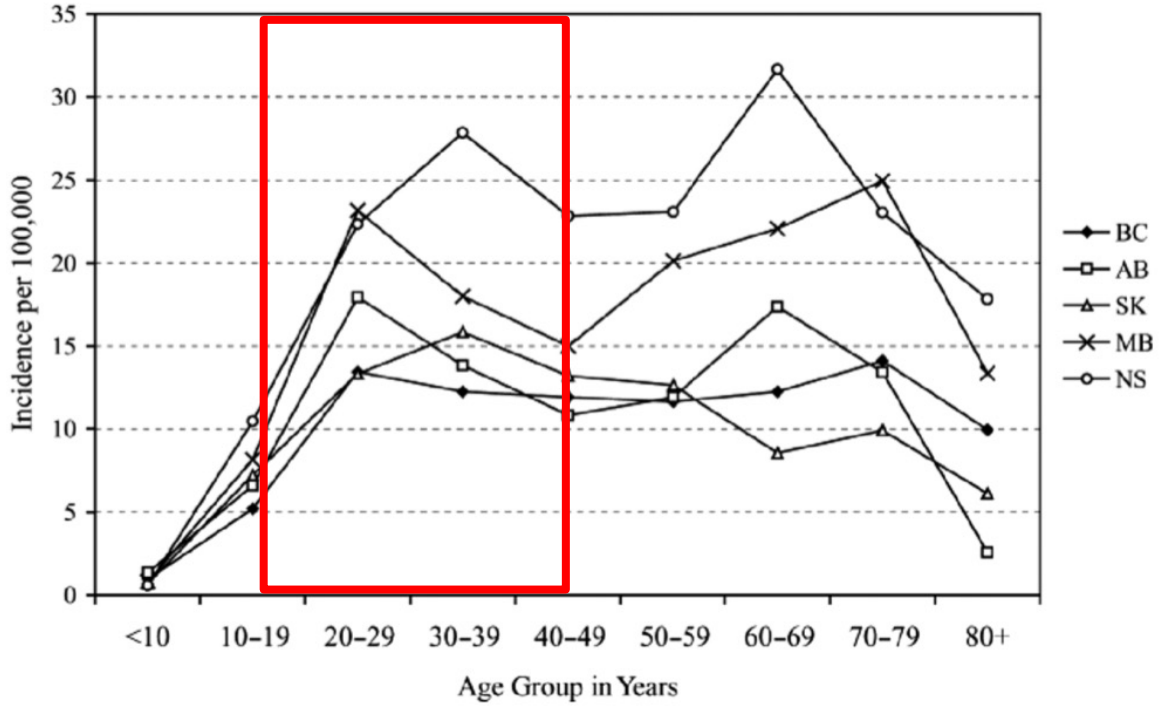
Objectives

- To discuss the “9 month” plan of the care of IBD during pregnancy
- To discuss the safety of advanced IBD therapies during pregnancy
- To discuss “flaring IBD” during pregnancy
- To discuss the role of disease monitoring during pregnancy

