



# IMPACT OF **i**BD ON HEALTHCARE SYSTEMS

Supported by an educational grant from Janssen Biotech, Inc.

# Chronic Care Management Approaches and Preventing Complications in IBD

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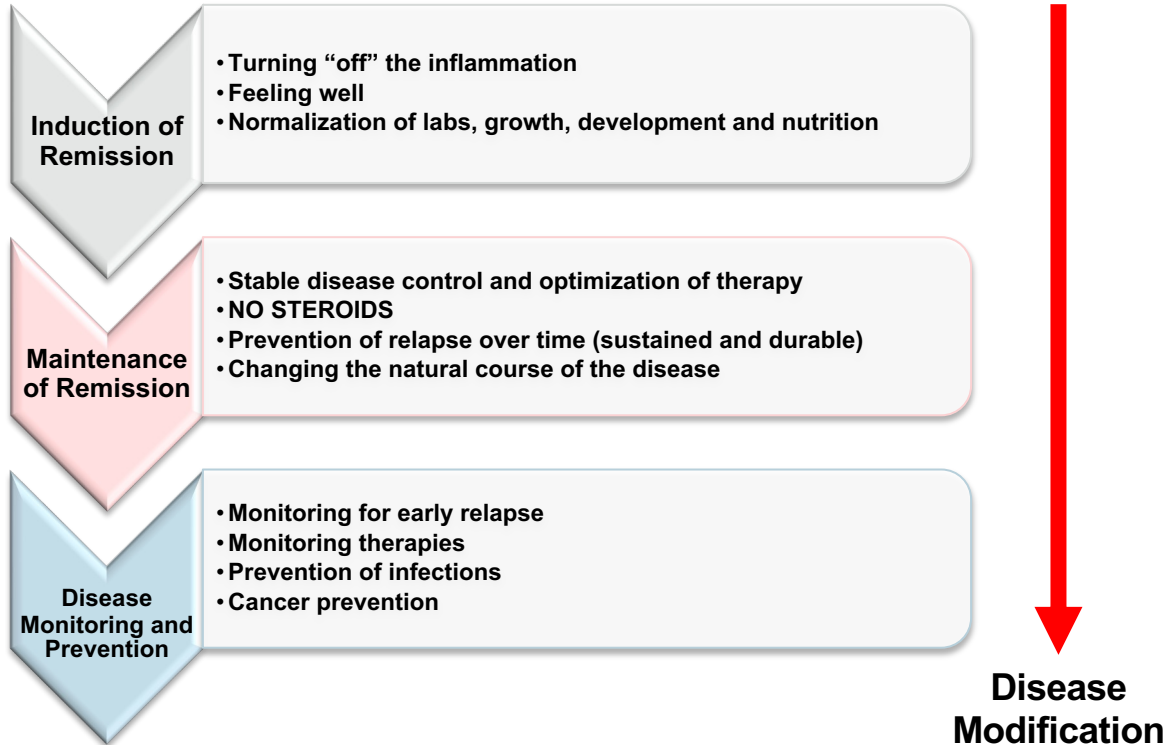
University of Chicago

# Disclosures

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# Modern Goals of IBD Management



SPECIAL ISSUE

Evolving Goals of  
Management for IBD

Reconsidering  
Disease Classification

Optimizing &  
Sequencing Therapies

Point-of-Care Testing &  
Monitoring Strategies

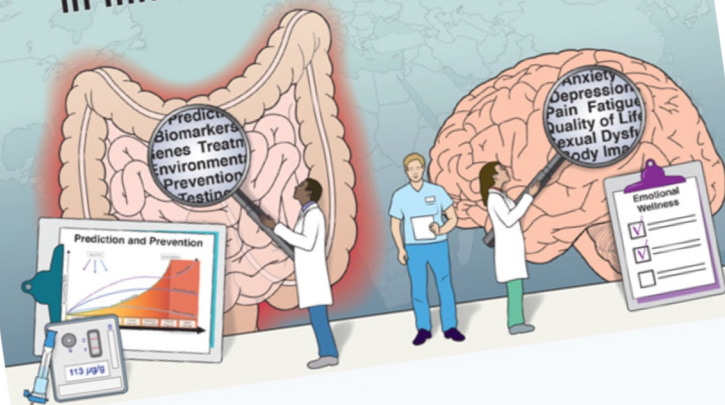
# Gastroenterology

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## Entering the Era of Disease Modification in Inflammatory Bowel Disease



# What Are the Preferred Outcomes in IBD?

## **Preferred Outcomes**

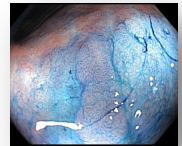
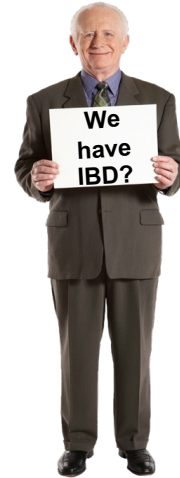
- Cure
- Improved quality of life
- Stable Remission
- No surgery/repeat surgery
- No cancer
- No hospitalization
- No infections
- Affordable care

## **Surrogates of Outcomes**

- Symptom improvement
- Avoidance of steroids
- Healed mucosa

# Why Outcomes ARE Improving in IBD

- **Improvements in therapies**
  - Achieve more stable disease control, modify natural history
  - Achieve deeper levels of remission, i.e. mucosal healing
- **Improvements in goals of management**
  - More emphasis on steroid-free care
  - Movement to proactive management rather than reactive management (from “crisis care” to “chronic care”)
  - Inclusion of long-term improved outcomes in goals
- **Better evidence**
  - Are we just performing better research? Asking better questions?
- **Other interventions have improved**
  - i.e. surgery, surveillance colonoscopy
- **The diseases have changed.**
  - People with IBD now are less ill than those of the past.



