Amsterdam UMC
Universitair Medische Centra

# IBD and issues at child bearing age

Krisztina B Gecse, Amsterdam UMC, Amsterdam, The Netherlands

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# Disclosures

- KB Gecse has received consultancy fees and/or speaker's honoraria from Amgen, AbbVie, Biogen, Boehringer Ingelheim, Ferring, Hospira, Immunic Therapeutics, Janssen, MSD, Pfizer, Sandoz, Samsung Bioepis, Takeda, Tigenix and Tillotts.

# Background

- Most patients with IBD will carry the diagnosis during their reproductive years

- There's fear surrounding
  - the impact of IBD and its therapies on pregnancy and infant outcomes
  - the impact of pregnancy on IBD and maternal health

- Improvement of care is best achieved by
  - objective information
  - multidisciplinary collaboration
  - shared decision making

Sellinger CP *et al. J Crohn Colitis* 2016; Mahadevan *et al. Gastroenterology* 2019

# IBD Pregnancy Clinical Care Pathway

## Preconception

- Effective contraception
- Genetic risks
- Fertility
- Disease management
- Medication management
- Interdisciplinary consultations
- Healthcare maintenance

## 9-month pregnancy plan

- Monitoring pregnancy
- Monitoring IBD
- Monitoring of medication
- Nutrition and weight gain

## Delivery

- Vaginal
- Cesarean

## Post-partum

- Lactation
- Monitoring infant
- Disease management
- Effective contraception

Adapted from Mahadevan *et al. Gastroenterology* 2019

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Adapted from Mahadevan *et al*. *Gastroenterology* 2019

# Genetic risks of IBD


- Patients typically overestimate the risk of having a child affected by IBD

- The absolute risk of an offspring developing
  - CD in the setting of maternal CD is 2.7%
  - UC in the setting of maternal UC is 1.6%
  - When both parents have IBD: >30%

Moller FT *et al. Am J Gastroenterol* 2015; Lahari *D et al.Gastroenterology* 2001

# Fertility

Issue 2

- IBD is not associated with decreased fertility in patients who have not undergone surgery

- Women with IBD are significantly more likely to remain voluntarily childless compared with the general population (up to 18% vs 6%) due to fear from:
  - infertility
  - genetic risks
  - effect of disease and medications on the outcome of the pregnancy

Sellinger CP *et al. J Crohn Colitis* 2016 ; Tavernier F *et al. Aliment Pharmacol Ther* 2013; Mountifield *et al. Inflamm Bowel Dis* 2009