Epidemiology



Incidence by age in CD



Incidence by age in UC

1% of the Canadian population will have IBD by 2030

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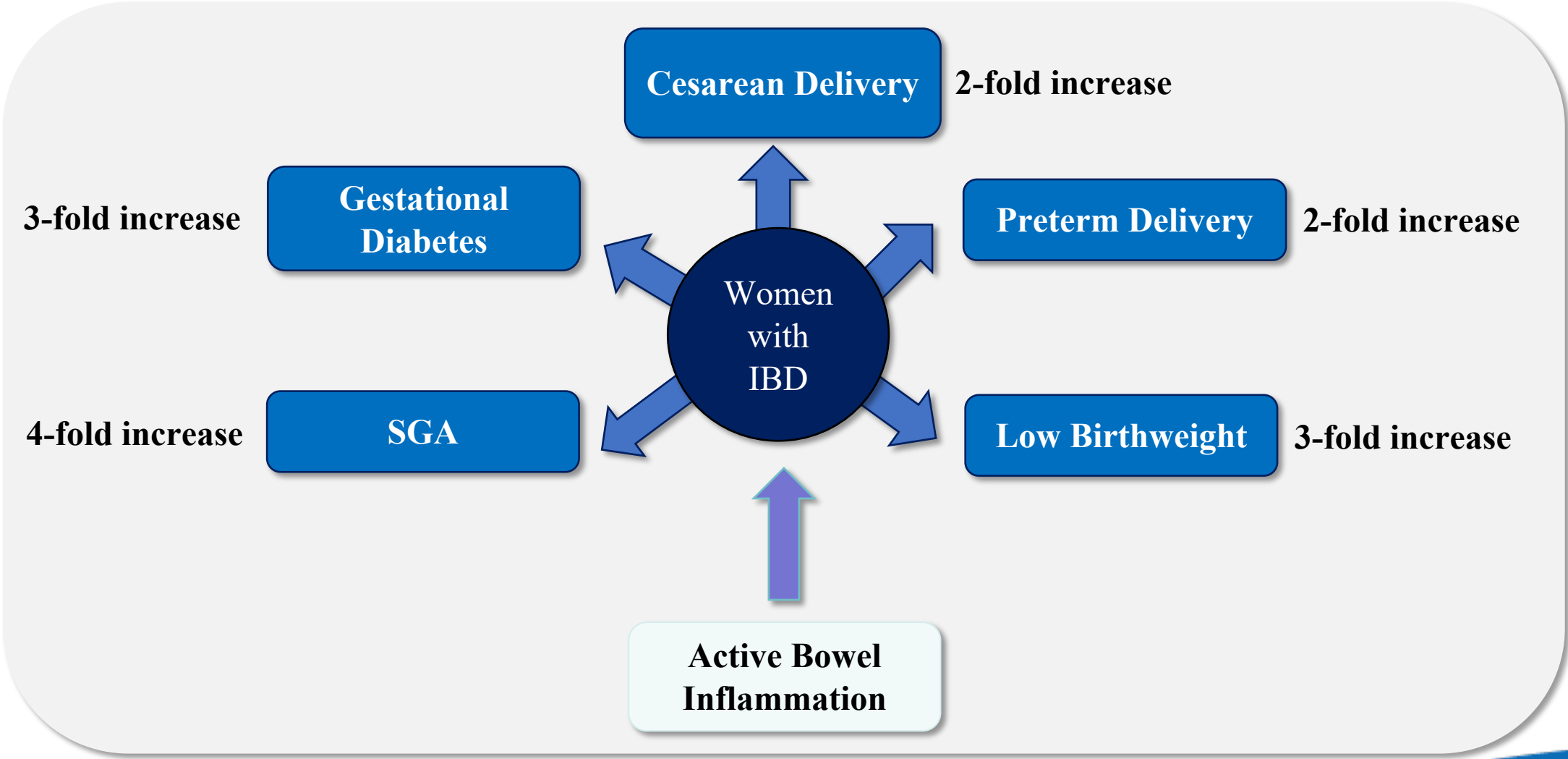
Kaplan et al. JCAG 2018.

Why Does It Matter?



