IMPROVECARENOW™

MODEL IBD CARE—A GUIDELINE FOR CONSISTENT RELIABLE CARE

Diagnostic and therapeutic interventions that are appropriate and recommended for a very large percentage of children and adolescents with Crohn's disease and ulcerative colitis.[1]

COMPLETE DIAGNOSTIC AND INITIAL EVALUATION:

- CBC, ESR, CRP, iron studies, and serum albumin.
- Esophagogastroduodenoscopy with biopsy and colonoscopy with biopsy.
- Imaging of the small intestine (MR enterography, CT enterography, or capsule endoscopy). Minimizing or avoiding exposure to ionizing radiation is recommended.
- If concern for perianal disease, consider pelvic imaging (MRI pelvis) and/or surgical exam under anesthesia.
- Obtain stool inflammation marker (fecal calprotectin or lactoferrin) to establish a baseline level.
- Other studies as indicated, including stool samples to rule out enteric infection.

EXTENT OF DISEASE: Documentation of disease location (esophagus, stomach, duodenum, jejunum, ileum, right colon, transverse colon, left colon, rectum, perianal).

CROHN'S DISEASE PHENOTYPE: Based on the Paris classification (age at diagnosis; disease above the distal ileum; non-stenosing, non-penetrating; both penetrating and stenosing).

SEVERITY: Physician Global Assessment (Quiescent, Mild, Moderate, Severe); short Pediatric Crohn's Disease Activity Index (sPCDAI); Pediatric Ulcerative Colitis Activity Index (PUCAI) at baseline and routine follow-up visits.

VISIT FREQUENCY: It is recommended that each patient be examined and evaluated at least once every 6 months (≤ 200 days).

ROUTINE DISEASE ACTIVITY AND SAFETY MONITORING: To assess disease activity and screen for extraintestinal manifestations of disease or side effects of therapy, consider monitoring the following lab tests periodically (at least every 6-12 months or more frequently if indicated).

CBC, CMP, gGTP, ESR, CRP, stool inflammation marker (calprotectin or lactoferrin), 25-hydroxy vitamin D, and iron studies (see iron deficiency section of model care guidelines).

[1] The guidance in this document does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, considering individual circumstances, may be appropriate.

TREATMENT WITH INFLIXIMAB AND INFLIXIMAB BIOSIMILARS:

1. It is recommended that tuberculosis testing (skin test (PPD) and/or Interferon-gamma release assays (IGRAs) and/or a chest radiograph) be obtained before initiation of infliximab therapy and annually if insurance mandates.
2. It is recommended hepatitis B immune status be assessed with a hepatitis B surface antigen, surface antibody, and core antibody before initiation of infliximab therapy and reimmunize as indicated. Reimmunization should not delay treatment.
3. For **induction of remission**, the FDA recommended dose is infliximab 5 mg/kg IV (or rounding up to the nearest 100 mg if consistent with the desired treatment range) used as an initial dose, with repeat doses of 5 mg/kg IV 2 and 6 weeks later (0, 2, and 6 weeks). In pediatrics, especially in the setting of more severe and/or extensive disease including perianal disease, higher starting doses and/or shorter intervals between infusions are often utilized to optimize response and should be considered.
4. For **maintenance of remission**, the FDA recommended dose is infliximab 5 mg/kg IV (or rounding up to the nearest 100 mg if consistent with the desired treatment range) given every 8 weeks. In pediatrics, especially in the setting of more severe and/or extensive disease including perianal disease, higher doses and/or shorter intervals between infusions are often utilized to optimize response and should be considered.
5. It is recommended that the infliximab trough level be measured just prior to the first maintenance dose (typically at week 14). Consider testing prior to week 14 if clinically indicated.
6. For patients treated with and poorly responsive to infliximab, it is recommended to measure infliximab trough and antibody to infliximab (ATI) levels. In patients responding well to infliximab but who lose response prior to the next infusion, consider dose adjustment followed by measurement of infliximab trough and antibody to infliximab (ATI).
7. The target trough level is generally a minimum of 5 µg/mL though higher trough levels may be necessary. A trough of > 10 µg/mL is associated with greater healing for perianal fistulizing disease.
8. If the measured trough is below the desired therapeutic range, consider increasing the dose and/or decreasing the interval between infusions. If the measured trough is significantly above the desired therapeutic range with good response, consider decreasing the dose and/or increasing the interval between infusions if clinically appropriate.
9. Shortened infusion times or rapid infusions have been shown to be both safe and cost-effective after infusion tolerance has been established.

