Pregnancy, Fertility and Family Planning

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Patient Questions

- Will my IBD get worse during pregnancy?
- Can I have a healthy pregnancy?
- Should I stop my medications?
- How will my medications impact my baby?

Highlights

- Most IBD patients can have normal pregnancy, healthy baby
- Plan ahead: Preconception counseling, multidisciplinary care-MFM, dietitian, mental health provider
- Best to be in remission before conception
  - Active ds associated with adverse outcomes – preterm birth, low birthweight, small for gestational age but not congenital abnormalities
  - Active ds at conception associated w/ ↑activity during pregnancy
  - Goal: 3 months of steroid-free remission before conception
- Continue most Rx

Fertility

- Quiescent IBD = preserved fertility
- ↓ Fertility in IBD
  - Active inflammation – fallopian tubes, ovaries
  - Surgical history: Proctocolectomy in males, IPAA in females
  - Certain Rx: MTX, SSZ in males

Checklist for pre-conception, pregnancy and post-partum states in women with IBD

Pre-conception

Medication management

- Stop methotrexate >3 months prior to conception
- Taper off corticosteroids
- Caution with small molecules (for example, tofacitinib, ozanimod, upadacitinib)
- Consider stopping concomitant immunomodulators
- Continue all other IBD therapies
- Measure serum drug concentrations for thiopurines or biologics

Disease management

- 3 months steroid-free remission prior to conception
- Confirm remission with objective markers (calprotectin, endoscopy)
- Can consider imaging surveillance of small-bowel Crohn's disease

Fertility

- Refer to reproductive endocrinologist for infertility after 6 months of timed intercourse

Health-care maintenance

- Up-to-date cancer screening as appropriate (Papanicolaou smear, skin, colonoscopy)
- Up-to-date vaccination status
- Start prenatal vitamins with folic acid 1 mg (2 mg with sulfasalazine)
- Additional pre-conception health care as guided by obstetricians

Pregnancy

Multidisciplinary care

- MFM referral
- Nutrition referral or mental health referral as needed
- Colorectal surgeon referral: history of IPAA or colostomy

IBD monitoring and management

- see Fig. 3

Mode of delivery

Vaginal

- Can resume biologic therapy 24 h after delivery if no infection
- No recommendation for holding therapy in third trimester
- Attention to ostomy care if present

Caesarean section

- Can resume biologic therapy 48 h after delivery if no infection
- No recommendation for holding therapy in third trimester
- Anticoagulant prophylaxis for VTE
- Attention to ostomy care if present

Post-partum period

Lactation

- Avoid breastfeeding while on methotrexate, metronidazole or small molecules (for example, tofacitinib, upadacitinib, ozanimod)
- All other IBD therapies low risk to continue
- Can consider spacing steroids and thiopurines 4 h from breastfeeding (not universally recommended or necessary)

Infant monitoring

- Avoid live vaccines for 6 months with biologic exposure
- All other vaccines should be given on schedule
- Standard monitoring for developmental milestones as guided by paediatricians

IBD, inflammatory bowel disease; IPAA, ileal pouch–anal anastomosis; MFM, maternal–fetal medicine; VTE, venous thromboembolism.

Image from Brondfield and Mahadevan. Nat Rev Gastroenterol Hepatol. 2023; 20(8): 504-53

IBD monitoring and management

Goal: 3 months steroid-free remission before conception

Stop MTX, avoid JAK inhibitors and S1P modulators as able

IBD remission

IBD monitoring
- Gastroenterologist visit and patient update in each trimester
- Laboratory tests every trimester with complete blood count, liver enzymes, albumin and obstetrician laboratory tests
- No role for routine imaging or endoscopy

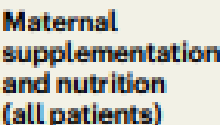
IBD management
- Continue mesalamines, thiopurines, biologics uninterrupted
- Routine metabolite monitoring on thiopurine + allopurinol co-therapy
- Counselling on mode of delivery with attention to perianal disease
- MFM consultation

IBD active disease and flare

IBD monitoring
- Stool studies for infection and fecal calprotectin
- Laboratory tests with complete blood count, liver enzymes, albumin, and CRP
- Consider serum drug monitoring if on biologic or thiopurine
- Imaging (preference for US or MRI where available, although single CT acceptable)
- Endoscopic evaluation if needed, preferably unsedated. Consult MFM if fetus >24 weeks

IBD management
- Gastroenterologist close follow-up every 2 weeks until flare resolved
- Antimicrobials as needed for pouchitis and perianal disease
- Initiate and optimize medications, including corticosteroids or change in biologic therapy if needed
- Counselling on mode of delivery with attention to perianal disease