SGA, small for gestational age

Leung K et al. IBDJ 2021; Varner et al. 2020

Before Conception

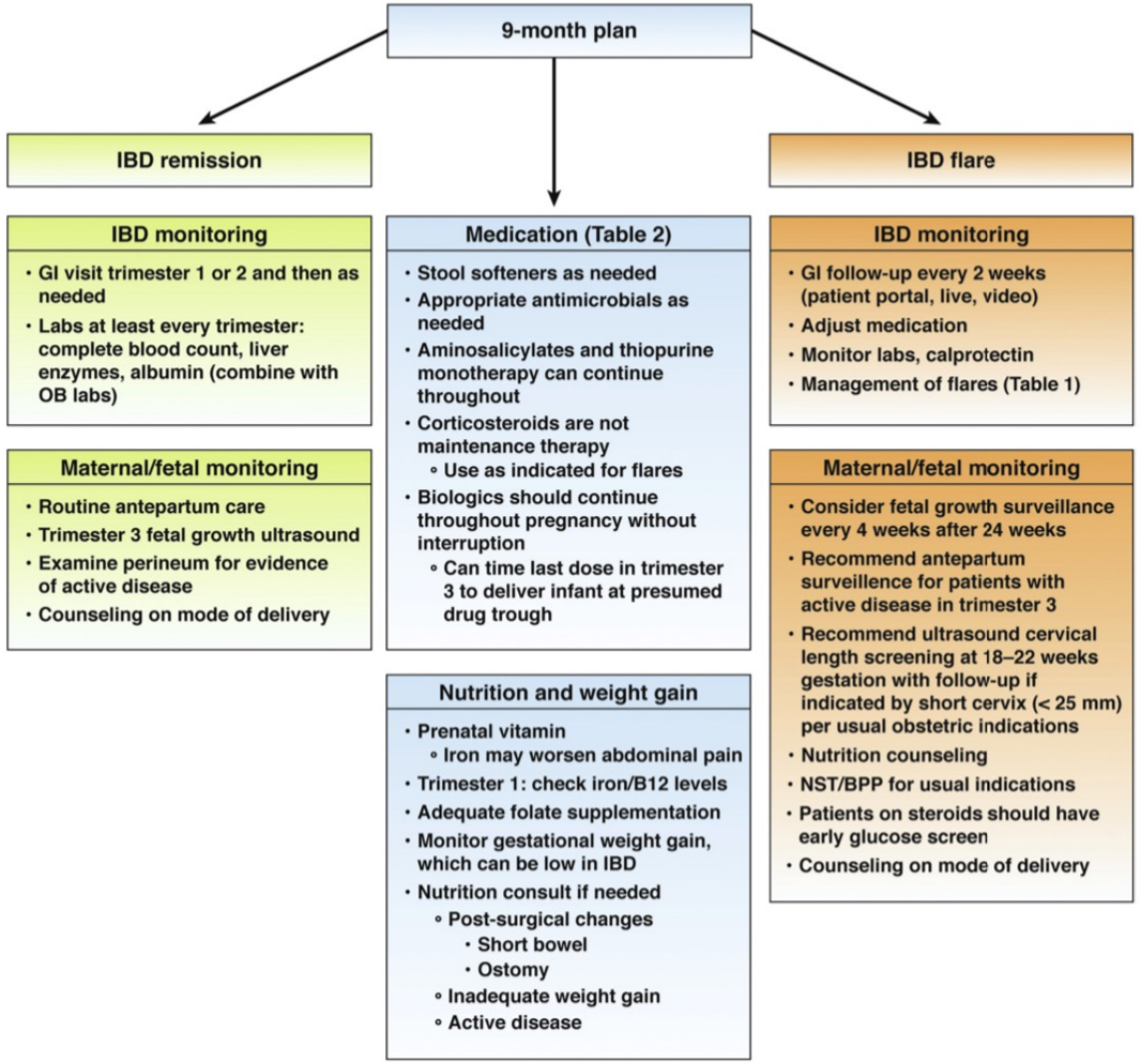
IBD remission at conception → 80% will remain in remission

Active IBD at conception → 2 in 3 will continue to have active IBD during pregnancy

Achieving disease remission in preconception for at least 3-6 months

Abhyankar et al. APT 2013

After Conception



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Mahadevan et al. Gastroenterology 2019

The Mount Sinai Hospital PC/PREG IBD Clinic

BIOLOGIC EXPOSED

Preconception
- **Drug level**
- **FCP**

1st Trimester
- **Drug level**
- **FCP**

2nd/3rd Trimester
- **Drug level**
- **FCP**

Preconception

Every 4 to 6 months
- Clinical
- CRP
- FCP
- Meds
- Investigations

Trimester 1

Trimester 2

Each Trimester
- Clinical
- CRP
- FCP
- Meds

Trimester 3

Delivery

Postpartum

Within 1 and 3 months
- Clinical
- CRP
- FCP
- Meds

At each visit, discuss adherence to therapy

If flaring, see as frequent as every 1-2 weeks

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Courtesy of Dr. Vivian Huang

5-Aminosalicylates

Safe

- Meta-analysis suggested no increased risk of
  - congenital malformations OR 1.16 (95% CI 0.76 – 1.77)
  - stillbirth OR 2.38 (95% CI 0.65 – 8.72)
  - spontaneous abortion OR 1.14 (95% CI 0.65 – 2.01)
  - preterm delivery OR 1.35 (95% CI 0.84 – 2.13)
  - low birth weight OR 0.93 (95% CI 0.46 – 1.85)

Rahimi et al Reprod Toxicol 2008

Immunomodulators: Thiopurines

Safe

- no differences in growth, # infections, allergies, adverse reactions to vaccinations, or chronic disease (at 1 yrs old)
  - prospective study 311 live births, 108 thiopurine exposed
- Yeaman et al. “Thiopurine Exposure During Pregnancy is Not Associated With Anemia in Infants Born to Mothers With IBD” CC 360; 2023
  - Prospective cohort study of 19 IBD patients on thiopurines, 50 IBD patients not on thiopurines, 37 controls
  - No risk of perinatal anemia or cytopenia as previously thought

