



# 2020 VIRTUAL GI AND LIVER SYMPOSIUM

IBD Updates:  
DDW 2020, ACG 2020 &  
Important publications of 2020

*Southern California Society of Gastroenterology*

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# Disclosures

None

# Topics

- Disease and Prognosis of IBD
- Therapeutic Drug Monitoring
- Pregnancy
- COVID-19 and IBD

# Prevalence of Incidental Terminal Ileitis in persons undergoing non-diagnostic colonoscopy: A meta-analysis

**Methods: A systematic search strategy of 3 biomedical databases to identify studies that reported prevalence of asymptomatic terminal ileitis in adults undergoing screening or surveillance colonoscopy.**

**8 studies identified with reporting of asymptomatic terminal ileitis in 46, 460 persons**

Results: 147 out 46,650 (1.5%) patients found to have asymptomatic ileitis.  
5 of the 147pts progressed to Crohn's disease.

**Three studies reports absence of symptoms as a predictor for lack of progression**

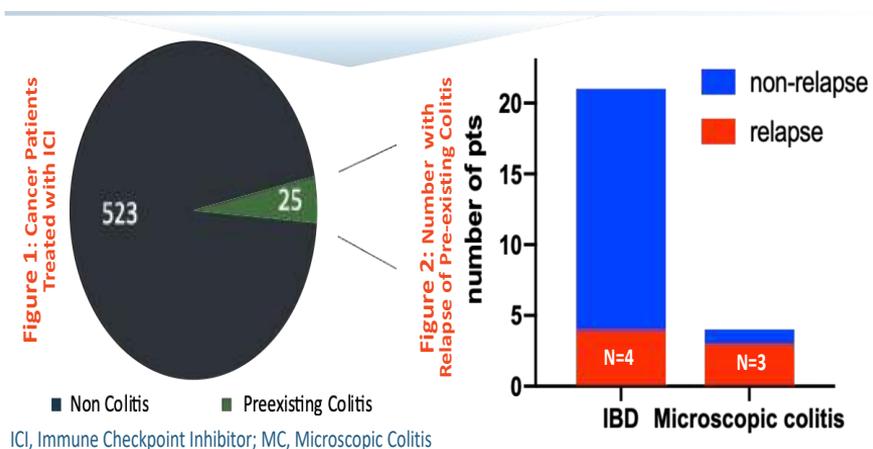
Conclusions: Rate of progression to Crohn's disease is low and watchful waiting is likely a reasonable strategy.

# Safety of Immune Checkpoint Inhibitors (ICI) in patients with IBD and microscopic colitis(MC)

**Methods:** Retrospective study of cancer pts treated with PD-1/PDL-1 Ligand inhibitor or CTLA-4 inhibitor between 2011-18

**Results:** 548 cancer pts treated with ICI  
25 pts had pre-existing IBD or MC  
¾ (75%) with MC and 4/21 (18%) with IBD relapsed

**Conclusions:** Cancer pts with history IBD/MC can be treated with ICI and will require close follow-up for potential flares.



# FMT for *C. difficile* Infection (CDI) in IBD: Systematic review and meta-analysis

**Methods:** Systematic review of 3 databases for studies up to Nov 2019.

**Primary outcome:** Pooled CDI cure rate

**Secondary outcomes:** IBD outcomes after FMT

**Results:**

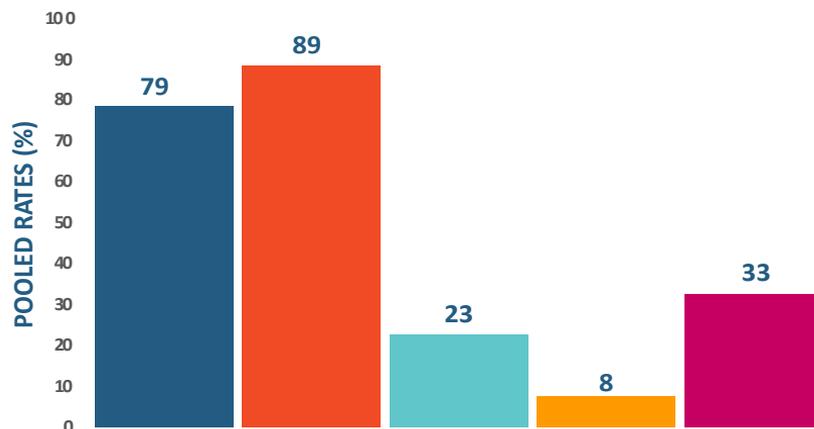
Total of 17 studies were included with 1 to 12 months followup.