Medically refractory disease
- Salvage therapy with infliximab, calcineurin inhibitor or JAK inhibitor
- Surgical consultation for potential colectomy
- Counselling on mode of delivery and risk of spontaneous delivery with surgery
- MFM consultation throughout



Maternal supplementation and nutrition (all patients)
- Vitamin D (400 IU per day)
- Folic acid (≥400 μg per day)
- Iron (dose varies)
- Aspirin prophylaxis from week 12 gestation
- Nutrition consultation if indicated
  - Short bowel (anatomically or reduced function)
  - Ostomy

Image from Brondfield and Mahadevan. Nat Rev Gastroenterol Hepatol. 2023; 20(8): 504-53

Slides Courtesy of:

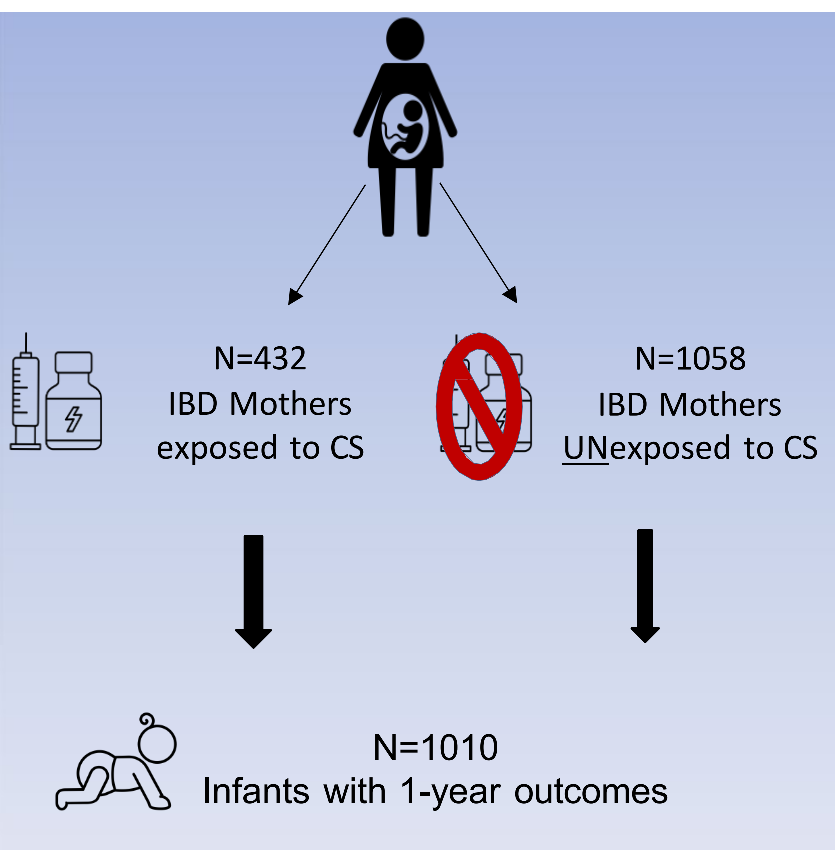
IBD Roadmap: Pregnancy and Beyond

Uma Mahadevan MD
Lynne and Marc Benioff Professor of Gastroenterology
Director, Colitis and Crohn's Disease Center
University of California, San Francisco

Medications to Continue?

Contraindicated Medications	Avoid	Medications to Continue
Methotrexate	Mesalamine w/ Dibutyl Phthalate	Mesalamine/sulfasalazine
Thalidomide	Corticosteroids	Azathioprine/6MP
	Ozanimod	Anti-TNF agents
	Tofacitinib	Ustekinumab/Risankizumab
	Upadacitinib	Vedolizumab

Exposure to Corticosteroids in Pregnancy is Associated with Adverse Perinatal Outcomes Among Infants of Mothers with Inflammatory Bowel Disease: Results From The PIANO Registry

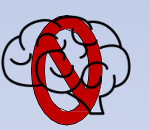


Maternal Outcomes with CS exposure

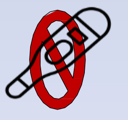
↑ Adverse Outcomes of Pregnancy

- Pre-term birth, OR 1.8 (1.2-2.7)
- Low birth weight, OR 1.8 (1.1-2.9)
- NICU admission, OR 1.5 (1.0-2.3)

No increased congenital malformations, OR 1.2 (0.8-1.9)