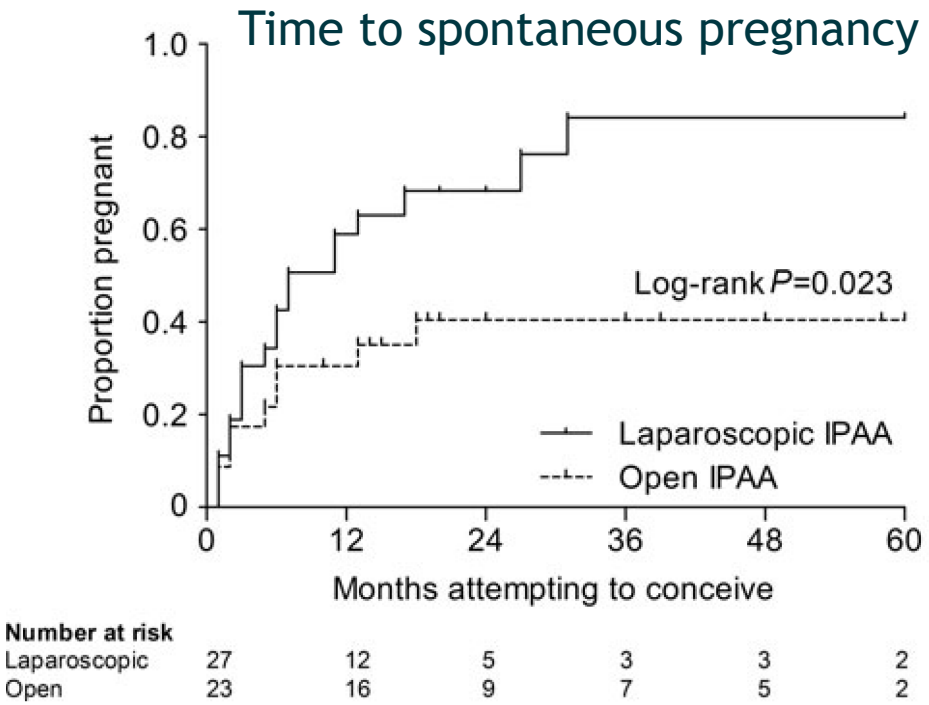
# Fertility

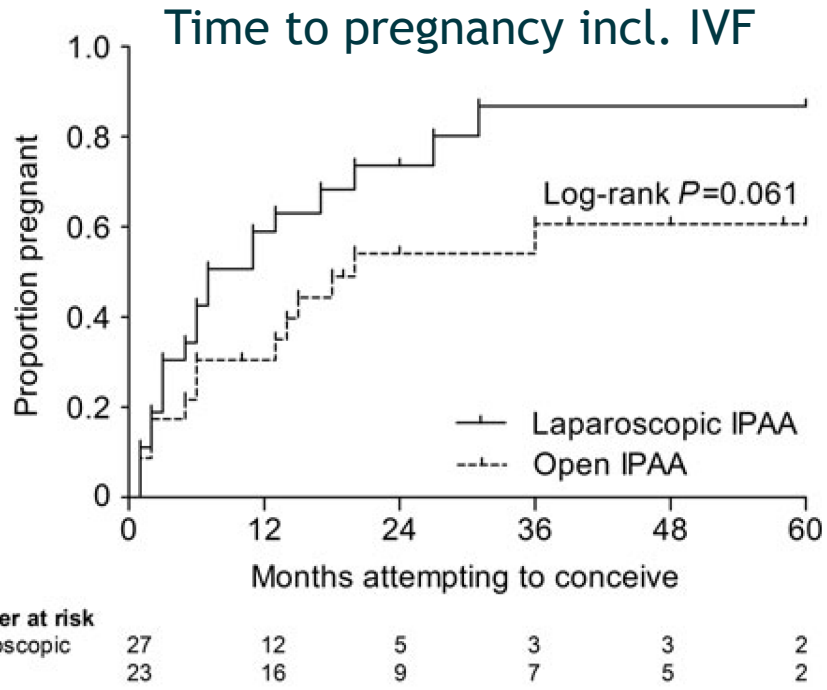
| Inflammatory Bowel Disease/Treatment Type | Effect on Fertility | |
|---|---|---|
| | Male | Female |
| Active disease | No effect | Reduces |
| Sulphasalazine | Significantly reduces | No effect |
| 5-Aminosalicylic acid | No effect | No effect |
| Corticosteroids | Reduces | No effect |
| Mercaptopurine/azathioprine | No effect | No effect |
| Biological agents | Unlikely | Unlikely |
| Small/large bowel resection | Unlikely | Unlikely |
| Ileal pouch anal anastomosis | Reduces | Reduces |

Heetun *et al. Aliment Pharmacol Ther* 2007; Mouyis M *et al. Semin Arthritis Rheum* 2019; van der Woude CJ *et al. J Crohn Colitis* 2015

# Fertility

- Infertility rates of 20% before open IPAA and 63% after open IPAA (RR of infertility after IPAA 3.91, 95CI 2.06–7.44)




Rajaratnam SG *et al. Int J Colorectal Dis* 2011, Mountifield RE et al. J Crohns Colitis 2010, Bartels SA et al. Ann Surg 2012

# Disease management

Issue 3

**IBD is associated with higher risk of adverse pregnancy outcomes compared to non-IBD pregnancies**

- Increased risk of prematurity: 1.87-fold increase (<37 weeks' gestation; 95% CI 1.52 to 2.31; p<0.001)
- Low birth weight: 2-fold increase (<2500 g; 95% CI 1.38 to 3.19; p<0.001).
- Congenital abnormalities: 2.37-fold increase (95% CI 1.47 to 3.82; p<0.001)
- Cesarean delivery: 1.5-fold (95% CI 1.26 to 1.79; p<0.001)

Cornish J etal. Gut 2006, Broms G *et al. Inflamm Bowel Dis* 2014, Stephansson O et al. Inflamm Bowel Dis 2011

# Disease management

Issue 4

| | Flaring UC | Flaring CD |
|---|---|---|
| Premature birth | OR 2.72 | OR 2.66 |
| Low birth weight | OR 2.10 | OR 3.3 |
| Stillbirth/miscarriage/abortion | 4-fold increase | 5-fold increase |

## Plan the pregnancy in remission!

**(at least 3 months of CSFR on stable therapy)**

Cornish J etal. Gut 2006, Broms G *et al. Inflamm Bowel Dis* 2014, Stephansson O et al. Inflamm Bowel Dis 2011

# Medication Management

Issue 5

## Active disease

- Discuss the risk of infertility
- Discuss the risk of continued/worsening disease activity during pregnancy
- Suggest delaying conception until disease is inactive

Optimize maintenance medication

## Inactive disease
(sustained CSF remission for at least 3 months)

Optimize maintenance medication

| Tofacitinib | DBP-containing SSZ | MTX | 5-ASA, thiopurines, anti-TNF |
|---|---|---|---|
| SEEK ALTERNATIVE | SWITCH | STOP | CONTINUE |

Adapted from Nguyen *et al. Gastroenterology* 2016

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- **Disease management**
- **Medication management**
- Interdisciplinary consultations
- Healthcare maintenence