**Conclusions:** Single or multiple FMT appears highly effective therapy for IBD pts with CDI.

No serious adverse events were reported

Tariq et al. DDW 2020 Abstract Mo 1794

**Figure 1:** Pooled Rates of FMT Outcomes



## LEGEND

	Resolution of CDI After 1 FMT (N=11 Studies)
	Resolution of CDI Following Multiple FMTs (N=13)
	Worsening of IBD After FMT Requiring Therapy Escalation (N=14)
	Worsening of IBD After FMT Requiring Surgery (N=13)
	Improvement of IBD Symptoms After FMT (N=6)

# Therapeutic Drug Monitoring (TDM)

- Reactive TDM
  - cost effective for primary non-response or secondary loss of response compared to empiric dose escalation
- Proactive TDM
  - May improve efficacy of anti-TNF and outcomes
  - May improve cost-effectiveness
  - Improve safety of biologic therapy

## MEETING SUMMARY

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### Appropriate Therapeutic Drug Monitoring of Biologic Agents for Patients With Inflammatory Bowel Diseases



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# Early Infliximab(IFX) Levels Predict Outcomes

**Methods:** Prospective multicenter (n=9) study in Europe  
IFX naïve pts with active CD or UC (n=62)

**Primary outcome:** Inter-individual variability of IFX during induction and correlation with remission at week 30.

**Samples done between baseline to week 30 including trough levels(TL), intermediate levels(IL), peak levels(PL)**

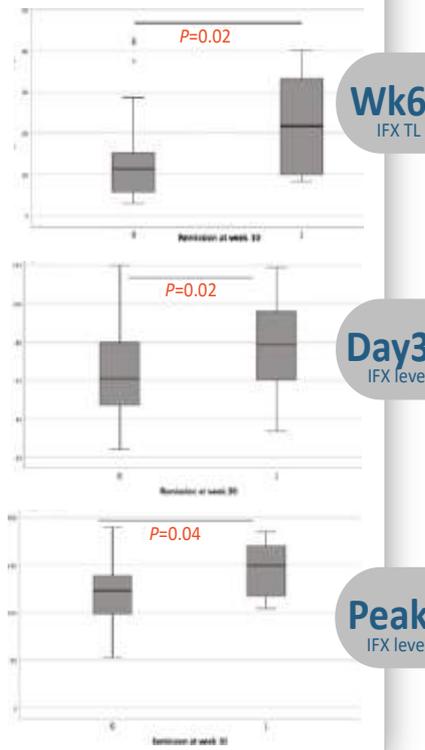
## Results:

33.9% ( 21/62) patients were remission at week 30  
Median wk 6 Trough Levels higher in pts in clinical remission at wk 30

Day 3 IL and PLs after 3<sup>rd</sup> infusion was higher in pts in clinical remission at week 30