# Preventing Complications in IBD

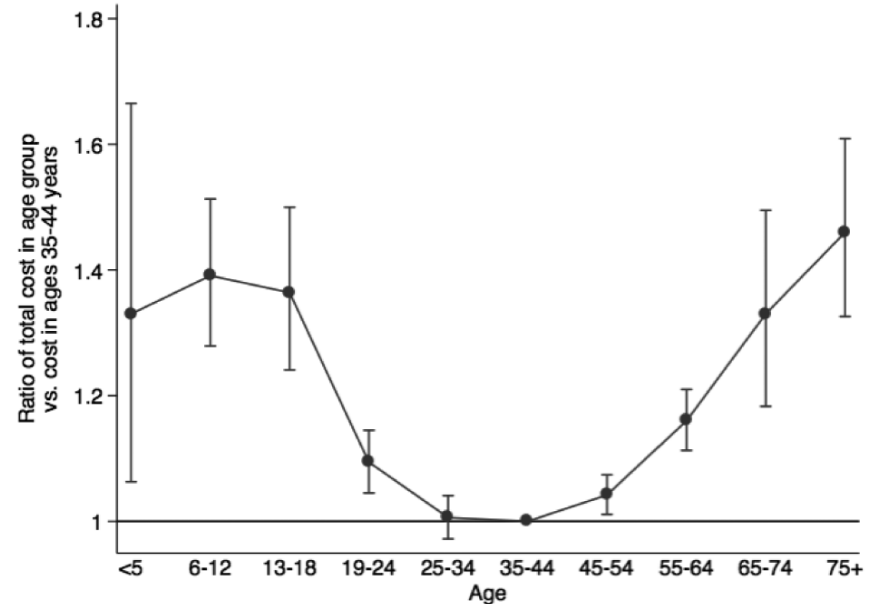
- Disease control: deep remission
- Disease monitoring, leading clinical recurrence/adverse events
- Drug monitoring (toxicity and efficacy)
- Vaccinations for vaccine preventable illnesses
  - Pneumococcal, influenza, herpes zoster, HPV, COVID-19
- Cancer prevention
  - Colorectal, lymphoma, skin, cervical, anal
- Mental health screening and treatment
  - Anxiety, depression
- Emerging co-existent medical issues
  - Cardiovascular morbidities
  - Sleep quality and disorders

## IBD Checklist for Monitoring & Prevention™

Name: _____		Date Completed	
MR#: _____		D.O.B.: _____	
<b>Vaccine Preventable Illnesses</b>		<b>Therapy Related Testing</b>	
<p><b>Diphtheria and Pertussis (Non-Live Vaccine)</b> Vaccinate with Tdap if not given within last ten years, or if Td a 2 years.</p> <p><b>Hepatitis A (Non-Live Vaccine)</b> Safe to administer to at-risk patients regardless of immunosuppression.</p> <p><b>Hepatitis B (Non-Live Vaccine)</b> Check hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody before initiating anti-TNF therapy. If non-immune consider vaccination series with non-live hepatitis B vaccine, 3 doses. If active viral infection or core Ab positive, check PCR and without anti-TNF therapy until active infection is excluded or treated appropriately.</p> <p><b>Herpes Zoster (Shingles) (Non-Live Vaccine)</b> Recombinant for all adults &gt; 50 yrs old regardless of immune suppression. Consider for patients &gt;18 yrs old based on their risk, particularly if on a JAK-inhibitor.</p> <p><b>HPV (Non-Live Vaccine)</b> Recommended for all patients 9-26 yrs old. Consider in patients up to 45 yrs old on a case-by-case basis for those at risk, regardless of immune suppression.</p> <p><b>Influenza (Non-Live Vaccine)</b> Annual dose for all patients during flu season. Avoid intranasal live vaccine in immunosuppressed patients.</p> <p><b>Meningococcal Meningitis (Non-Live Vaccine)</b> Vaccinate at-risk patients (college students, military recruits) if not previously vaccinated regardless of immunosuppression.</p> <p><b>MMR (Live Vaccine)</b> Contraindicated in immunosuppressed patients and those planning to start immunosuppressants within 4 weeks.</p> <p><b>Pneumococcal Pneumonia (Non-Live Vaccine)</b> For adults who have never received a pneumococcal vaccine or if unknown vaccination history, administer 1 dose PCV20 or 1 dose PCV15 followed by 1 dose PPSV23 at least 1 year later. (The minimum interval (8 weeks) can be considered in immunocompromised patients). For adults who previously received PPSV23 but not any pneumococcal conjugate vaccine (e.g. PCV13, PCV15, PCV20), administer one dose of PCV13 or PCV20 at least 1 year from PPSV23. For adults who received PCV13 but not all recommended doses of PPSV23, administer a single dose of PPSV23 &gt;8 weeks after PCV13. If the patient &lt;65 yrs old at first dose of PPSV23 and still &lt;65 yrs old, administer a 2nd PPSV23 &gt;5 years after 1st dose PPSV23. At 65 yrs old and &gt;5 years since last PPSV23, administer final dose PPSV23.</p> <p><b>SARS-CoV-2</b> Recommended for any age meeting local vaccine approval criteria, with any mRNA, non-replicating viral vector, or subunit vaccine, regardless of immune suppression.</p> <p><b>Varicella (Chicken Pox) (Live Vaccine)</b> Check Varicella Zoster Virus IgG. If negative consider vaccination. Can be considered in patients on low-dose immunosuppression (prednisone &lt;10mg/day, MTX, 6-MP, azathioprine), but not on biologics. Can administer &gt; 4 weeks prior to starting biologics.</p>		<p><b>Anti-TNFs/Anti-IL-12/23</b> Tuberculosis (TB) screening prior to initiating therapy with PPD skin testing and/or QuantiFERON-TB Gold assay, Chest X-Ray if high-risk and/or indeterminate PPD or QuantiFERON-TB Gold. Perform annual TB risk assessment and consider re-testing if high risk (including travel to endemic region). Also, see Hepatitis B vaccine, CBC, liver, and renal function prior to initiating therapy and routine monitoring while on therapy.</p> <p><b>Corticosteroids</b> – Also See Bone Health Document plan and use of corticosteroid-sparing therapy. Consider ophthalmology exam.</p> <p><b>Mesalamines</b> Annual renal function monitoring.</p> <p><b>Methotrexate</b> CBC, liver, and renal function prior to initiating therapy. Routine CBC, liver, and renal function monitoring while on therapy.</p> <p><b>Natalizumab</b> Enroll in TOUCH program. Check JCV antibody and treat if negative. Repeat JCV antibody every 6 months after initiating therapy. Routine CBC and liver function monitoring while on therapy.</p> <p><b>Ozanimod</b> Perform ECG and check BP prior to initiating therapy and routine monitoring while on therapy. CBC, liver function, urology, and TB prior to initiating therapy and routine monitoring while on therapy. In patients with a history of uveitis or macular edema, obtain an evaluation of the fundus, including the macula.</p> <p><b>Thiopurines</b> TPMT, CBC, and liver function prior to initiating therapy. Routine CBC and liver function monitoring while on therapy. Consider NUDT15 polymorphism prior to dosing.</p> <p><b>Tofacitinib</b> CBC, liver, fasting lipid profile, and tuberculosis (TB) screening with PPD skin testing and/or QuantiFERON-TB Gold assay prior to initiating therapy. Chest X-Ray if high risk and/or indeterminate PPD or QuantiFERON-TB Gold. Perform annual TB risk assessment and consider re-testing if high risk (including travel to endemic region). Routine CBC and liver function monitoring while on therapy. Fasting lipid profile 4-8 weeks after initiating therapy. Screen for risks of thrombosis at <a href="https://www.medicines.com/canada/canadian-consumer-thromboboolein-2005">https://www.medicines.com/canada/canadian-consumer-thromboboolein-2005</a>. Consider alternative therapies if high risk. Vaccination against HZV should be strongly considered when treating with tofacitinib.</p> <p><b>Vedolizumab</b> CBC, liver, and renal function prior to initiating therapy and routine monitoring while on therapy.</p>	
<b>Bone Health</b>		<b>Cancer Prevention</b>	
<p><b>Vitamin D 25-OH Level</b> Serial monitoring of vitamin D levels, supplement if deficient.</p> <p><b>Bone Density Assessment</b> Assess bone density if the following conditions are present: 1. Steroid use &gt; 3 months 2. Inactive disease but past chronic steroid use of at least 1 year within the past 2 years 3. Inactive disease but maternal history of osteoporosis 4. Inactive disease but malnourished or very thin 5. Inactive disease but amenorrheic 6. Post-menopausal women, regardless of disease status.</p> <p><b>Prescription of Calcium &amp; Vitamin D</b> Co-prescription of calcium and vitamin D tablets for all patients with each course of oral corticosteroids and if vitamin D deficient or insufficient.</p>		<p><b>Colon Cancer</b> If ulcerative colitis beyond the rectum or Crohn's is present in at least 1/3 of the colon, perform surveillance colonoscopy for neoplasia detection after 8 years of disease. Interval varies based on risk factors (annually to every 2-3 years). High-definition scopes preferred; augmented imaging (NBI or dye-spray) and targeted biopsies recommended.</p> <p><b>Cervical Cancer</b> If immunocompromised, perform annual PAP smears. If results of 3 consecutive PAPs are normal, perform every 3 yrs. If not immunocompromised and situated low-risk for cervical dysplasia, follow general population screening guidelines.</p> <p><b>Skin Cancer</b> Annual visual exam of skin by dermatologist if immunocompromised and recommend sun exposure precautions.</p>	
<b>Miscellaneous</b>		<b>Assessment of Anatomic Location and Activity</b>	
<p><b>Smoking Cessation</b> Discuss at every visit.</p> <p><b>Nutritional Assessment</b> B12 if ileal disease or resection, iron panel. Assess for risk of malnutrition.</p> <p><b>Behavioral Health</b> Screen and address mental health co-morbidities.</p>		<p>Discusses at every visit.</p>	