Reminder: Methotrexate is contraindicated and should be stopped at least 3 months prior to conception

Kanis et al. Clin Gastro Hep 2017
Jharap et al. Gut 2014, Yeaman et al. CC 360; 2023

"Traditional" Biologics

Safe

- Anti-TNFα
  - infliximab (Remicade®, Inflectra®, Renflexis, Avsola)
  - adalimumab (Humira® and biosimilars)
  - golimumab (Simponi®)

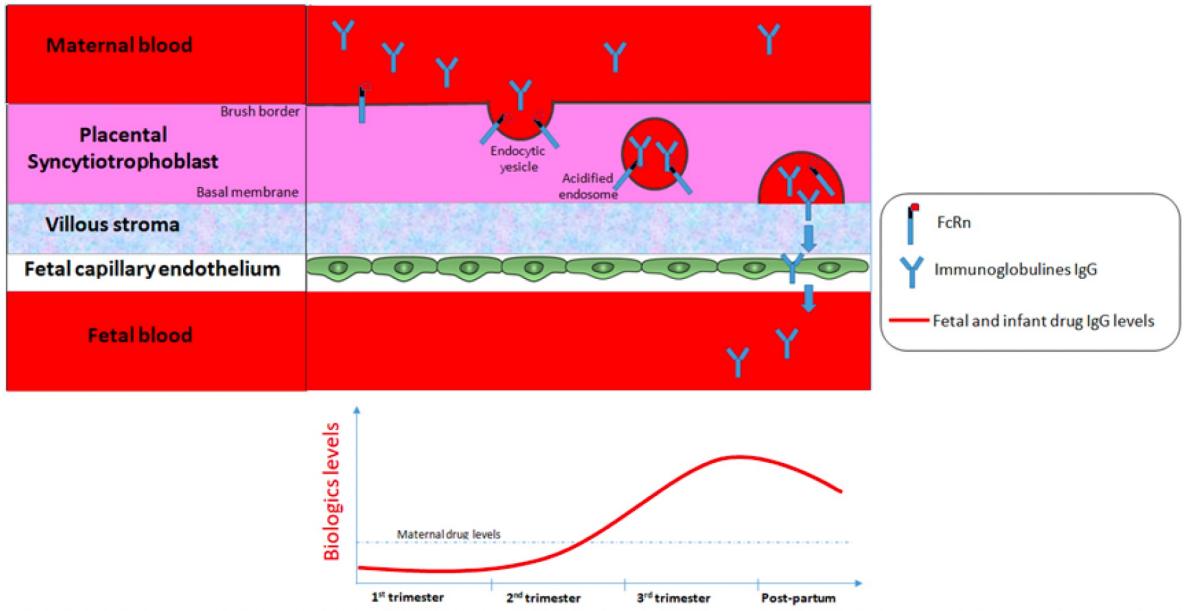
Safe

- Anti-integrin
  - vedolizumab (Entyvio®)

Safe

- Anti-IL-12/23 p40
  - ustekinumab (Stelara®)