Wk 2, 6, and 10 TL lower in pts who developed ATI at a later point

Figure 1:  
**Levels & Wk30 Remission<sup>1</sup>**



**Conclusion:**  
Intermediate levels at early as Day 3 can predict remission at wk 30.

Low IFX levels during induction were correlated to development of ATIs

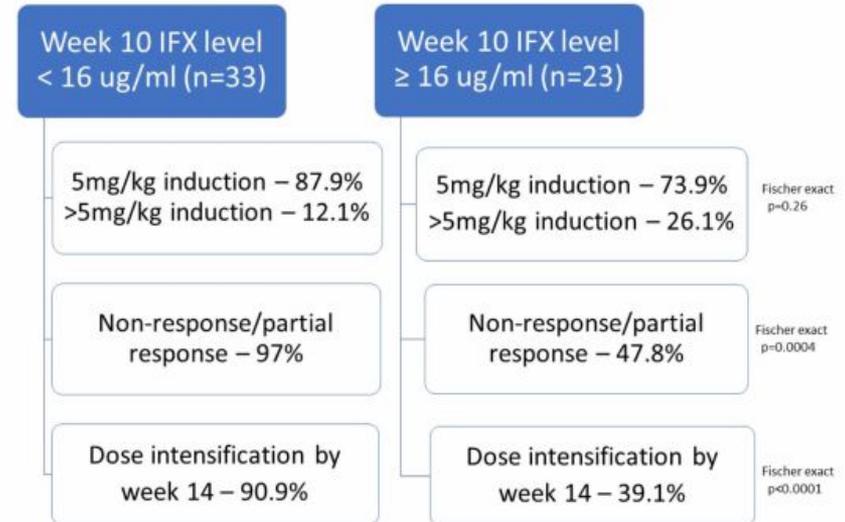
# Week 10 Infliximab Concentration Identifies Pts with Partial or Non-response and Allows for Early Optimization of Therapy in IBD

**Methods:**  
Single center study with 56 pts with IBD  
Serum IFX levels assessed at Wk 10  
Clinical and biochemical response assessed at Wk 14

Results: Median Wk 10 IFX level was lower in non-responders/partial responders compared to complete responders

**Wk 10 IFX level <16ug/ml more likely to have non-response/partial response**

Figure 1- Response and need for dose intensification based on week 10 IFX level



# Diagnostic accuracy of serum biomarker panel for endoscopic activity in UC and CD

EHI, Endoscopic Healing Index, 13 protein serum panel from Promethues Biosciences validated to detect endoscopic healing. Scores range 0-100, higher scores indicating more severe activity.

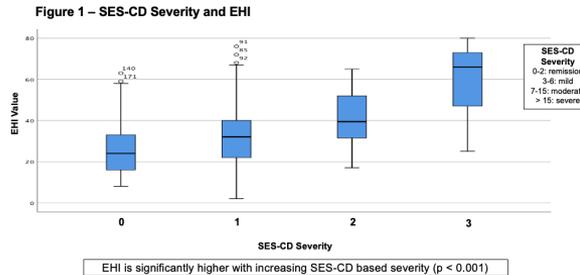
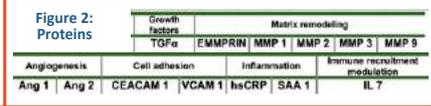
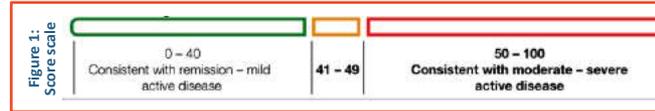
## CD

Methods: EHI in 205 with CD paired with endoscopy

Subcomponents of SES-CD score evaluated

Results:  
EHI values significantly higher with increasing ulcer size ( $P < .001$ )

EHI < 20: modest sensitivity (85%, CI 77-91) for ruling out any ulcers  
EHI > 50: modest sensitivity (85%, CI 76-92) for ruling in presence of any ulcers



## UC

Methods: EHI in 114 pt with UC paired with endoscopy scores

Results: EHI < 20 **ruling out** moderate to severe endoscopic activity

EHI > 40 had 90% specificity for **ruling in** mild to severe endoscopic activity