# Key Drivers for Costs in IBD Patients

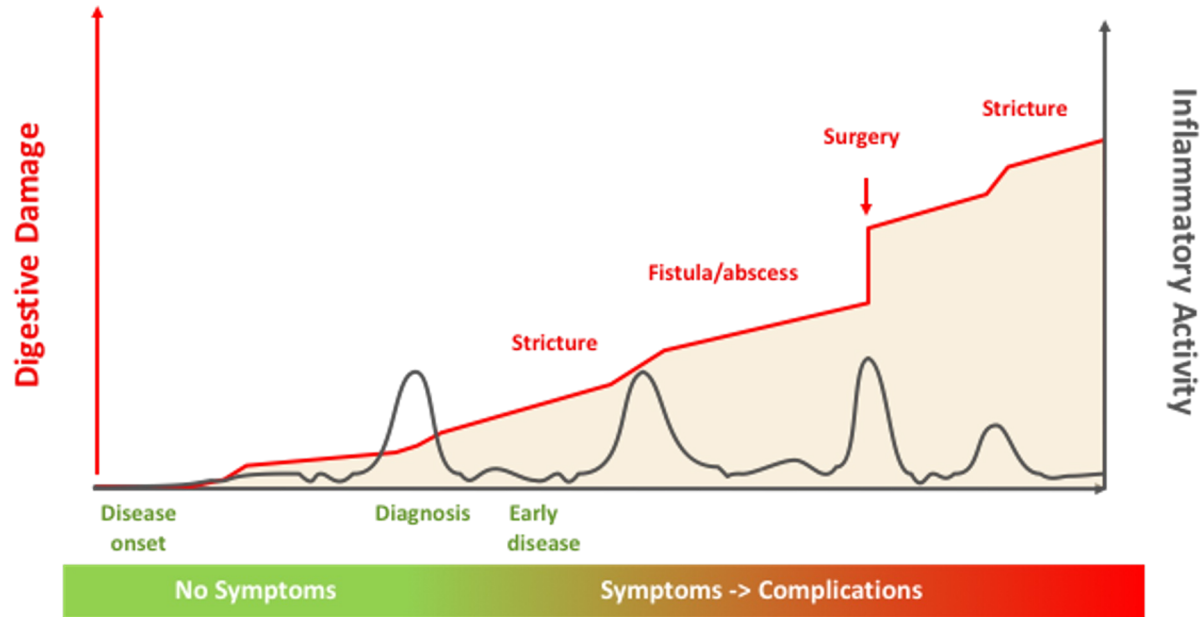
- Age
- Treatment with Specific therapeutics (biologics, opioids or steroids)
- ED use
- Healthcare services associated with relapse, anemia, mental health comorbidities