- Monoclonal antibodies are IgG antibodies
  - cross placenta 2nd trimester



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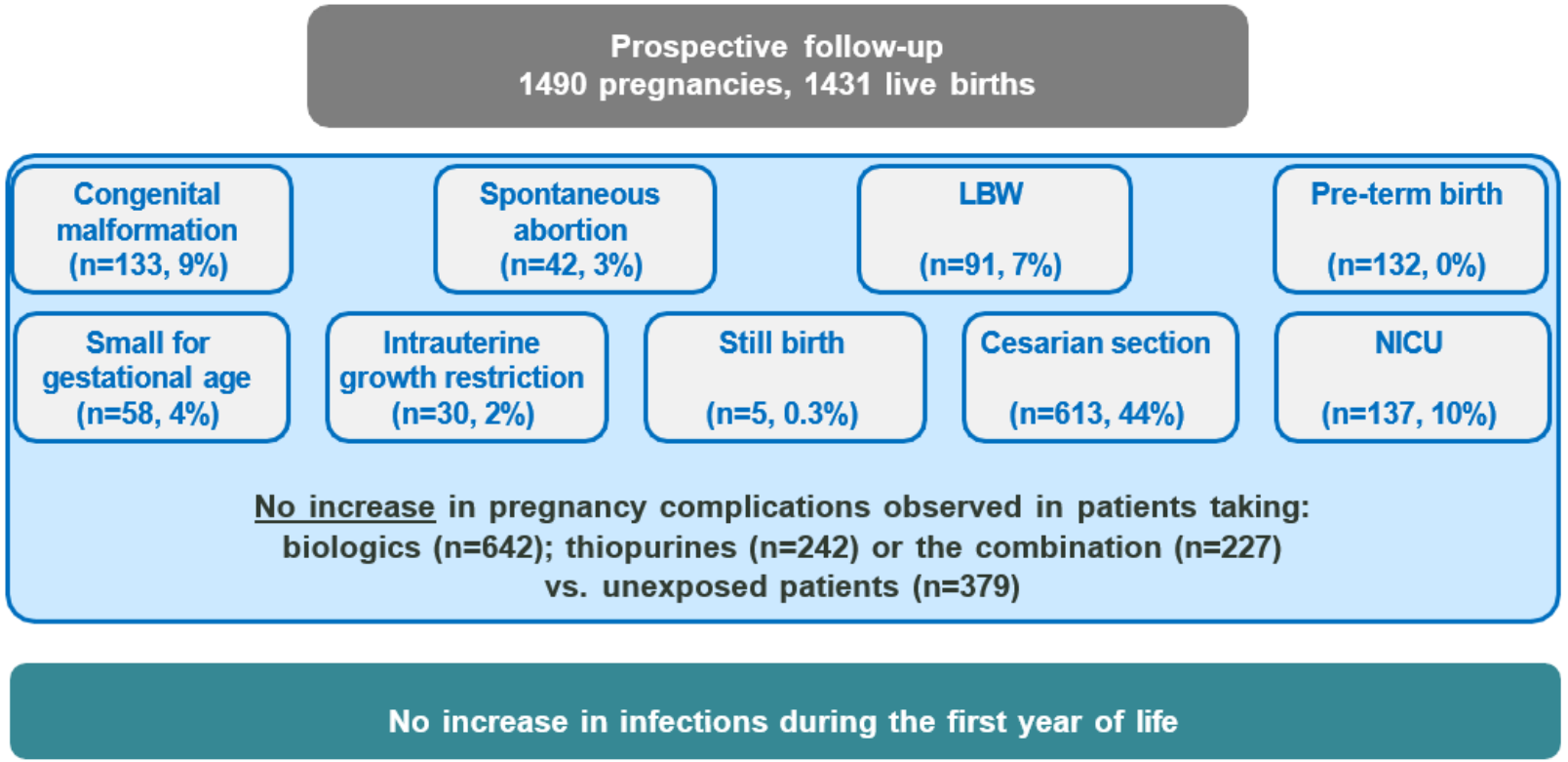
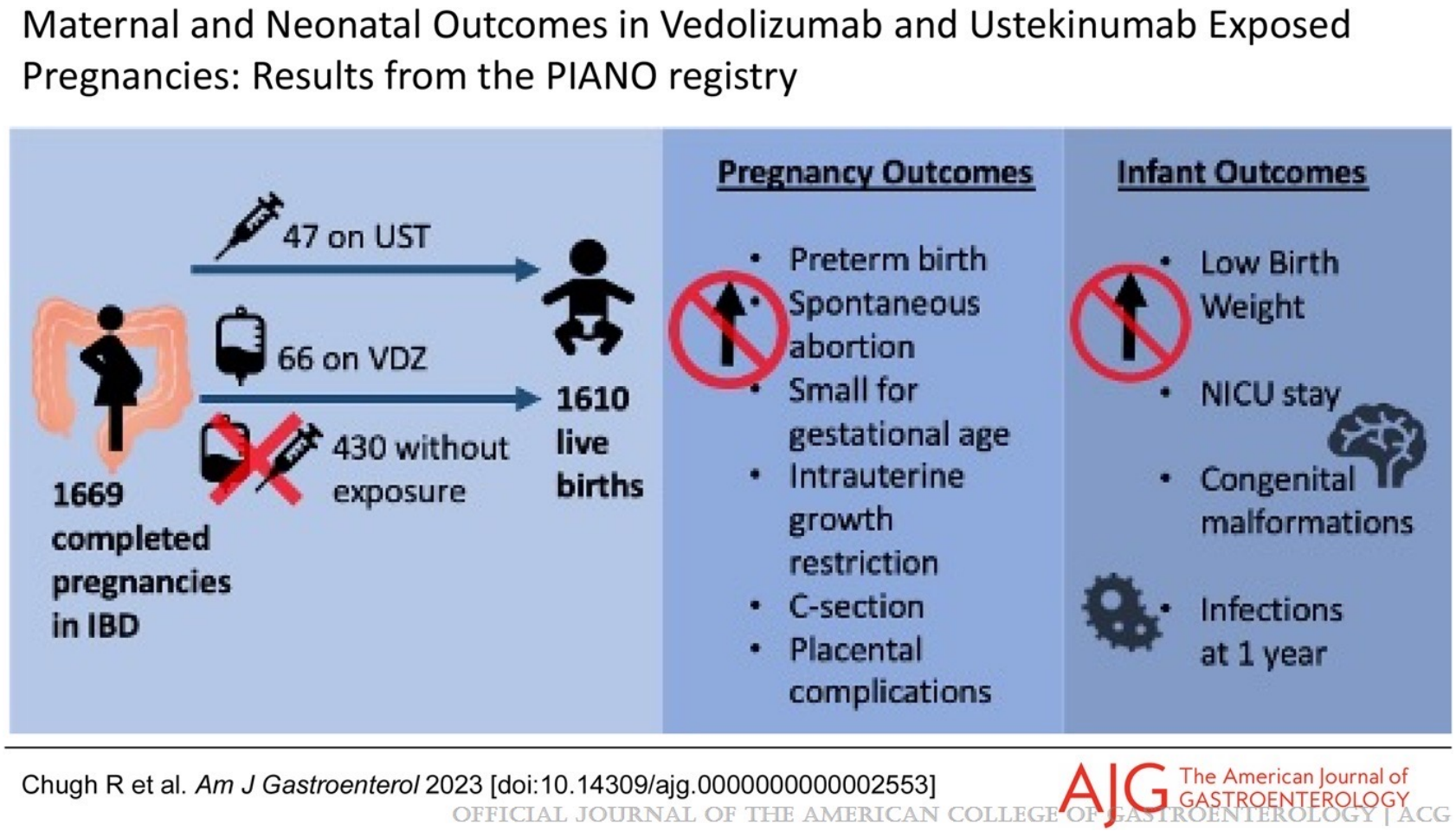
Mahadevan et al. Clin Gastro Hep 2012
Julsgaard et al. Gastroenterol 2016
Barrau et al. J Clin Med 2023

