

COVID-19 and Its Impact on Patient Care in IBD: What Clinicians Need to Know

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Learning Objective

Examine the latest evidence on current and emerging treatment and prevention strategies for COVID-19 and its associated symptoms in GI patients.

COVID-19: Key Facts

- There are hundreds of coronaviruses
 - Most circulate among animals (pigs, camels, bats, cats)
 - Sometimes jump to humans (SARS 2002-2004) (MERS 2012)
 - COVID-19 caused by SARS-CoV-2
- Incubation median 4-5 days, range 2-11.5 days
- Clinical presentation
 - Respiratory tract infection (fever, cough)
 - New loss of taste or smell
 - Bilateral pneumonia, lymphopenia
 - Gl involvement
- May cause immune-mediated reaction and cytokine-like syndrome





When to Suspect COVID-19

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle of body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

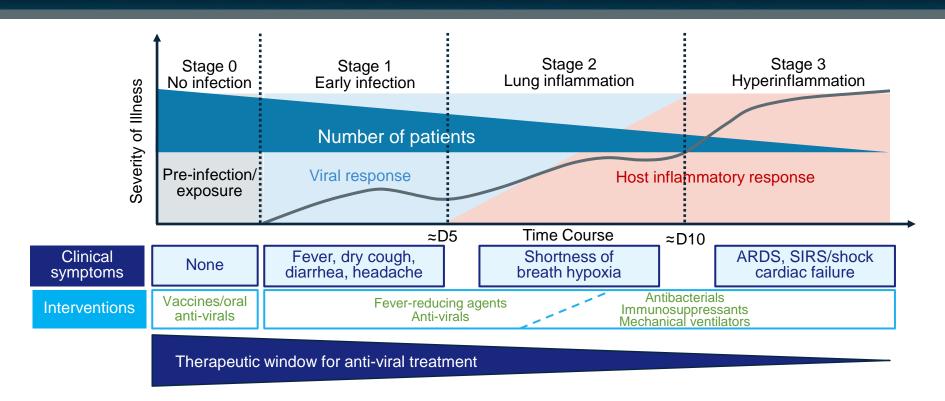
- Known exposure to infected person
- Abnormal chest imaging
- Lymphopenia (low WBC)
- Elevated CRP

Emergency warning signs

- Trouble breathing
- Persistent pain or pressure in the chest
- New confusion
- Inability to wake or stay awake
- Bluish lips or face



Stages, Symptoms, and Potential Treatments





Current World Numbers



Total Cases

67,916,341

Total Deaths

1,551,120

192 countries/regions







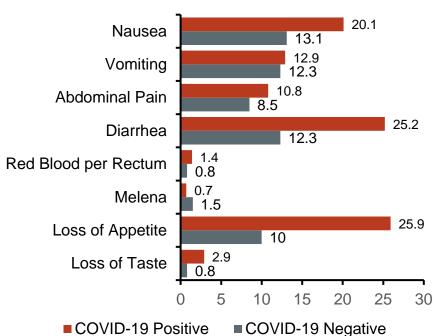
COVID-19: GI Involvement

- 55% of patients have fecal samples positive for SARS-CoV-2 RNA; live virus has been detected
- Stools remain positive for a mean of 28 days (vs. 17 days for respiratory) after first symptom
- Around 30% of hospitalized patients have GI symptoms:
 - Anorexia, diarrhea, vomiting, abdominal pain
 - Can precede URI/fever
 - Can be sole manifestation
 - Severe disease/ICU more common with GI symptoms
 - Consider COVID-19 in patients with IBD if fever, URI, unusual GI symptoms or flare, or history of exposure



GI Manifestations in Patients with COVID-19: Real-World Experience

GI Symptoms on Admission



- 7% of patients who are COVID-19 positive present with isolated GI symptoms
- Presence of GI symptoms is associated with higher risk for cytokine release syndrome
- No difference in mortality between those with and without GI symptoms