# Biologic Serum Concentrations Inversely Correlate with EHI in CD

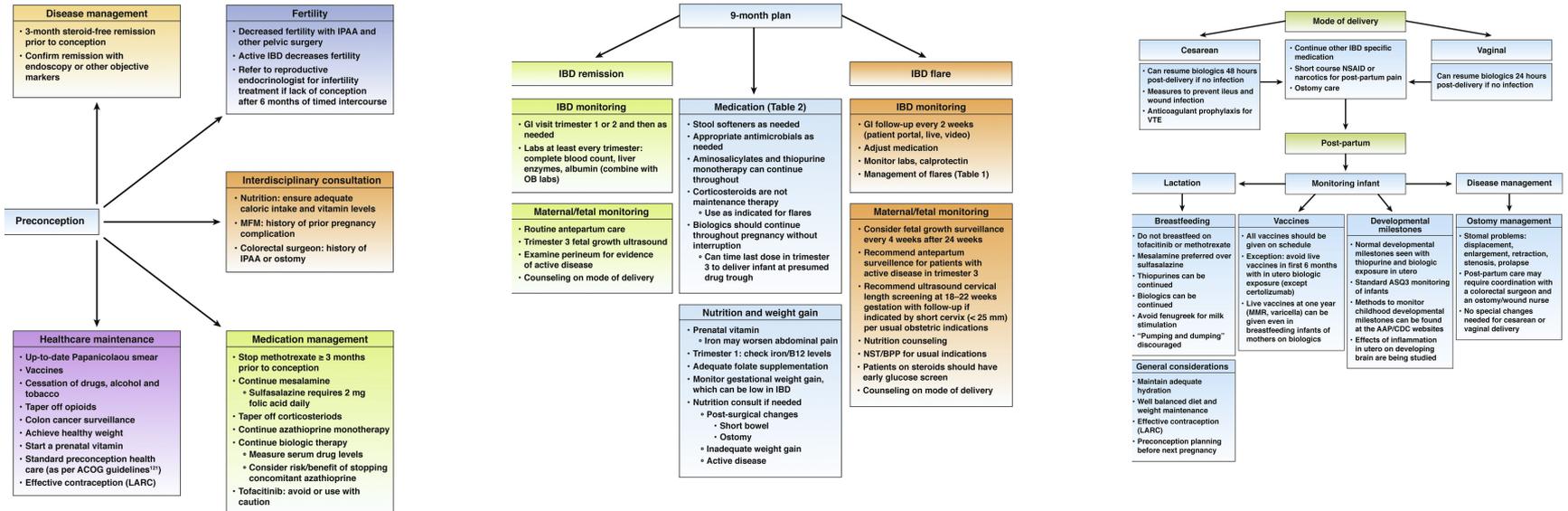
Infliximab <sup>1</sup>	Adalimumab <sup>1</sup>	Vedolizumab <sup>2</sup>	Ustekinumab <sup>3</sup>
N= 591 Threshold for EHI <20	N= 853 Threshold for EHI <20	N= 272 Threshold for EHI <20	N= 353 Threshold for EHI <20
Adults: IFX level >3.45 ug/ml AUC 0.702, Sensitivity 53.1% and Specificity 88%	Adults: ADA level >5.95 ug/ml AUC 0.682, Sensitivity 59% and Specificity 73.8%	Adults: Vedolizumab level >15.7ug/ml AUROC 0.67, Sensitivity 65% and specificity 74%	Adults: Ustekinumab level > 3.75 ug/ml AUROC 0.735, Sensitivity 59% and specificity 85%

Conclusions: Combined testing of EHI and anti-TNF level could identify pts with EHI >50 who may benefit from dose escalation.  
Higher VDZ levels correlated with lower EHI  
Exposure response relationship exists with UST levels and EHI reflecting endoscopic activity.

1. Abreu et al DDW 2020 Abstract 241
2. Yarur et al DDW 2020 Abstract Sa 1865
3. Walshe et al DDW 2020 Abstract Sa 1870

# Pregnancy

## AGA Care Pathway published in 2019

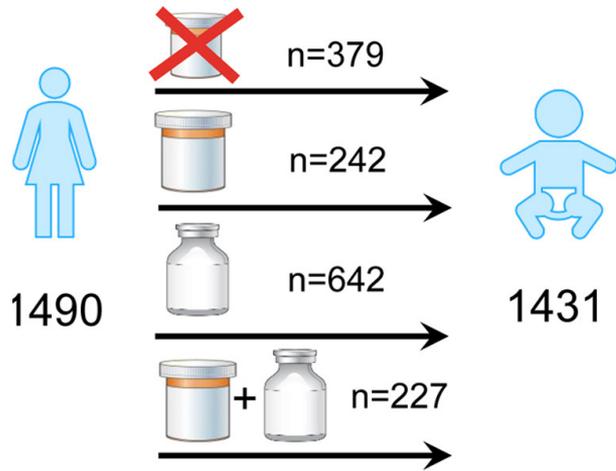


# PIANO Registry

- Pregnancy in IBD And Neonatal Outcomes
- Prospective Observational study enrolled pregnant women with IBD at 30 US center from Jan 2007 to March 2019.
- Medication use, disease activity, pregnancy outcomes, neonatal outcomes and developmental milestones collected, serum maternal, neonatal and cord drug levels,