Pregnancy and Neonatal Outcomes After Fetal Exposure to Biologics and Thiopurines Among Women With Inflammatory Bowel Disease (PIANO)



Mahadevan et al. Gastroenterology 2021

Maternal and Neonatal Outcomes in Vedolizumab- and Ustekinumab-Exposed Pregnancies: Results From the PIANO Registry



Chugh R et al. *Am J Gastroenterol* 2023 [doi:10.14309/ajg.0000000000002553]

AJG The American Journal of GASTROENTEROLOGY
OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY | ACG

Safety of vedolizumab and ustekinumab compared with anti-TNF in pregnant women with inflammatory bowel disease

Pregnant women with IBD between 2014 and 2021

398 pregnancies exposed to **vedolizumab** were compared to 1,592 pregnancies exposed to anti-TNF

propensity score matching for maternal, IBD, and pregnancy characteristics

464 pregnancies exposed to **ustekinumab** were compared to 1,856 pregnancies exposed to anti-TNF

Pregnancy complications

No increased risk of:
- Abortion
- Caesarean section
- Stillbirth
- Preterm birth
- Small for gestational age

No increased risk of:
- Abortion
- Caesarean section
- Stillbirth
- Preterm birth

Increased risk of small for gestational age births (aHR 1.45; 95%CI: 1.03-2.06)

Children complications

No increased risk of:
- serious infections
- malignancies
- congenital abnormality

No increased risk of:
- serious infections
- malignancies
- congenital abnormality

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Meyer et al. CGH 2024

Anti-IL-23

Likely safe

- selectively blocks the p19 subunit of IL-23 receptor
- animal studies –
  - no adverse finding on female reproductive organs or on male fertility[1]
  - fetal losses and neonatal deaths when exposed to 13X to 99X (Risankizuamb) and 69X to 232X (Mirikizumab) greater than human exposure[1,2]
- clinical trials human pregnancy exposure → 72 RZB exposed pregnancies[1]
  - 30 (41.6%) live w/o congenital anomalies (CA);
  - 13 (18.1%) elective termination, 2 (2.8%) elective termination w/ fetal defects
  - 10 (13.9%) miscarriages