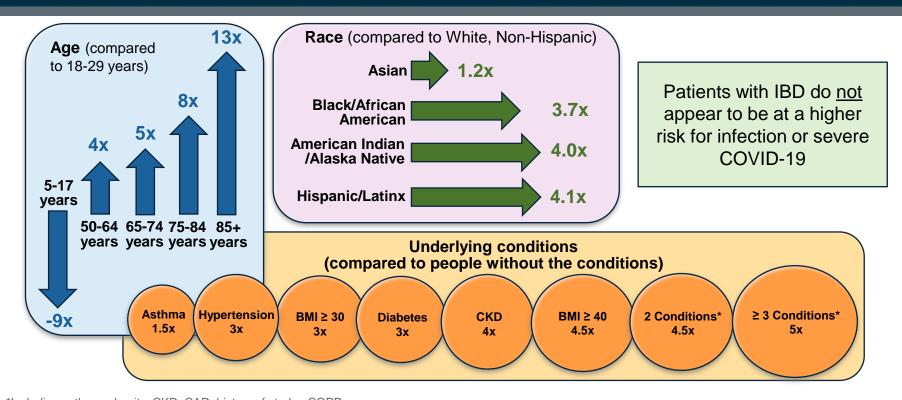


SARS-CoV-2 Detection in Stool: Evidence for Fecal Transmission Is Limited

Author	Journal	Year Published	No. of Patients	Findings
Jin X, et al	Gut	2020	651	 11.45% with one GI symptom (nausea, vomiting, diarrhea) Identified novel methylation site in S protein that changed from SARS to Wuhan and some differences to the strain in Zhenjiang Province → may account for change in frequency of GI symptoms
Xiao F, et al	Gastroenterology	2020	73	 39 (53%) had positive stool RNA Stool remained positive in 17 patients (23.29%) after respiratory samples were negative
Wu Y, et al	Lancet Gastroenterol Hepatol	2020	74	 41 (55%) had positive stool samples Fecal samples were positive for a mean of 27.9 days (vs. respiratory samples – mean of 16.7 days)
Wolfel R, et al	Nature	2020	9	 Viral RNA detected in sputum and stool samples Live virus was not isolated from stool samples Virus in stool is not thought to be infectious



Risks for COVID-19 Hospitalization



^{*}Including asthma, obesity, CKD, CAD, history of stroke, COPD

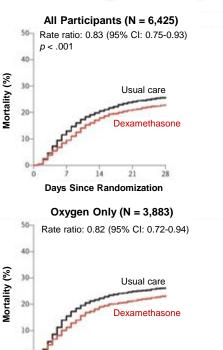
BMI = body mass index; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease

CDC Website. 2020. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/index.html.

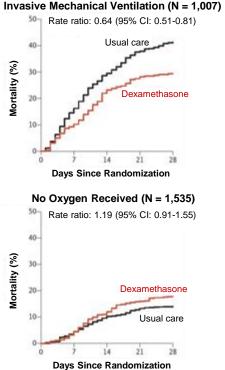


Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report

- Randomized, controlled, open-label, adaptive, platform trial
- Dexamethasone 6 mg given once daily for up to 10 days vs. usual care alone
- Primary outcome: 28-day mortality
- Conclusion: In patients hospitalized with COVID-19, dexamethasone reduced 28-day mortality among those receiving invasive mechanical ventilation or oxygen at randomization, but not among patients not receiving respiratory support



Days Since Randomization

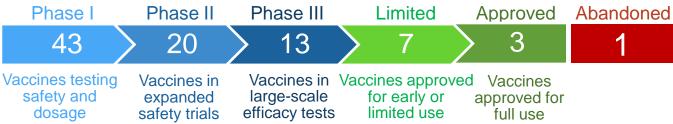




Vaccine Updates

- Approved or limited-use vaccines:
 - Pfizer/BioNTech (approved in Canada and other countries; emergency use in United States and other countries)
 - Moderna (approved in Canada; emergency use in United States)
 - Gamaleya (Russia, Belarus, Argentina)
 - Oxford-AstraZeneca (UK, India, Argentina)
 - CanSino (China)
 - Vector Institute (Russia)
 - Sinopharm/Beijing Institute of Biological Products (China, UAE, Bahrain, Egypt)
 - Sinopharm/Wuhan Institute of Biological Products (China, UAE)
 - Sinovac (China)
 - Bharat Biotech (India)

FDA = U.S. Food and Drug Administration; UAE = United Arab Emirates



Recorded December 8, 2020

New York Times Website. 2020. https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html. https://www.pfizer.com/news/press-release-detail/pfizer-and-biontech-announce-vaccine-candidate-against. 2020. https://investors.modernatx.com/news-releases/news-release-details/modernas-covid-19-vaccine-candidate-meets-its-primary-efficacy. 2020.