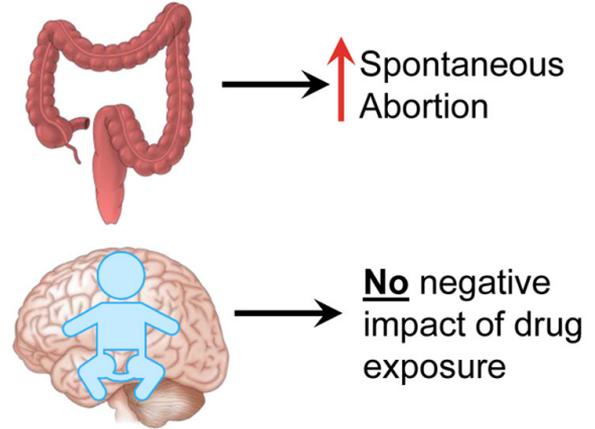
# PIANO Registry Results

## 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



Gastroenterology

# Pregnancy outcomes in women exposed to Ustekinumab for IBD, Psoriasis (Pso) and Psoriatic Arthritis(PsA)

**Methods:** Pregnancies with exposure to ustekinumab during pregnancy or within 3 months prior to conception reported to manufacturer through April 2019  
Data from spontaneous reporting, clinical studies and registries

**Results:** n=478 pregnancies ( 124 CD, 11 UC, 2334 PsO, 9 PsA)

71.7% resulted in live births

Rate of spontaneous abortion (SA) 18.4%

Rate of congenital anomalies (CA) 3.9%

Pregnancy outcome rates similar in CD/UC and PsO and PsA

**Conclusions:** Pregnancy outcome after maternal exposure to UST with prevalence of live birth, SA and CA consistent with general population.

Exposure of UST throughout pregnancy was not associated with any apparent safety signals.

**Figure 1: Rates of Pregnancy Outcomes for UST-treated patients (All, Prospective, Retrospective) Compared to US General Population**

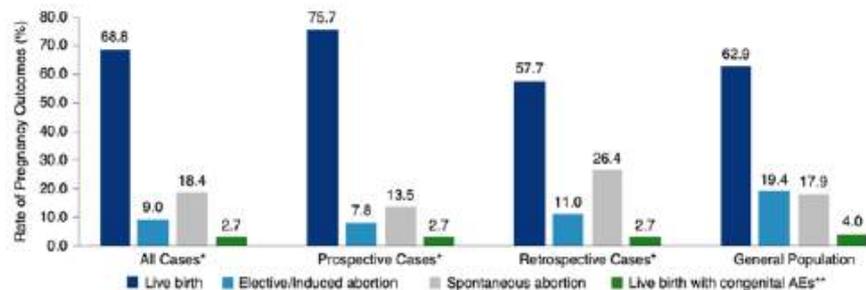


Table 1: Safety (Total Cases N=478)	n/N (%)	Congenital Anomaly
Live Birth	341/478 (71%)	12
Elective/Induced Abortion	42/478 (9%)	1
Spontaneous Abortion	88/478 (18%)	3
Ectopic Pregnancy	3/478 (0.6%)	0
Still birth	2/478 (0.4%)	1
Ongoing (fetal congenital anomaly)	1/478 (0.2%)	1
<b>Total</b>	<b>100%</b>	<b>18</b>

# Vedolizumab Pregnancy Exposure Registry: An OTIS Pregnancy Study Update

## Methods:

Prospective observational study conducted by OTIS comparing 100 VDZ exposed to 100 disease matched patients to 100 healthy controls from Dec 2015 to March 2020

Results: N=263, 73 VDZ, 103 with IBD, 87 Healthy

Major Structural birth defects: 3 (4.2%) in VDZ, 8 (7.8%) in disease matched, 4 (5%) in healthy controls.