[1]Abbvie Medical Information August 2023
[2]Lilly Medical Information August 2023
[3]Kimball et al. JAMA Dermatol 2021;157(3):301-306 (PSOLAR)

JAK Inhibitors

STOP

- Small molecules cross placenta starting in Trimester 1

- Animal studies – feticidal and teratogenic – soft tissue and skeletal fetal malformations

Tofacitinib[2]

74 maternal exposures
- 1 in 5 miscarriage rate
- 1 in 5 elective termination
- Only 1 congenital anomaly

84 paternal exposures
- 1 in 10 miscarriage rate

Upadacitinib[3]

40 maternal exposures
- 1 in 5 miscarriage rate
- 1 in 5 elective termination
- 1 case of ectopic pregnancy
- Many pregnancies still ongoing

[1]Spiewak et al. Curr Res Pharmacol Drug Discov 2022;3:100096 [2]Mahadevan et al. Inflamm Bowel Dis 2018;24(12):2494-2500 [3]Abbvie Medical Information August 2023

Guidance on Last Dose of Biologic Therapy During Pregnancy

AGA Clinical Care Pathway

Infliximab – Plan final pregnancy infusion 6-10 weeks before EDC and resume post-partum
Adalimumab – Plan final pregnancy injection 2-3 weeks before EDC and resume post-partum
Golimumab – Plan final pregnancy injection 4-6 weeks before EDC and resume post-partum
Vedolizumab – Plan final pregnancy 6-10 weeks before EDC and resume postpartum
Ustekinumab Plan final pregnancy dose 6-10 weeks before EDC and resume postpartum

Likely do not need adjust intervals during pregnancy

If adjusted, ensure therapy is restarted after delivery as soon as safely possible


OAG
GAMIFICATION
Tandon - Game Code:
POWDER

THE FLARING PREGNANT IBD PATIENT

General Principles

- Same principles apply as the non pregnant IBD patient
- Increased urgency to reduce intestinal inflammation
- Involve maternal-fetal medicine, obstetrics, and perhaps colorectal surgery

Treatment

- Same management as the non-pregnant IBD patient
- Avoid JAKi, thiopurines, MTX, S1P

Odufalu et al. Gut 2021
- Corticosteroid use associated with:
  - Preterm birth (OR 1.79, 1.18-2.73)
  - Low birth weight (OR 1.76, 1.07-2.88)
  - Neonatal intensive care unit admission (OR 1.54, 1.03-2.30)
  - Late exposure (2nd and/or 3rd trimester) associated with serious infections at 12 months age

Minimize corticosteroid exposure during pregnancy

Investigations

Bloodwork	Stool Tests	Endoscopy	Imaging
CBC CRP (*) Albumin (*) TDM	C+S CDIFF O+P Fecal calprotectin	Flex sig Colonoscopy (*)	XRAY CT abdomen MRI (no contrast) Bowel ultrasound

Can I Perform Endoscopy During Pregnancy?

- Yes, if it will lead to a diagnosis and/or change in therapeutic plan.

De Lima et al. JCC 2015
- Prospective study of 42 pregnant women
- 12 colonoscopies, 35 sigmoidoscopies (throughout Pregnancy
- No increase in adverse pregnancy outcomes Including miscarriages

Ko et al. DDS 2020
- Retrospective cohort study at UCSF
- 50 lower endoscopies performed, 78% resulted in change in treatment
- No increase in adverse pregnancy outcomes Including miscarriages

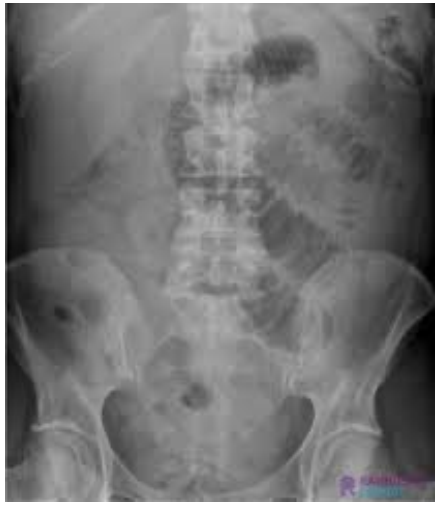
Flexible sigmoidoscopy without sedation may be performed if indicated