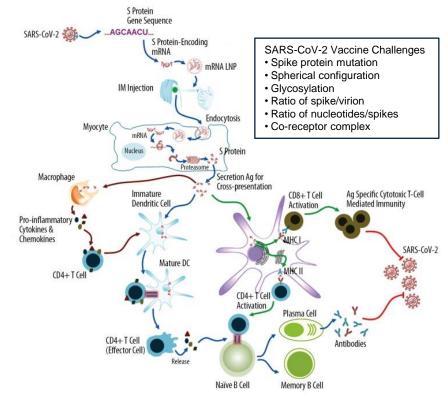
SARS-CoV-2 Vaccines

Developer	Route	Method	Number of Doses (Timing)
AstraZeneca/ University of Oxford	Injection	Replication-deficient viral vector vaccine (adenovirus from chimpanzees)	2 (0, 28 days)
Bharat Biotech	Injection	Inactivated SARS-CoV-2 vaccine	2 (0, 28 days)
CanSino/Beijing Institute of Technology	Injection	Recombinant vaccine (adenovirus type 5 vector)	1
Johnson & Johnson	Injection	Non-replicating viral vector	1
Moderna/NIAID	Injection	mRNA-based vaccine	2 (0, 28 days)
Pfizer/BioNTech	Injection	mRNA-based vaccine	2 (0, 28 days)
Sinovac	Injection	Inactivated SARS-CoV-2 vaccine combined with an immunological agent	2 (0, 14 days)

CME Outfitters

How Do the Pfizer BNT162b2 and Moderna mRNA-1273 Vaccines Work?

- mRNA-based vaccines
- The mRNA describes the spike protein on the outer surface of SARS-CoV-2
- Prepares the immune system to fight COVID-19
- The Pfizer vaccine must be stored at -70°C while the Moderna vaccine must be stored at -20°C
- Each has 2 doses





Wang F, et al. Med Sci Monit. 2020;26:e924700-e924700.





Pfizer Vaccine BNT162b2 Update

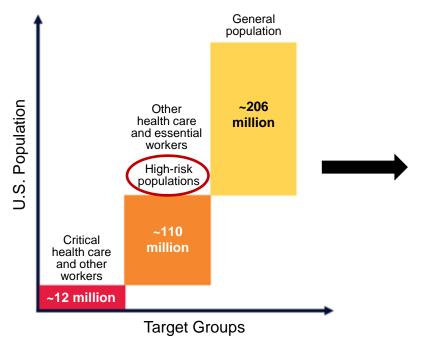
- 95% effective in preventing COVID-19 (p < .0001)
- \bullet N = 43,538
 - 94 cases of COVID-19 have been confirmed (this was split between vaccinated individuals and those who received the placebo)
- Protection is achieved 28 days after initiation or the 2-dose schedule vaccine



Moderna Vaccine mRNA-1273 Update

- 94.5% effective in preventing COVID-19 (p < .0001)
- N > 30,000
 - 95 cases of COVID-19 have been confirmed (5 cases were seen in vaccinated individuals; 90 cases were seen in those who received the placebo)
- Protection is achieved 28 days after initiation or the 2-dose schedule vaccine

Advisory Committee on Immunization Practices: Considerations for Vaccine Prioritization



- High-priority target group includes:
 - Highest risk medical, national security, and other essential workers
 - Rationale: protect health care infrastructure and other critical societal functions
- High-risk populations include patients in an immunocompromised state from:
 - Blood or bone marrow transplant
 - Immune deficiencies
 - Human immunodeficiency virus (HIV)
 - Use of corticosteroids
 - Use of other immune-weakening medications

Summary

- Risks of severe COVID-19 vary depending on age, ethnicity, and presence of certain comorbidities
- Pharmacologic management is only recommended in hospitalized patients requiring supplemental oxygen
- At least 149 prophylactic vaccines are currently in development, many in late stages





Questions Answers

Recorded on December 8, 2020



Learning 2 Objective

Apply optimal strategies to manage patients with IBD during the COVID-19 pandemic.