No increased risk of neurocognitive deficits in first 12 months of life

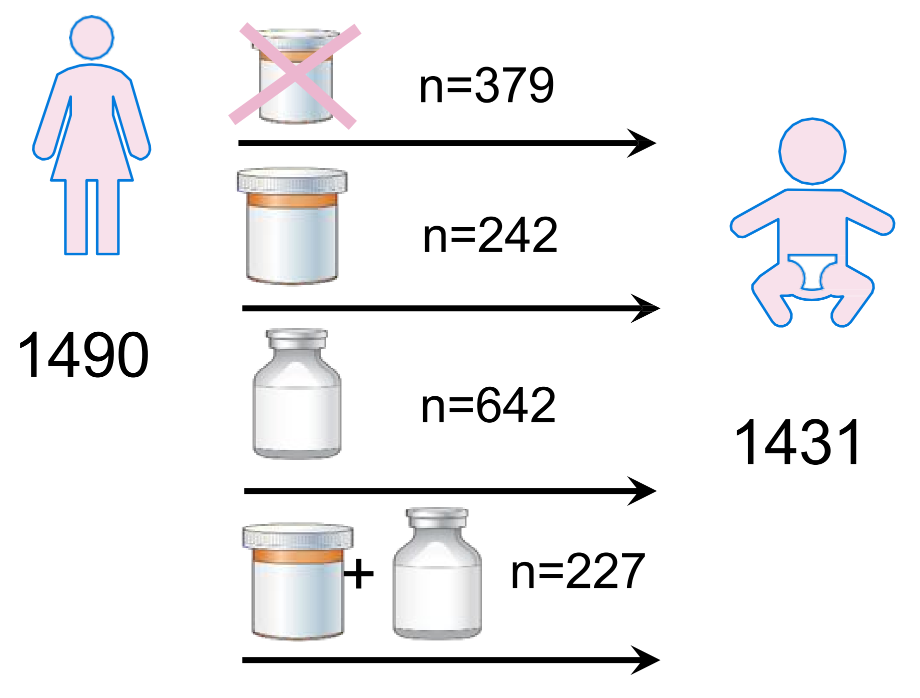


No increased risk of infection in first 12 months of life, OR 1.1 (0.9-1.4)

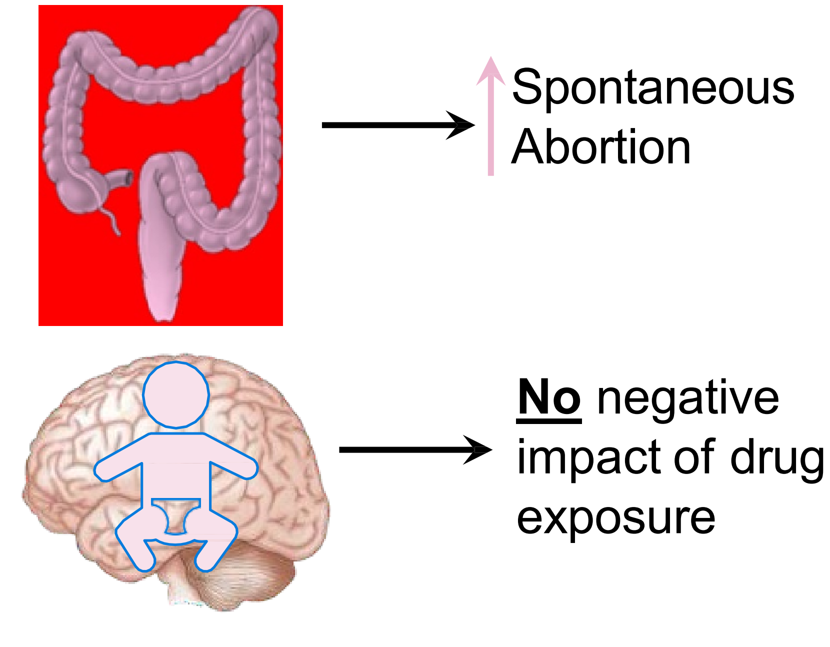
CS Corticosteroids; OR Odds Ratio; T1 First Trimester

Odufalu FD *Gut* 2021. doi: 10.1136/gutjnl-2021-325317

Pregnancy and Neonatal Outcomes After Fetal Exposure To Biologics and Thiopurines Among Women with Inflammatory Bowel Disease



No increase in:
- Congenital malformations
- Spontaneous abortions
- Preterm birth
- Low Birth Weight
- Infections in year
  - But ↑ with preterm birth