## Conclusions:

Women in 1st trimester have similar outcomes compared to disease matched and healthy outcomes.

**Table 1: Pregnancy Outcomes in the Study Cohort**

	Vedolizumab-Exposed-Total (N=73)	DM-Total (N=103)	HC-Total (N=87)
Pregnancies ending with live born infant - n/N (%)	68/73 (93.2)	99/103 (96.1)	79/87 (90.8)
Spontaneous abortion - Left Truncation Accounted Rate <sup>a</sup>	12.6%	6.2%	6.2%
Termination - n/N (%)	0/73 (0.0)	0/103 (0.0)	0/87 (0.0)
Stillbirth - n/N (%)	0/73 (0.0)	1/103 (1.0)	0/87 (0.0)
Lost to follow-up (LTFU) - n/N (%)	1/53 (1.9)	0/88 (0.0)	6/82 (7.3)
Preterm delivery - Rate <sup>b</sup>	13.6%	6.1%	7.9%
Birth weight full term infants - mean g (SD)	3395.4 (442.5)	3429.0 (455.3)	3300.0 (439.0)
Number of pregnancies with major birth defects among all pregnancies excluding LTFU - n/N' (%)	3/71 (4.2)	8/103 (7.8)	4/80 (5.0)
Serious infections in live born infants up to 1 year of age - n/N' (%) <sup>c</sup>	1/70 (1.4)	1/99 (1.0)	1/82 (1.2)
Ages and Stages Screening at 1 year of age with concern - n/N' (%) <sup>c</sup>	7/38 (18.4)	15/74 (20.3)	8/51 (15.7)

<sup>a</sup>Spontaneous abortion rate computed using Kaplan-Meier estimate at 20 weeks' gestation, accounting for left truncation because women can enroll at various times in gestation

<sup>b</sup>Computed using Kaplan-Meier estimate at 37 weeks' gestation

<sup>c</sup>Includes twins

% = (n/N') \* 100. N' at each category: Number of pregnancies meeting the criteria specified in the row title

# Inflammatory Bowel Disease Is Not Associated With Severe Outcomes of COVID-19: A Cohort Study From the United States Epicenter

**Methods: Prospective study of IBD pts with Covid 19 and pts without IBD from March 3 to May 10, 2020**

**Results: 83 pts with IBD and 8277 non-IBD pts with Covid 19 identified.**

IBD pts had higher rates of IMM and biologic use  
IBD pts had lower rates of hospitalizations ( 14% vs 51%,  $p < 0.001$ )

IBD pts had lower rates of ICU Admission (2% vs 13%,  $p = 0.04$ )

**Multivariable analysis Results**

Presence of IBD was not associated with severe outcomes (OR 0.55)

Age, male gender, thiopurine use, # of comorbidities were predictors of severe Covid 19 outcomes

Anti-TNF agents maybe be protective from severe outcomes of Covid 19.