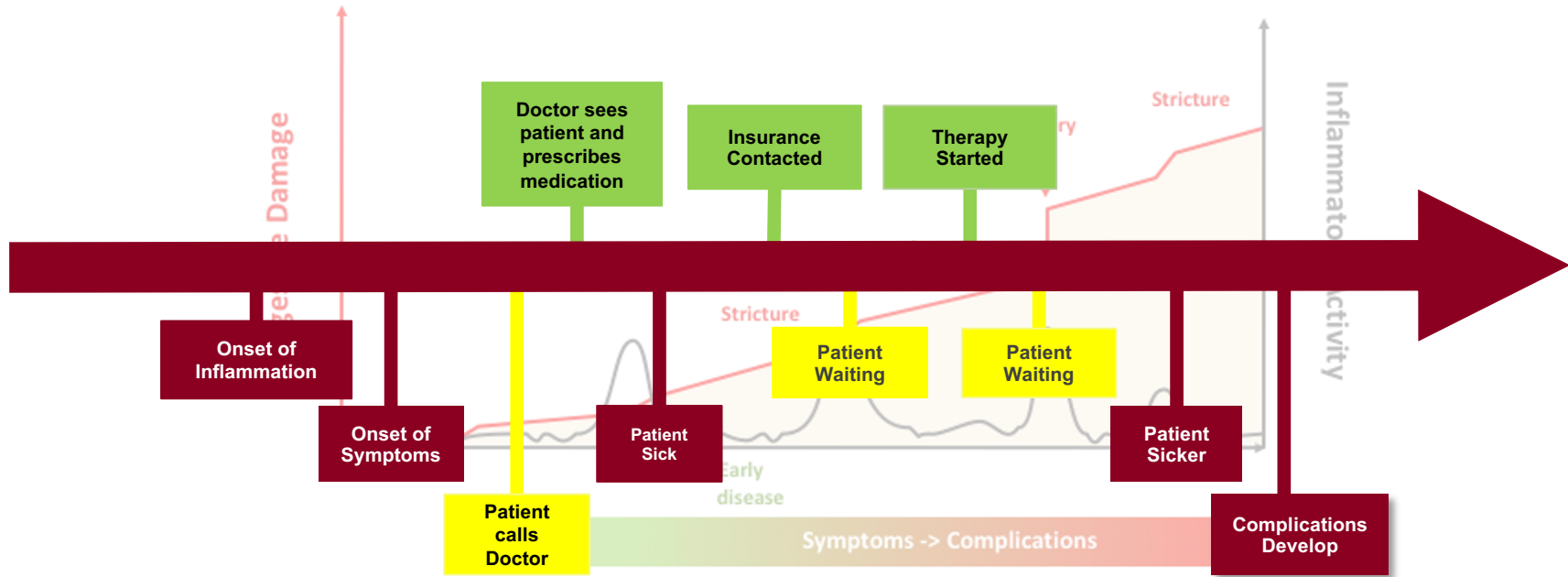
# Challenges to Preventing Complications in IBD

- Limitations of existing therapeutics
- Current disease management paradigms are too slow
- Available testing
- Diffusion of responsibility: who is the appropriate person to arrange vaccines, dermatology visits, etc?
- Time!
- Payers
- Patient acceptance and adherence

# How IBD Is Currently Managed: Delays and Disease Progression



# How IBD Is Currently Managed: Delays and Disease Progression

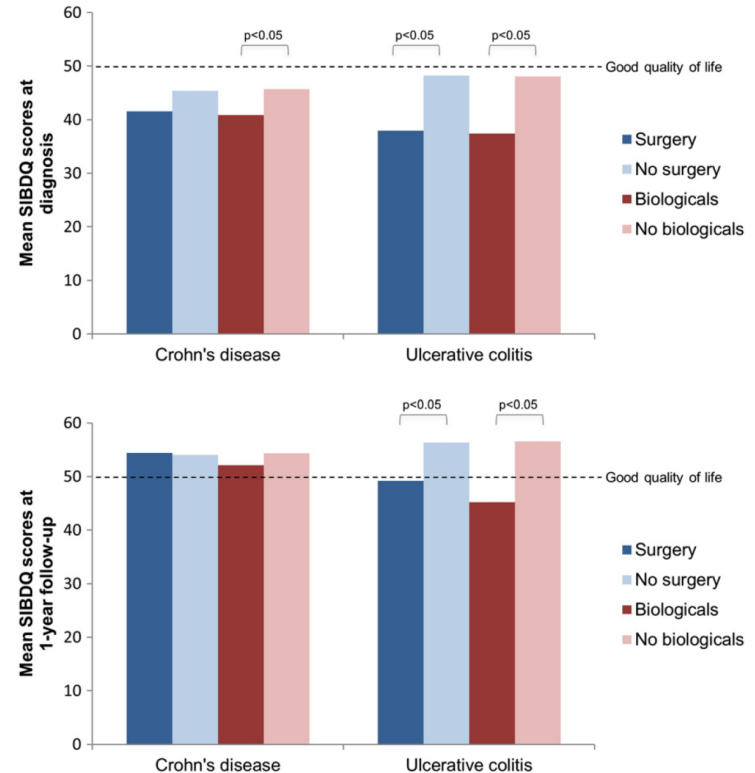


# What We've Learned About Therapy and Achieving Preferred Outcomes in IBD

- Effective therapies improve QoL (of course!)
- Proactive disease monitoring is essential
- As therapies evolve, so does our ability to achieve preferred outcomes
- A personalized approach to management can optimize therapy
- Timing matters
- Individual pharmacokinetics matter
- Adherence to therapy matters

# Improvements in Quality of Life in IBD Associated With Effective Therapy

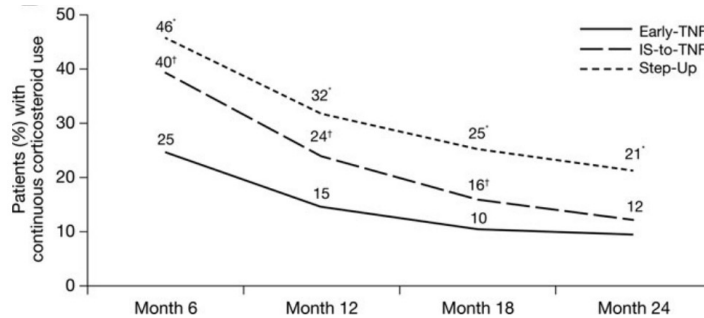
- ECCO-Epicom Study (2014) compared quality of life of 1560 unselected IBD patients from Eastern and Western Europe.
- Quality of life during the first year of diagnosis improved if disease activity reduced.