Mahadevan U, et al. *Gastroenterology.* 2021 Mar;160(4):1131-1139

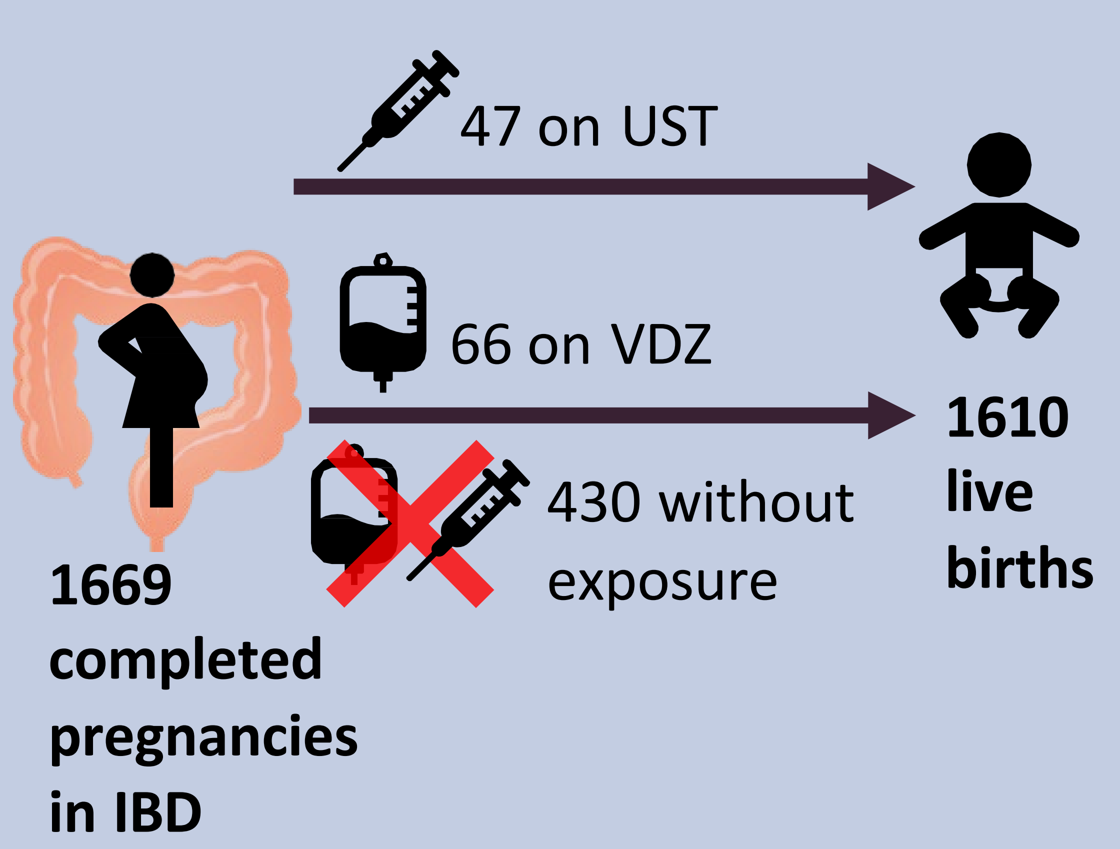
ECCO Guidelines 2022

Statement 18

For women with active disease just before or during pregnancy, or with disease that is difficult to control, continuation of anti-TNF [EL3] or non-TNF biologics [EL5] throughout pregnancy is recommended. The last dose of anti-TNF in the third trimester should be timed in accordance with the presumed due date to reduce foetal exposure [EL5].

Torres et al. JCC August 2022

Summary

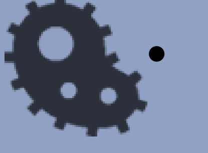


Pregnancy Outcomes

- Preterm birth
- Spontaneous abortion
- Small for gestational age
- Intrauterine growth restriction
- C-section
- Placental complications

Infant Outcomes

- Low Birth Weight
- NICU stay
- Congenital malformations



- Infections at 1 year

Small Molecules

	Tofacitinib	Upadacitinib	Ozanimod
Animal Reprotox: Feticidal, teratogenic Rats and Rabbits	73x and 6.3x [10 mg BID]	1.6x, 15x [15 mg AD] **0.8x, 7.6x [30 mg QD]** 0.6x, 5.6x [45 mg QD]	0, 0.2, 1, or 5 mg/kg/day 60x, 2x [0.92 mg]
Human Data	158 exp (24 IBD)	54 exposures	60 (12 IBD) exposures
Pregnancy	Avoid, ? lowest dose	Avoid, ? 15 mg dose	Avoid
Lactation	No	No	No