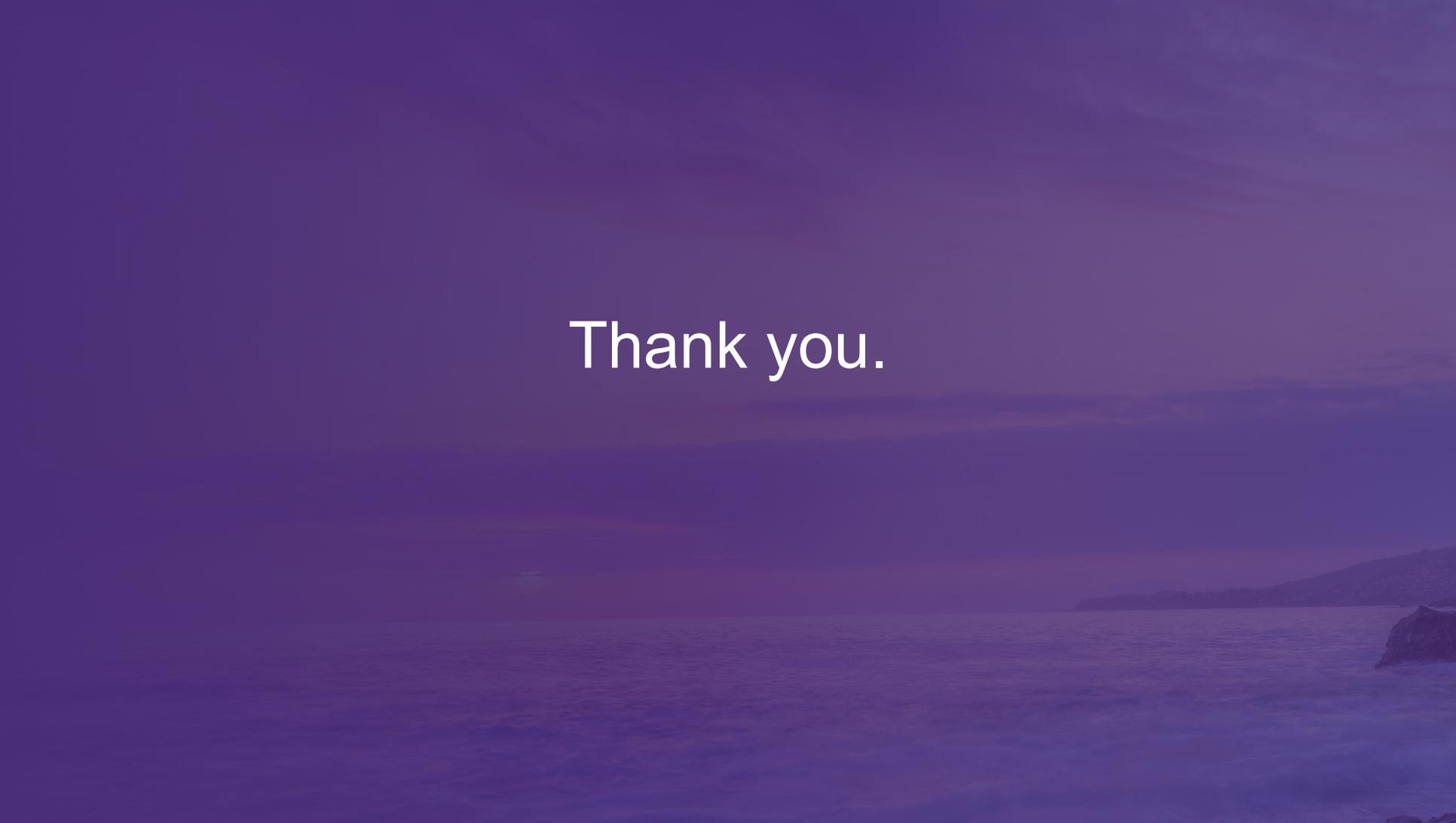
**Table 2 - Outcomes of COVID-19 Patients**

Outcome	Non-IBD Controls (N = 8,277)	IBD Patients*			
		Confirmed COVID-19 (N = 44)	P-value	Confirmed or Suspected COVID-19 (N = 83)	P-value
Hospitalization	4210 (50.9)	6 (13.6)	<0.001	6 (7.2)	<0.001
Ventilator used	865 (10.5)	1 (2.3)	0.08	1 (1.2)	<0.01
ICU	1058 (12.8)	1 (2.3)	0.04	1 (1.2)	<0.01
Death	927 (11.2)	2 (4.5)	0.23	2 (2.4)	0.01

\*P-values represent Chi-square comparison with non-IBD controls



- International pediatric and adult database to monitor and report outcomes of COVID-19 occurring in IBD
- As of 12/2/2020: 3493 cases reported
- COVID 19 risk calculator.

A purple-tinted landscape of a sea at sunset or sunrise. The sky is a gradient of purple and blue, with some light clouds. The sea is calm with gentle ripples. In the distance, a low landmass is visible. The text "Thank you." is centered in white.

Thank you.