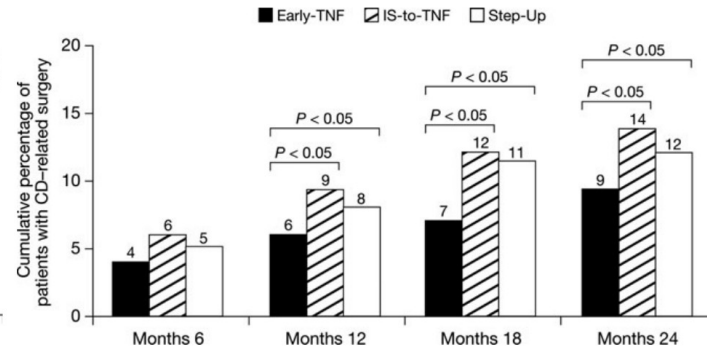
# Earlier Use of Anti-TNF Biologic Therapy in Crohn's Disease Has Better Outcomes

- Claims data assessment
- >3700 patients all who received anti-TNF at some point

**Continuous corticosteroid use during anti-TNF therapy.**



**CD-related Surgery during anti-TNF therapy**

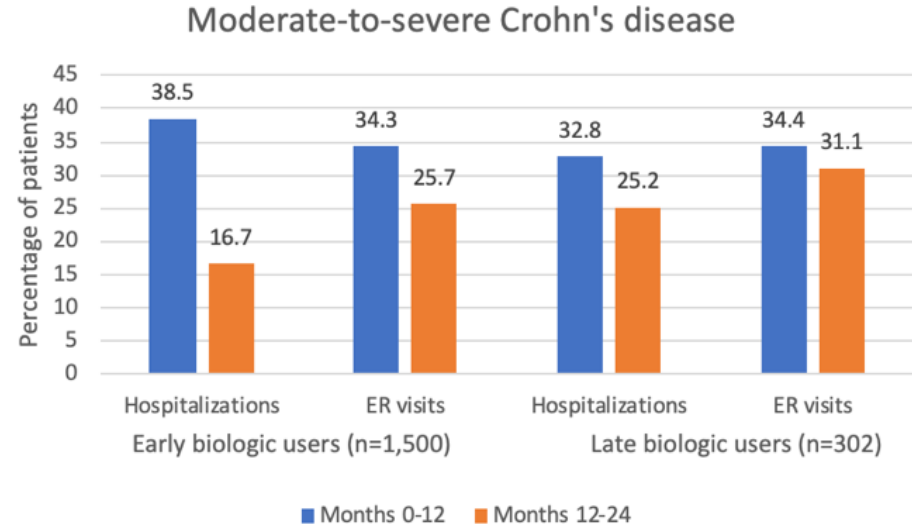


\*P < 0.05 IS-to-TNF group versus other groups.

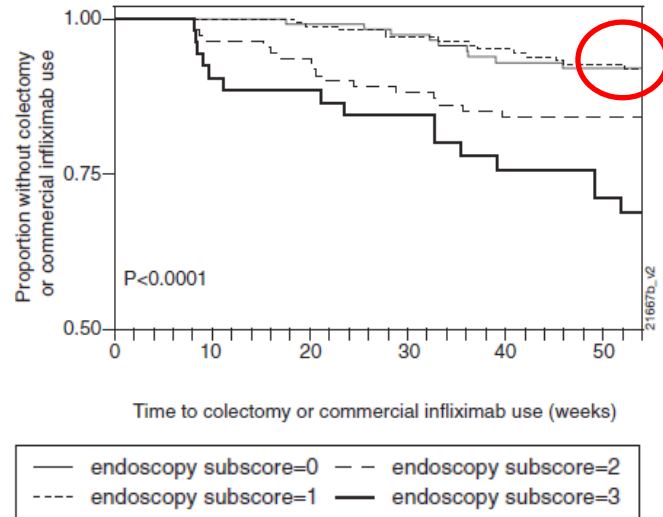
Rubin DT et al. *Inflamm Bowel Dis.* 2012;18(12):2225-2231.

# Early Initiation of Biologics in Crohn's Disease Associated With Decreased Hospitalization and ER Visits

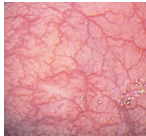
- Retrospective study on CD patients from 2010-2016
- Groups:
  - Early biologic users ( $\geq 1$  biologic claim  $\leq 12$  months post diagnosis)
  - Late biologic users ( $\geq 1$  biologic claim 12-24 months post diagnosis)
  - Non-biologic users
- Results:
  - **Early biologic users** had a statistically significant **decrease in ER visits and hospitalizations** compared to **late biologic users** in 12-24 month period relative to 0-12 month period



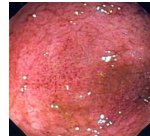
# Mucosal Healing With Infliximab Associated With Less Colectomy in Ulcerative Colitis



0 = NORMAL



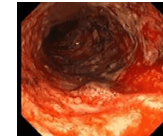
1 = MILD



2 = MODERATE



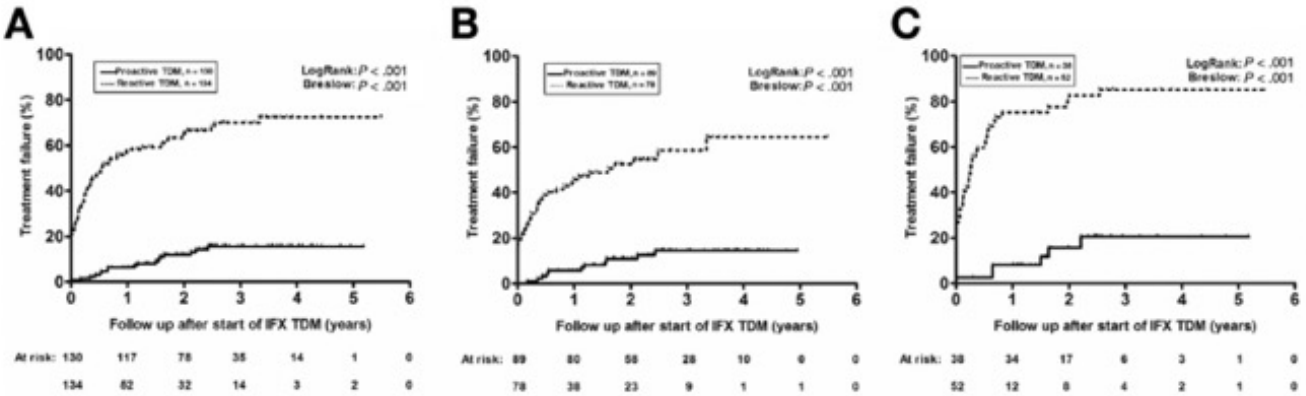
3 = SEVERE



# Improved Long-term Outcomes of Patients With Inflammatory Bowel Disease Receiving Proactive Compared With Reactive Monitoring of Serum Concentrations of Infliximab