Case Study 1: Meet Jackie

- Jackie is a 24-year-old Caucasian woman diagnosed with pan-UC 2 years ago
- Has been on infliximab since the diagnosis and is currently in remission
- Current symptoms: abdominal pain, bloody diarrhea (6 times/day)
- Infliximab trough level 2.3 µg/ml, ATI 0 U/mL
- Physical exam with mild tenderness in LLQ
- Clostridioides difficile (C. diff) negative
- SARS-CoV-2 negative



Audience Response

How would you proceed with Jackie?

- A. Increase infliximab dosage
- B. Switch to another anti-TNF
- C. Switch to vedolizumab
- D. Switch to ustekinumab
- E. I don't know; tell me the answer



Are Patients with IBD at Increased Risk of COVID-19?

- No increased rates of COVID-19 among patients with IBD
 - Madrid study: Patients with IBD had a significantly lower standardized risk of COVID-19 compared to the general population
- Moderate-to-severe IBD activity and steroid use were associated with higher rates of infection

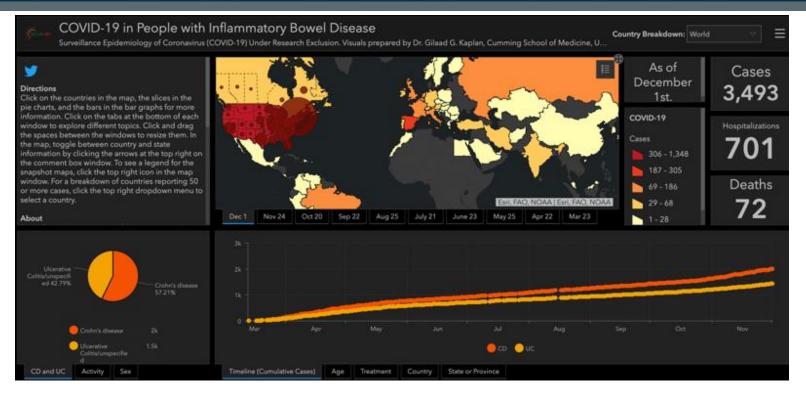


Presentation of COVID-19 in Patients with IBD

- COVID-19 can present as a flare in patients with IBD
 - Higher rates of new-onset diarrhea, abdominal pain, endoscopically active disease, and elevated biomarkers in patients with COVID-19 compared to patients without COVID-19
- Careful clinical evaluation, SARS-CoV-2 testing, and endoscopy may be required to distinguish between an IBD exacerbation and COVID-19 symptoms
- Fecal calprotectin can be elevated in patients with COVID-19 and diarrhea (current or resolved) vs. in patients without diarrhea



SECURE-IBD Registry: COVIDIBD.org



SECURE-IBD = Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion SECURE-IBD Database. 2020. https://covidibd.org. Brenner EJ, et al. *Gastroenterology*. 2020;159(2):481-491.e483. Ungaro RC, et al. *Gut*. 2020 Oct 20. [Epub ahead of print].



SECURE-IBD Registry: COVIDIBD.org

 > 3,500 patients with IBD in SECURE-IBD by beginning of December

Factors Associated with Severe COVID-19

- Older age, comorbidities
- Systemic corticosteroids
- Thiopurine mono and thiopurine/anti-TNF combo
- Any mesalamine or sulfasalazine

Factors **NOT** Associated with Severe COVID-19

- Anti-TNF monotherapy
- Ustekinumab (compared to anti-TNF)
- Vedolizumab (compared to anti-TNF)



Targeted Therapies Are NOT Associated with Worse IBD Outcomes: New York City Data

- Prospective case series of 86 patients with IBD, RA, PsA, AS, PsO with suspected or confirmed COVID-19
- 72% on biologics or JAK inhibitors
 - Higher percentage of hospitalized patients receiving targeted therapy vs. outpatients (76% vs. 50%, respectively)
- On multivariate analysis, hospitalization was associated with oral steroids, methotrexate, and hydroxychloroquine
- Hospitalization rate consistent with general population