Full colonoscopy, or endoscopy with sedation, requires discussion with patient, MFM team, anesthesia

Left lateral tilt to avoid compression of IVC and aorta

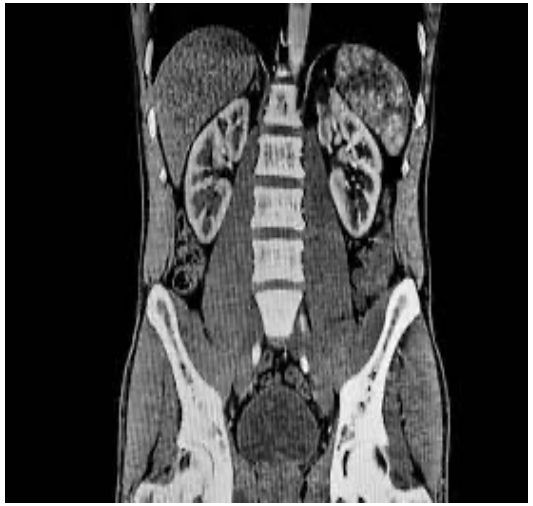
Is Imaging Safe During Pregnancy?

XRAY

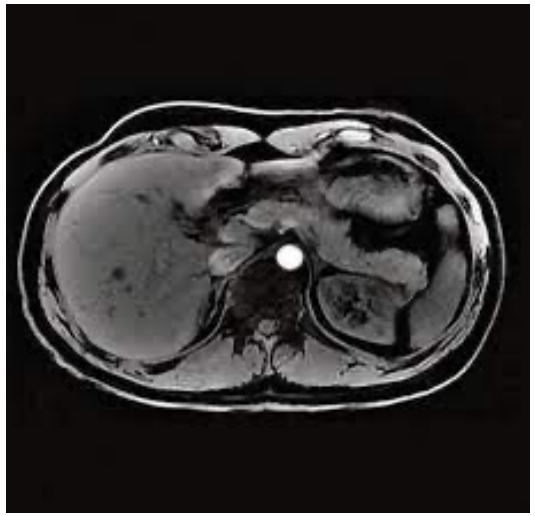


Radiation exposure "ok" with XRAY/CT if test will change management

CT scan

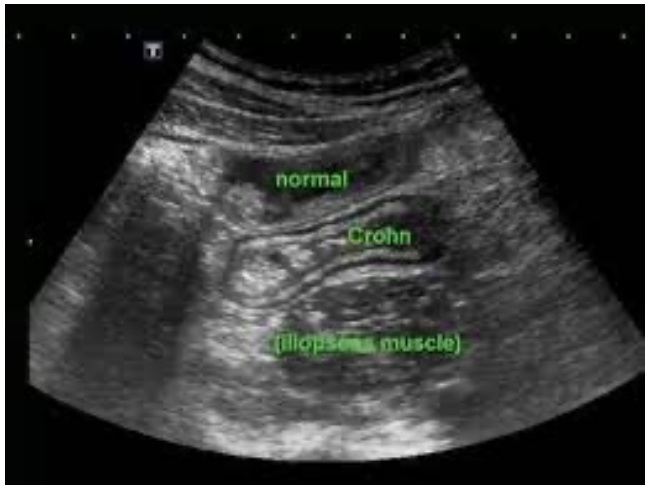


MRI



MRI can be used safely without Gadolinium

Ultrasound



IBD Ultrasound may be modality of choice (where available)

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ACOG Guideline Number 723 October 2017

Summary

- To discuss the “9 month” plan of the care of IBD during pregnancy
  - Close monitoring, objective disease assessment, prevent flares
  - Multidisciplinary care is key to achieving optimal disease outcomes

- To discuss the safety of advanced IBD therapies during pregnancy
  - Most biologics appear to be safe to continue during pregnancy – can continue without adjusting intervals in most settings
  - Limited evidence for small molecules – STOP!

Summary

- To discuss the “flaring IBD” during pregnancy
  - Increased urgency to induce remission
  - Minimize corticosteroid use but may be used in the short-term to induce remission quickly

- To discuss the role of disease monitoring during pregnancy
  - Objective disease assessment is critical to prevent flares during pregnancy
  - Endoscopy and imaging can be performed with safe monitoring, appropriate discussion of risks

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