Konstantinos Papamichael,<sup>\*</sup> Karen A. Chachu,<sup>‡</sup> Ravy K. Vajravelu,<sup>§</sup> Byron P. Vaughn,<sup>||</sup> Josephine Ni,<sup>§</sup> Mark T. Osterman,<sup>§,b</sup> and Adam S. Cheifetz<sup>\*,b</sup>



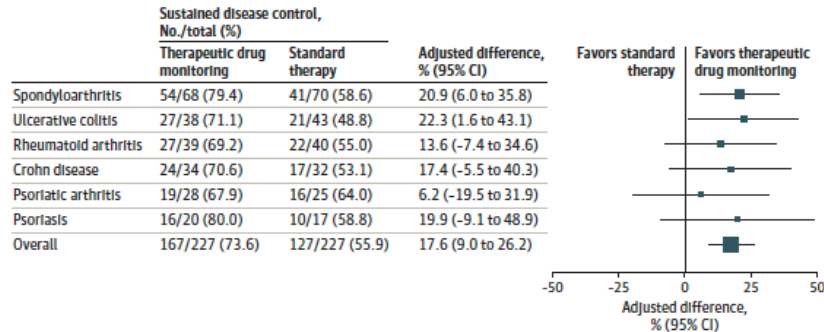
**Figure 2.** Kaplan-Meier cumulative probability curves of treatment failure in patients undergoing either reactive (*dotted line*) or proactive therapeutic drug monitoring (TDM) (*solid line*) based on the first infliximab (IFX) concentration measured (A), stratified also by the type of IBD, Crohn's disease (B) or ulcerative colitis (C).

## Effect of Therapeutic Drug Monitoring vs Standard Therapy During Maintenance Infliximab Therapy on Disease Control in Patients With Immune-Mediated Inflammatory Diseases: A Randomized Clinical Trial

Silje Watterdal Syversen, MD, PhD; Kristin Kaasen Jørgensen, MD, PhD; Guro Løvik Goli, MD, PhD; Marthe Kirkesæther Brun, MD; Øystein Sandanger, MD, PhD; Kristin Hammersbøen Bjørlykke, MD; Joseph Sexton, PhD; Inge Christoffer Olsen, PhD; Johanna Elin Gehin, MD; David John Warren, PhD; Rolf Anton Klaasen, PhD; Geir Noraberg, MD; Trude Jannecke Bruun, MD; Christian Kvikne Dotterud, MD, PhD; Maud Kristine Aga Ljoså, MD; Anne Julsrud Haugen, MD, PhD; Rune Johan Njålla, MD; Camilla Zetteli, MD; Carl Magnus Ystrøm, MD; Yngvill Hovde Bragnes, MD; Svanaug Skorpe, MD; Turid Thune, MD; Kathrine Aglen Seeberg, MD; Brigitte Michelsen, MD, PhD; Ingrid Marianne Blomgren, MD; Eldri Kveine Strand, MD; Pawel Mielnik, MD, PhD; Roald Tøp, MD; Cato Mørk, MD, PhD; Tore K. Kvien, MD, PhD; Jørgen Jahnsen, MD, PhD; Nils Bostad, MD, PhD; Espen A. Haavardsholm, MD, PhD

Randomized 1:1  
Proactive TDM (dose/interval adjustments based on scheduled serum drug levels and ADAs (TDM group; n = 228) or Standard infliximab therapy without drug and ADA monitoring (standard therapy group; n = 230).

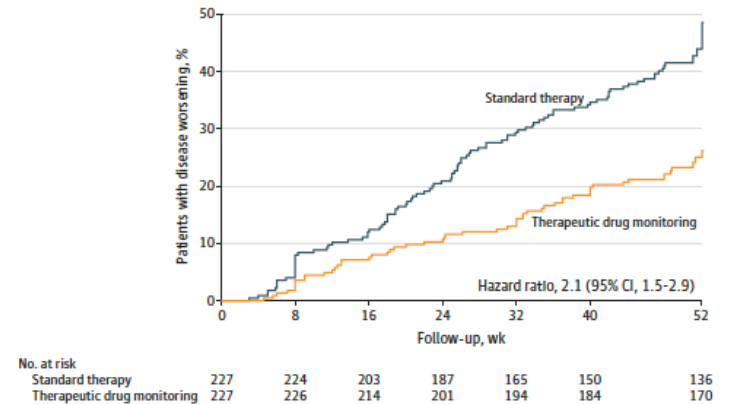
Figure 2. Sustained Disease Control With No Disease Worsening (Primary Outcome)



### Disease worsening:

- major change in treatment, consensus btw pt and MD
- HBI/partial Mayo score

Figure 3. Time to Disease Worsening

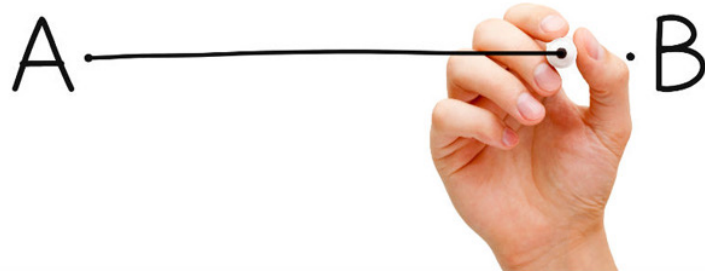


The primary outcome of sustained disease control without disease worsening was observed in 167 patients (73.6%) in the TDM group and 127 patients (55.9%) in the standard therapy group.