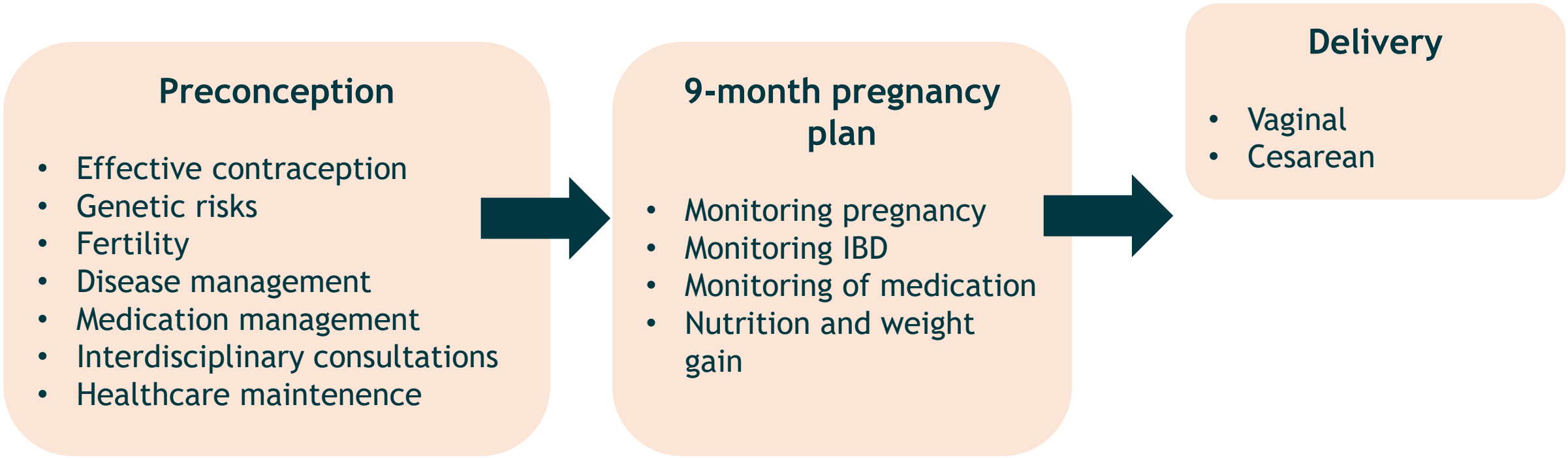
## 9-month pregnancy plan

- Monitoring pregnancy
- Monitoring IBD
- Monitoring of medication
- Nutrition and weight gain

**Issue 6**

Adapted from Mahadevan *et al. Gastroenterology* 2019

# IBD Pregnancy Clinical Care Pathway

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# Delivery

- **Previous rectovaginal fistula**
- **Current perianal disease (perianal fistula, abcess, rectovaginal fistula, anal fissure, anal stenosis)**

- **IPAA**

- **Absence of the above**

**Issue 7**

Recommend cesarean delivery

Consider caesarean or vaginal delivery (surgical back-up)

Vaginal delivery, caesarean for usual indications

**Issue 8**

**In case of caesarean delivery:**

- Anticoagulant prophylaxis for VTE
- Can resume biologics after 48h

**In case of vaginal delivery:**

- Can resume biologics after 24h

Adapted from Mahadevan *et al. Gastroenterology* 2019, Mahadevan et al. Gastroenterology 2017

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- **Lactation**
- **Monitoring infant**
- Disease management
- Effective contraception

Adapted from Mahadevan *et al. Gastroenterology* 2019

# Lactation

Issue 9

- **Mesalamine** is preferred to sulfasalazine (sulfapyridine metabolite is excreted into milk at higher concentrations and has hemolytic and antimicrobial properties)
- **Thiopurines** can be continued due to their low concentration in the breast milk
- **Biologicals** have undetectable or very low (<1% of serum concentration) with no negative impact of breastfeeding on infant health outcomes
- **Methotrexate** concentrations in milk appear to be clinically insignificant; however, in the absence of data, use is contraindicated
- **Tofacitinib** is contra-indicated during breastfeeding as a precautionary measure

Nguyen *et al. Gastroenterology 2016;* Matro *et al. Gastroenterology* 2018; SmPC Xeljanz, November 2018

# Vaccination

Issue 10

All vaccines should be given on schedule, ***except*** if the mother is exposed to any biologic therapy (other than certolizumab) during the third trimester of pregnancy (ie, after 27 weeks gestation):

- avoidancance of live vaccines is recommended for the first 6 months of life (oral rotavirus, BCG)

Nguyen *et al. Gastroenterology 2016*

# Conclusions

- **Plan together, in remission**
  - during durable deep remission (at least 3 months)
  - with the right drugs in the right dosis (preferably no new start of medication during pregnancy)

- **Assess risks and benefits** of stopping/continuing (co-)medication and possibility of relapse

- **Control regularly**
  - each trimester outpatient visits (blood check, FCP)

- **Team** with the gynecologist and the surgeon