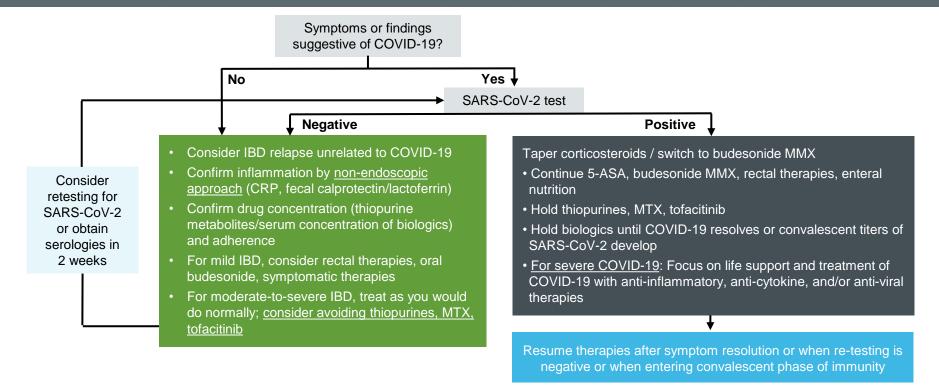


Outcomes of COVID-19 in 79 Patients with IBD in Italy

Risk Factor	COVID-19-Related Death		
NISK I ACIOI	OR (95% CI)	P Value	
Age > 65	19.6 (2.95, 130.6)	.002	
CCI score > 1	16.66 (1.8, 153.9)	.01	
UC diagnosis	2.95 (0.31, 27.73)	.34	
Active IBD	8.45 (1.26, 56.56)	.02	
Corticosteroids	6.28 (0.89, 44.24)	.064	
Thiopurines	-	-	
Anti-TNF	0.4 (0.04, 3.78)	.42	
Vedolizumab	-	-	



Management of IBD Relapse During the COVID-19 Pandemic: AGA Guidance





IBD Therapies to Treat COVID-19?

- Infliximab used in two patients for both IBD and COVID-19 successfully
- Anti-TNFs and JAK inhibitors are being evaluated as potential COVID-19 therapies
 - Tofacitinib: NCT04469114, NCT04332042, NCT04415151
 - Infliximab: NCT04425538
 - Adalimumab: ChiCTR2000030089
- Interleukin (IL)-23 blockade may potentially suppress cytokine storm syndrome; ustekinumab successfully used in a patient with PsA to treat COVID-19



Summary

- Patients with IBD are **not** at increased risk for COVID-19
- IBD biologics should be continued during the pandemic, except if positive for SARS-CoV-2
- Consider avoiding thiopurines, methotrexate, and tofacitinib



Case 1: Jackie

- Jackie is a 24-year-old Caucasian woman diagnosed with pan-UC 2 years ago
- Has been on infliximab since diagnosis and is now in remission
- Current symptoms: abdominal pain, bloody diarrhea (6 times/day)
- Infliximab trough level 15.4 μg/mL, ATI 0 U/mL
- Colonoscopy reveals moderately severe pan-UC (Mayo 2)
- C. diff negative
- SARS-CoV-2 negative



Audience Response

How would you proceed with Jackie?

- A. Increase infliximab dosage
- B. Switch to another anti-TNF
- C. Switch to vedolizumab
- D. Switch to ustekinumab
- E. I don't know; tell me the answer