# Why Don't We Achieve Preferred Outcomes in Everyone?

- We are too late
- Therapies don't work
- Therapies are not optimized
- We are treating the wrong problem – symptom improvement is “enough”

**Errors of  
commission  
vs.  
Errors of omission**



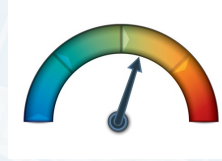
# Treating to a Target as a Way to Individualize Therapy

- Systematic assessment of an identified “target” and serial adjustment of therapy until the target is reached or until the patient refuses or we run out of options
- Primary goal: maximize health-related quality of life
  - Control of symptoms
  - Normalization of function and social participation
  - Prevention of progressive structural damage
- Presumption is that achievement of target may improve QoL, and change the natural history of the disease





# How Do We Monitor IBD?



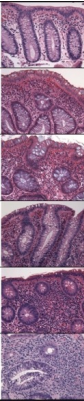
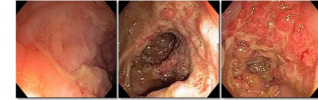
- **Symptom assessment**

- Patient Reported Outcomes
- Extra-Intestinal Manifestations
- Quality of Life (includes mental health)



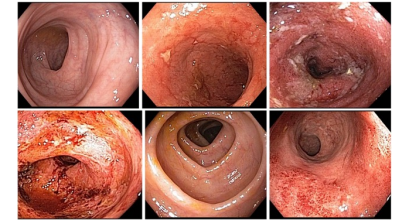
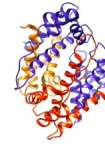
- **Endoscopic assessment**

- SES-CD
- Mayo Endoscopic Score, UCEIS
- Histological assessment (evolving)

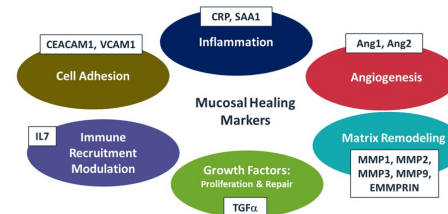


- **Biomarkers**

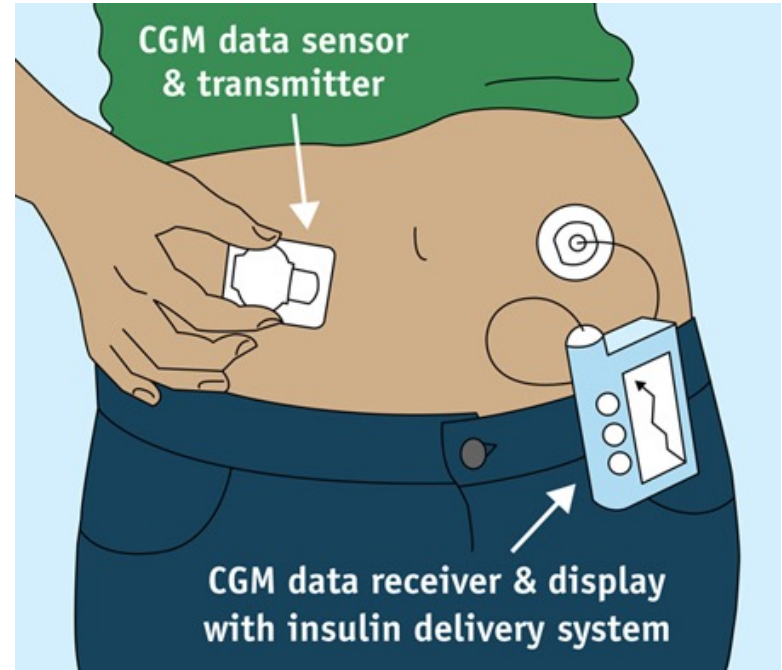
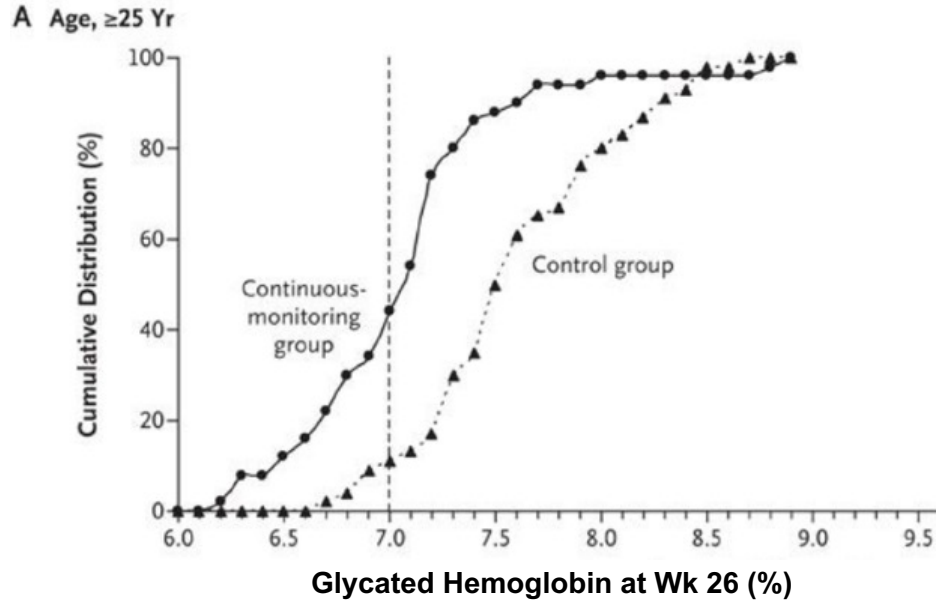
- Serum (CRP, hemoglobin, albumin)
- Stool (calprotectin, lactoferrin)
- Composite markers (Endoscopic Healing Index<sup>1</sup>)



- **Drug concentrations**

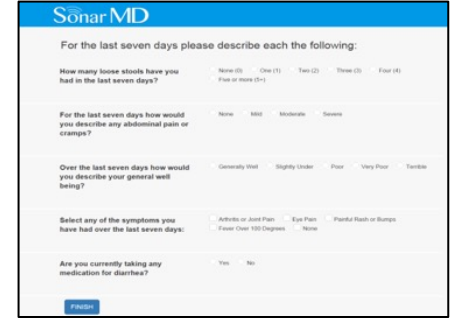
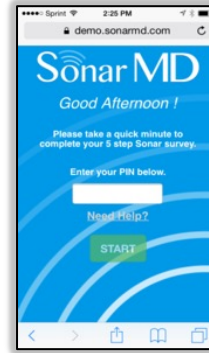