At least 4 weeks between stopping therapy and attempting conception

Summary

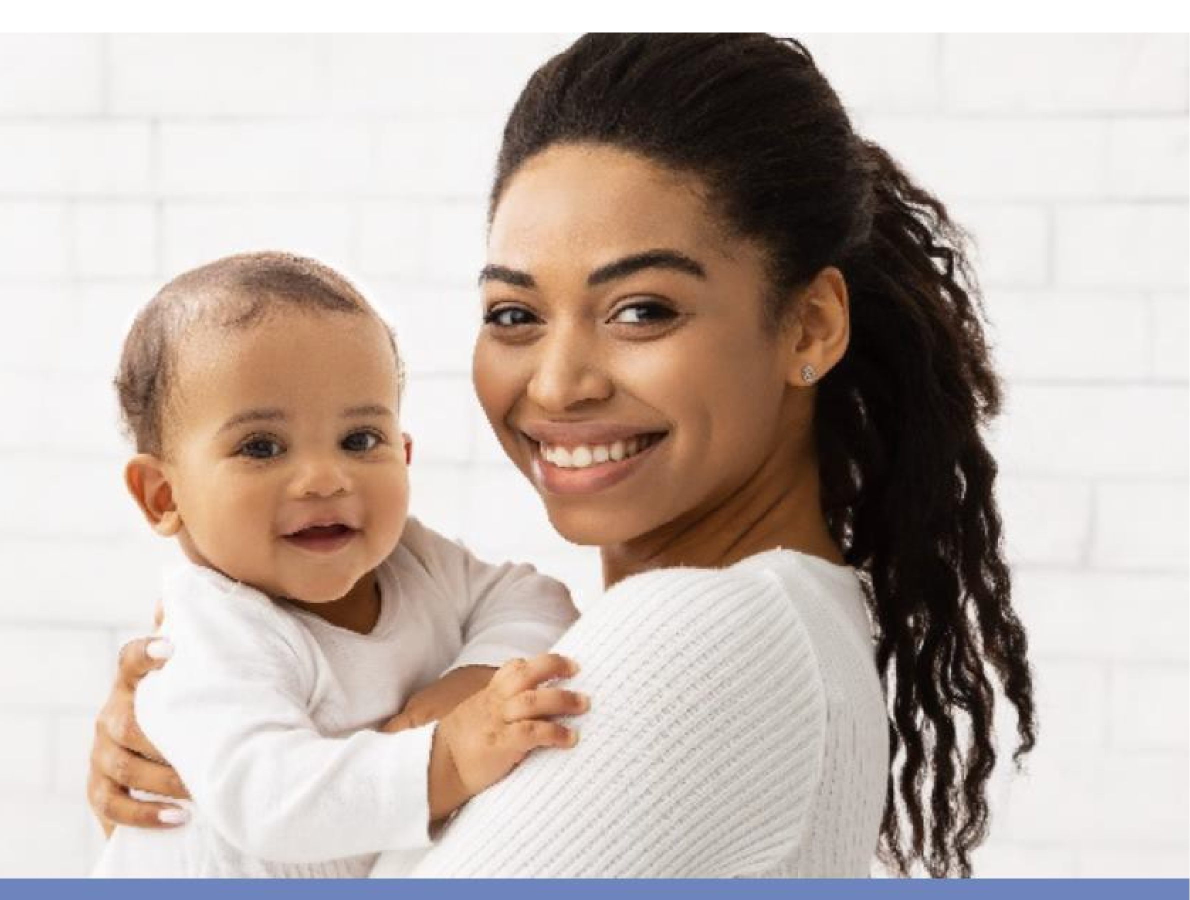
1. Continue biologics through pregnancy?
   - Yes! US/ECCO guidelines in agreement
2. Continue small molecules through pregnancy?
   - Avoid. Not an absolute contraindication
3. Continue biologics and small molecules in lactation?
   - Biologics: Yes!
   - Small Molecules: No! No safety data

Vaccinations?

- All Inactive vaccines should be given on schedule
- Live Vaccines
  - In utero Biologic exposure
    - After 6 months, yes
      - CZP no limitation; Vedolizumab?
      - If concerned, can check levels
  - Exposure via breastmilk should not limit live vaccine
- Small Molecules: Should be cleared by 4 weeks
  - Live vaccines after 4 weeks can be given on schedule

www.pianostudy.org

A national study of women with IBD and their children.



The PIANO research study looks at the safety of IBD medications in pregnancy and short- and long-term outcomes of the children.