TREATMENT WITH ADALIMUMAB:

1. It is recommended that tuberculosis testing (skin test (PPD) and/or IGRA and/or a chest radiograph) be obtained before initiation of adalimumab therapy and annually if insurance mandates.
2. It is recommended hepatitis B immune status be assessed with a hepatitis B surface antigen, surface antibody, and core antibody before initiation of adalimumab therapy and reimmunize as indicated. Reimmunization should not delay treatment.
3. **Crohn's Disease: Induction phase:**
    a. For patients weighing ≥ 40 kg it is recommended that adalimumab 160 mg SQ be given once, then 80 mg SQ two weeks later.
    b. For patients weighing < 40 kg it is recommended that adalimumab 80 mg SQ be given once, then 40 mg SQ two weeks later.
4. **Crohn's Disease: Maintenance phase**:
    a. For patients weighing ≥ 40 kg FDA recommended dosing is adalimumab 40 mg SQ be given every other week.
    b. For patients weighing < 40 kg FDA recommended dosing is adalimumab 20 mg SQ be given every other week.
5. **Ulcerative Colitis: Induction phase:**
    a. For patients **< 18 years of age and weighing ≥ 40 kg** it is recommended that adalimumab 160 mg be given once, then 80 mg weekly for two weeks.
    b. For patients **< 18 years of age and weighing < 40 kg** it is recommended that adalimumab 80 mg be given once, then 40 mg weekly for two weeks.
    c. For patients **> 18 years of age**, current FDA dosing guidelines are identical to those for Crohn's disease.
6. **Ulcerative colitis: Maintenance phase**:
    a. For patients **< 18 years of age and weighing ≥ 40 kg** FDA recommended dosing is that adalimumab be given as 80 mg every other week or 40 mg weekly.
    b. For patients **< 18 years of age and weighing < 40 kg** FDA recommended dosing is that adalimumab be given as 40 mg every other week or 20 mg weekly.
    c. For patients **> 18 years of age**, current FDA dosing guidelines are identical to those for Crohn's disease.
7. Consider checking a drug trough level just prior to one of the first maintenance doses in weeks 6-12.
8. For patients treated with adalimumab, when disease is active it is recommended that the adalimumab trough level and antibody to adalimumab be measured.
9. The target trough level is generally > 7.5 µg/mL though higher trough levels may be necessary. Higher trough levels are associated with greater healing for perianal fistulizing disease.
10. If the measured trough is below the desired therapeutic range, consider increasing the dose and/or decreasing the interval between injections. If the measured trough is significantly above the desired therapeutic range, consider decreasing the dose and/or increasing the interval between injections if clinically appropriate.
11. In pediatrics, especially in the setting of more severe and/or extensive disease including perianal disease, higher doses and/or shorter intervals between injections are often utilized to optimize response and should be considered.

TREATMENT WITH VEDOLIZUMAB:

1. The FDA has approved in patients ≥ 18 years of age for treatment of Crohn's disease and ulcerative colitis.
2. Induction Dosing:
    a. 6 mg/kg with a maximum dose of 300 mg IV (1,2)
    b. Induction dosing at 0, 2, and 6 weeks
3. Maintenance:
    a. q 8 weeks (some patients may require interval to be shortened to every 4-6 weeks to achieve remission)

TREATMENT WITH USTEKINUMAB:

1. The FDA has approved in patients ≥ 18 years of age for treatment of Crohn's disease and ulcerative colitis. It is recommended that tuberculosis testing (skin test (PPD) and/or Interferon-gamma release assays (IGRAs) and/or a chest radiograph) be obtained before initiation of ustekinumab therapy and annually if insurance mandates.
2. IV induction:
    a. 6 mg/kg (< 40 kg)
    b. 260 mg (≥ 40 and < 55 kg)
    c. 390 mg (55-85 kg)
    d. 520 mg (> 85 kg)
3. Maintenance:
    a. 45 mg sub-Q (< 40 kg) every 8 weeks (some patients may require interval to be shortened to every 4-6 weeks to achieve remission)
    b. 90 mg sub-Q (≥ 40 kg) every 8 weeks (some patients may require interval to be shortened to every 4-6 weeks to achieve remission)

TREATMENT WITH TOFACITINIB:

1. The FDA has approved in patients ≥ 18 years of age for treatment of ulcerative colitis.
2. Labs prior to initiation:
    a. TB test, complete blood count with differential, lipid panel and liver enzymes. Reassessment of lipid parameters should be performed approximately 4–8 weeks following initiation.
    b. Shingrix vaccination when eligible
3. Induction:
    a. 10 mg BID for at least 8 weeks
4. Maintenance:
    a. 5 mg BID (some patients may need to continue 10 mg twice a day to achieve remission)

TREATMENT WITH THIOPURINES:

1. Prior to initiation of a thiopurine, determine thiopurine methyltransferase (TPMT), preferably by phenotype.
2. Consider testing for EBV status prior to initiation. Caution use in EBV naive patients due to increased risk of lymphoma and HLH.
3. Choose a starting dose of azathioprine or 6-mercaptopurine (6MP) based on TPMT. If there is:
    a. Absent or very low TPMT activity, do not use a thiopurine.
    b. Intermediate TPMT activity, start azathioprine at 1.0-1.5 mg/kg/day or 6MP 0.5-0.75 mg/kg/day.
    c. Normal to high TPMT activity, start azathioprine at 2.0-3.0 mg/kg/day or 6MP 1.0-1.5 mg/kg/day.
4. For the maintenance dose of thiopurine use either at least the starting dose as defined above or adjust the dose based on blood concentrations of thiopurine metabolites or evidence of toxicity.
5. Monitor for toxicity at regular intervals with CBC and ALT.
6. For patients treated with a thiopurine, when disease is moderately or severely active it is recommended that the 6-TGN level be measured (if not done in the previous 90 days).

TREATMENT WITH METHOTREXATE:

1. For induction of remission, the recommended dose of methotrexate is 15 mg/m^2, up to 25 mg, IM, subcutaneous or oral once a week.
2. For maintenance of remission, the recommended dose of methotrexate is 10-15 mg/m^2, up to 15-25 mg, IM, subcutaneous or oral once a week.
3. Folic acid supplementation is recommended in a dose of 1 mg daily.
4. Monitor for toxicity at regular intervals with CBC and ALT.
5. Weekly low dose oral methotrexate can be considered for combination therapy with biologics (common dose ranges include 7.5-15 mg weekly as determined by patient weight).

TREATMENT WITH 5-ASA:

When using the following medications, use the recommended doses:

1. Mesalamine 80 (60-100) mg/kg/day up to 4.8 g/day for active colitis.
2. Mesalamine at least 30 (30-100) mg/kg/day up to 4.8 g/day for maintenance of quiescent or inactive colonic disease.
3. For distal colonic disease, consider mesalamine suppository or enema.
4. Sulfasalazine 70 (50-80) mg/kg/day up to 4 g/day for active colitis.
5. Sulfasalazine at least 25 (25-80) mg/kg/day up to 4 g/day for maintenance of quiescent or inactive colonic disease.
6. Patients on sulfasalazine should be on folic acid supplementation at a dose of 1 mg daily.
7. Annual BUN, Cr, and urinalysis for patients on 5-ASA to assess for renal toxicity.

TREATMENT WITH EXCLUSIVE ENTERAL NUTRITION (EEN):

1. EEN can be used to induce remission in pediatric patients with Crohn's disease.
    a. EEN is as effective as corticosteroids for inducing clinical remission and may lead to higher rates of mucosal healing.
2. Polymeric formula is as effective as elemental formula.
3. EEN can be administered by mouth (PO) or by nasogastric tube (NGT).
    a. Remission rates and compliance rates appear similar between these 2 routes.
4. Consider using 100% EEN (formula only) to start, but no less than 80% formula with up to 20% regular diet during treatment.
    a. Partial enteral nutrition (PEN) is not recommended for induction of remission.
5. Utilization of EEN should be undertaken in conjunction with a registered dietitian.