# Continuous Glucose Monitoring



# Sonar MD

- Patients automatically sent a survey to assess disease activity once a month
- Physician dashboard shows patients with risk assessment
- Providers instantly alerted with any potential downward trend

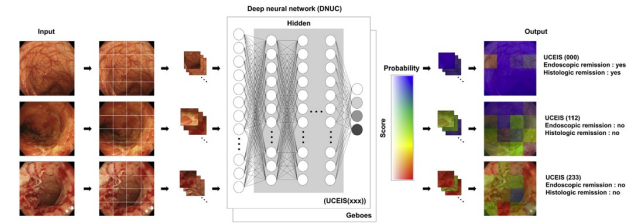
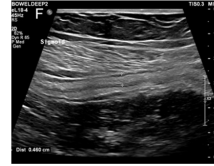
A screenshot of a physician dashboard. At the top, it says "Dr. John, Janet" and "Henry Gastroenterology Group". There are tabs for "Management", "Reports", and "Administration". A "Patients" dropdown menu is visible. Below that is a table with columns: "No.", "Last Ping", "Risk", "Score", "Disease", "Inflammation", "Comorbidity", "Assess", "Notes", "History", and "Edit". The table contains several rows of data with color-coded risk levels (Low, High) and assessment buttons (ASSESS).

No.	Last Ping	Risk	Score	Disease	Inflammation	Comorbidity	Assess	Notes	History	Edit
1	06/10/2015	Low	3.5	IBD	High	High	ASSESS			
2	06/10/2015	Low	3.5	IBD	High	High	ASSESS			
3	06/10/2015	Low	3.5	IBD	High	High	ASSESS			
4	06/10/2015	Low	3.5	IBD	High	High	ASSESS			
5	06/10/2015	Low	3.5	IBD	High	High	ASSESS			
6	06/10/2015	Low	3.5	IBD	High	High	ASSESS			



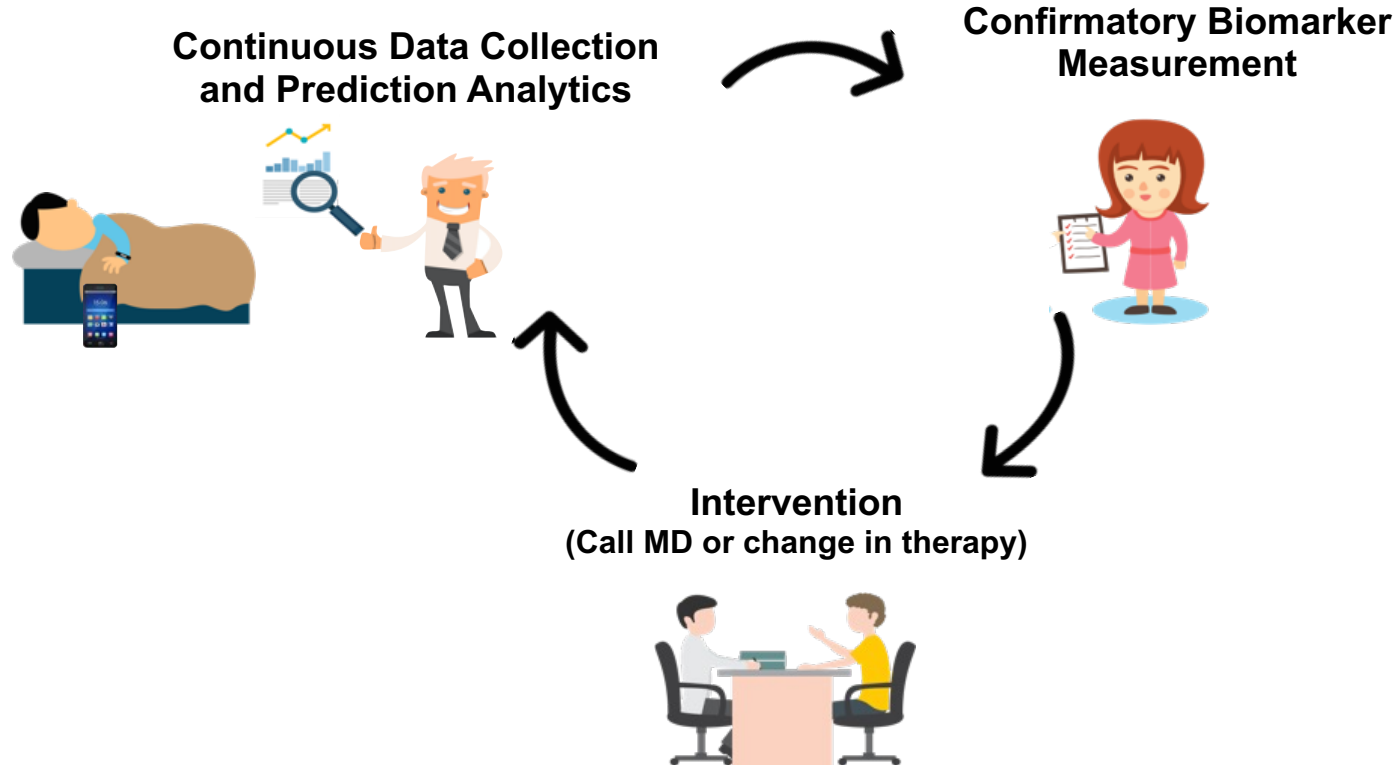
# The Near Future of Disease Monitoring in IBD

- Point of care testing
  - intestinal ultrasound
  - finger stick assessments
- At home testing
- Artificial intelligence for endoscopic scoring
- Predictive therapeutic biomarkers
- Companion diagnostics
- Passive biosensors



Wearable sweat sensor worn on lower arm

# Vision for Future IBD Management



# Summary: Chronic Care Management Approaches and Preventing Complications in IBD

- Outcomes of IBD patients have improved for multiple reasons, one of which has been the evolution of treatment goals emphasizing objective disease control.
- We must shift from reactive care to proactive care in order to prevent disease- and drug-related complications
- We need managed care partnership to support preventive care and informed treatment adjustments
- Future modifications will include proactive therapeutic drug monitoring and more specific targets of inflammation control.



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