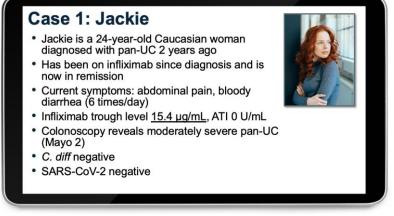


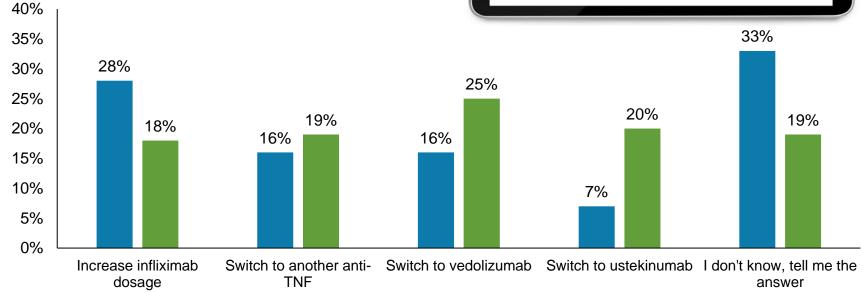


Questions Answers

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How would you proceed with Jackie?







Learning 3 Objective

Identify tips and tools for providers and patients in community settings during the COVID-19 era.

Case Study 2: Meet Anastacia

- Anastacia is a 37-year-old woman just diagnosed with moderately active Crohn's colitis
- Current symptoms: 10-12 bowel movements (BMs)/day (1-2x nocturnal frequency), urgency, frequent blood, abdominal cramps
- Colonoscopy: scattered ulcerations throughout the colon with rectal sparing consistent with moderately active Crohn's colitis
- C. diff and SARS-CoV-2 negative
- Was prescribed an intravenous (IV) biologic but is concerned about going to an infusion center out of fear of infecting her elderly mother who lives with her

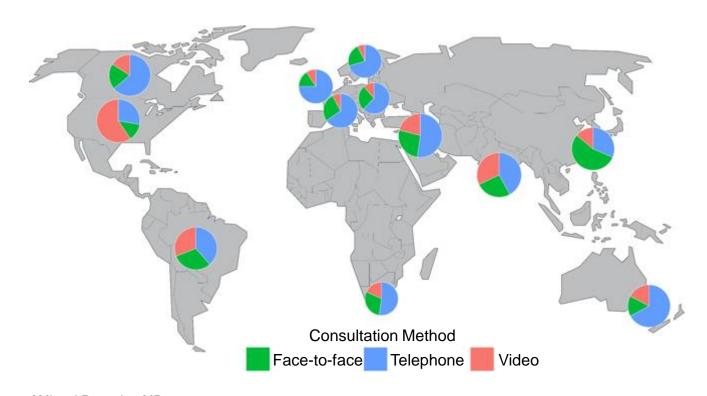
Audience Response

How would you approach your conversation with Anastacia?

- A. Address her concerns and explain relative risks and benefits of getting her medication
- B. Recommend switching to an option that does not require trips to an infusion center
- C. Recommend continuing her medication but only if she can be completely isolated from her mother
- D. I don't know; tell me the answer



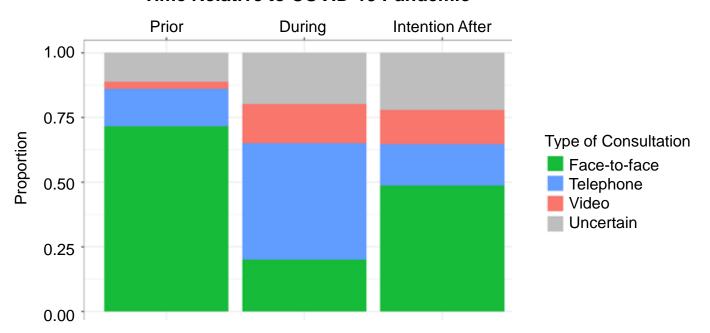
Mode of Patient Care During COVID-19





IOIBD Survey: *Pre-COVID -* Mostly Face to Face *During Pandemic -* Mostly Telephone or Video

Time Relative to COVID-19 Pandemic





Telehealth Before and After the Pandemic

Prior to COVID-19

- Almost universal that patients have access to a computer or cell phone
 - According to Pew Research Center's Internet and American Life Project, 91% of adults have access to a cell phone
 - Outcomes in chronic illness care are suboptimal
 - Patients seek more efficient and convenient ways to receive care

Survey on Use of Telehealth When the Pandemic Is Over

- 41% of GIs plan to use telehealth more often
- 63% of patients would like to have the option of seeing doctors in person and having telehealth appointments
- 25% of patients preferred telemedicine to in-office visits

Post COVID-19

- Practices had to rapidly implement telehealth to replace office visits
- CMS eased restrictions on types of programs to conduct telehealth visits (Skype for Business, FaceTime, Doximity now allowed)
- States waived licensing requirements so that providers could practice across state lines
- CMS and commercial payers agreed to reimburse for virtual visits at a rate equivalent with office visits*
- No requirements for existing relationship



^{*}Exception is that longer telehealth visits via telephone not reimbursed at a higher level CMS = Centers for Medicare & Medicaid Services Raine L. Pew Research Center Website. 2013. http://www.pewresearch.org/fact-tank/2013/06/06/cell-phone-ownership-hits-91-of-adults.

Advantages and Disadvantages of Telehealth

Advantages

- Patients often prefer virtual visits
 - Reduced travel and wait time
 - Convenient access from home
 - Fewer cancelled visits
- Providers can improve efficiency and increase volume
- Providers can bill for phone calls
 - New revenue opportunities
- Limits person-to-person contact

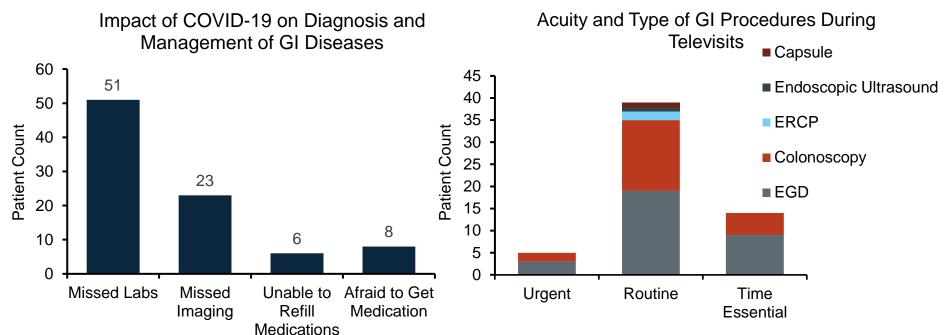
Disadvantages

- Privacy issues
- Difficult to develop a strong bond virtually
- Greater burden on administrative staff
- Inability to perform physical exam
- Challenges reaching patient population who are less technologically inclined
- Language barrier and lack of access to interpreter services
- Inability to recruit for research as well as inability to collect biospecimens
- Decreased point-of-care vaccinations and phlebotomy
- Challenges integrating trainees into visits
- Social isolation and fatigue of providers



Impact of Telehealth on Patient Management During COVID-19 Pandemic

Retrospective Analysis of Outpatient GI Visits in New York City (n = 151)





Best Practices in Using Telehealth

Telemedicine Setup

Choose a telemedicine platform that:

- Can provide a secure, private connection
- · Is compliant with local government regulations of telemedicine
- Can be easily implemented by both patients and provider

Pre-visit Preparation

- Develop a workflow to identify patients who are appropriate for telemedicine visit
- Provide instructions to patient how to access telemedicine platform, including tips for troubleshooting
- Clinic staff may opt to perform a "dress rehearsal" with patient
- Utilize electronic tools to collect history and data from patient
- Clinic staff can "pre" chart and input clinical information, i.e., IBD scores
- Find a space that is quiet, private, and without distractions to conduct visit
- Determine if telemedicine visit must be performed by provider in a clinic space (rather than from home)

During the Visit

- Medical assistant may "room" the patient and review insurance, demographics, preferred pharmacy and perform medication reconciliation
- Obtain verbal consent to perform video visit
- · Obtain history and limited physical examination
- Complete visit, communicating follow-up plan

Best Practices in Using Telehealth (continued)

Addressing Technology Challenges

- Can mostly be avoided by pre-visit trial with medical staff and/or providing a tip sheet for troubleshooting ahead of time
- Trial of alternate platform (e.g., FaceTime, WhatsApp)
- · If all else fails, convert to telephone visit

After the Visit

- Provide electronic copy of after-visit summary
- Route prescriptions and laboratory orders electronically
- Drive-through pharmacy and delivery options
- Instruct staff to contact patient to schedule follow-up care

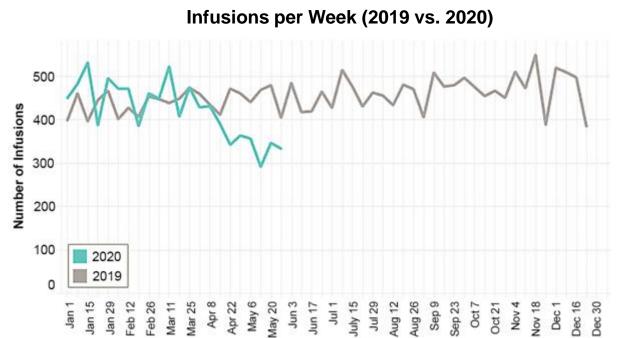
During the Visit

- Use similar note template to in-person documentation
- Use a physical exam template appropriate for video visit
- Document that patient provided consent for the modality used for the visit



Decreased Adherence to Infusible Biologics

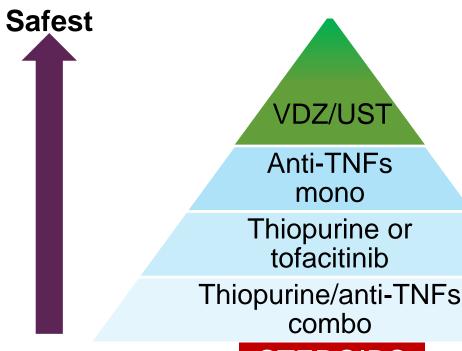
- U.S. nationwide VA cohort: up to 25% of patients had intervals of > 10 weeks between infusions
- Non-adherence to infusible biologics increased by 70%



Week of *



Safety Pyramid of Current IBD Medications



Inadequate treatment is an adverse event

STEROIDS



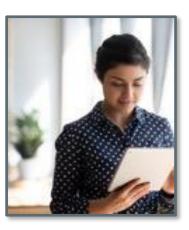
Summary

- Adherence rates to infusible biologics are decreased due to COVID-19 pandemic
- Telehealth approaches "are here to stay" after the pandemic



Case Study 2: Anastacia

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- Current symptoms: 10-12 BMs/day (1-2x nocturnal frequency), urgency, frequent blood, abdominal cramps
- Colonoscopy: scattered ulcerations throughout the colon with rectal sparing consistent with moderately active Crohn's colitis
- C. diff and SARS-CoV-2 negative
- Was prescribed an IV biologic but is concerned about going to an infusion center out of fear of infecting her elderly mother who lives with her



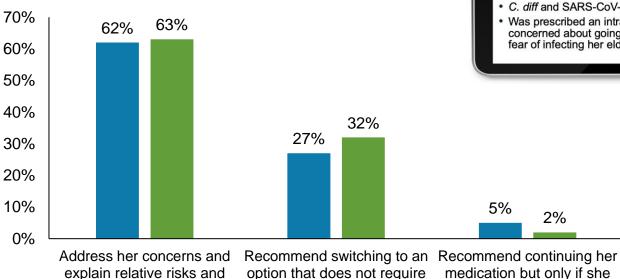
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How would you approach your conversation with Anastacia?

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- D. I don't know; tell me the answer



How would you approach your conversation with Anastacia?



trips to an infusion center

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medication but only if she can completely be isolated from her mother

2%

5%

I don't know; tell me the answer

3%

6%

benefits of getting her

medication

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Stay current on the recommended treatment and prevention approaches in COVID-19
- During the COVID-19 pandemic, continue IBD therapies and infusions; avoid high-dose steroids and weigh the risks and benefits of thiopurines, methotrexate, and tofacitinib
- Expand the use of telehealth during the pandemic when appropriate
- We will recommend the SARS-CoV-2 vaccine to our IBD patients

CME Outfitters

THE SHOW

Questions & Answers
Recorded on December 8, 2020

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Visit the COVID-19 and GI Hubs

Free resources and education to educate health care providers and patients on COVID-19

https://www.cmeoutfitters.com/covid19/

https://www.cmeoutfitters.com/gastrohub/

https://www.cmeoutfitters.com/gastro-patient-education-hub/

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