Please refer to the ICN Nutrition Care Manual for detailed information on EEN and center examples. You need an ICN Hub account to access this manual.

TREATMENT WITH STEROIDS:

1. Prednisone may be used for induction of remission, although minimizing steroid exposure is a priority. Long-term treatment with prednisone can induce significant adverse effects and is ineffective for maintenance of remission. Prednisone resistance or dependence warrants consideration of escalation of medical therapy.
2. To induce remission the dose of prednisone is 1-2 mg/kg/day, rounding up to the nearest 5 mg, up to 40 to 60 mg per day, PO for 1-4 weeks (induction phase).
3. Taper prednisone and discontinue it within 16 weeks after treatment was begun.
    a. Prednisone resistance is defined as an inadequate improvement after 2-4 weeks of treatment with prednisone.
    b. Prednisone dependence is present when a patient, who initially improves in response to prednisone treatment, develops a recurrence when the dose is being tapered or within 6 months after prednisone is discontinued.
    c. Prednisone resistance or dependence warrants consideration of escalation of therapy
4. Oral, ileal-release budesonide may be used for induction of remission for mild ileocecal disease with lower likelihood of adverse events than conventional steroids.
    a. Typical dosing for patients > 40 kg – 9 mg once daily for 6 weeks, then tapered to 6 mg once daily for 2 weeks, then 3 mg once daily for 2 weeks. Currently, dosing for children < 40 kg is not defined and therefore should be determined by care provider.
5. Oral, colonic-release budesonide (MMX 9 mg) may be used for induction of remission for mild ulcerative colitis refractory to 5-ASA before oral prednisone. Typical dosing is 9 mg daily for 8 weeks without a taper, however alternate day tapering over 2-4 weeks can be considered.

TREATMENT AND SCREENING FOR IRON DEFICIENCY ANEMIA:

1. Evaluate and treat for both iron deficiency anemia (IDA) and iron deficiency without anemia (IDWA).
2. At diagnosis, obtain complete blood count, reticulocyte count, ferritin, and transferrin saturation (Tsat). Repeat every 3-months for patients with active disease. Monitor every 6-12 months with inactive disease.
3. Serum ferritin levels may be elevated despite empty iron stores as it is an acute phase reactant.
4. Consider obtaining Vitamin B12 and folate levels if vitamin deficiency is suspected.

5. Treatment goals include normalizing Hgb, replenishing iron stores, correcting vitamin deficiencies, and improving quality of life.
6. There is no current standardized treatment approach and therefore oral or IV iron can be considered based upon the clinical situation.
    a. Consider IV iron in patients with active inflammation, moderate-to-severe anemia, those requiring blood transfusions to replenish iron stores, and in patients who are intolerant or unresponsive to oral iron products.

TREATMENT AND MONITORING CONSIDERATIONS AFTER BOWEL RESECTION IN PATIENTS WITH CROHN'S DISEASE:

1. It is recommended that post-operative medical therapy be started or continued in patients after a surgical resection, particularly in those with high risk factors for disease recurrence.
2. Monitor patients who have undergone resection for postoperative disease recurrence with ileocolonoscopy within 6-12 months following resection. Alternative methods of post-resection monitoring may include MR enterography and/or fecal calprotectin/lactoferrin.

HEALTH MAINTENANCE RESOURCES:

Health maintenance is an important part of IBD care. The Crohn's and Colitis Foundation has provided thorough health maintenance resources available for both practitioners (Pediatric Health Maintenance Technical Guide) and parents (Health Maintenance for Pediatric IBD Patients: Discussion guide for parents) to review.

NUTRITIONAL AND GROWTH ASSESSMENT

The Pediatric IBD Nutritional Status Algorithm and Pediatric Growth Status Algorithm have been taken from the ICN Nutrition Care Manual.

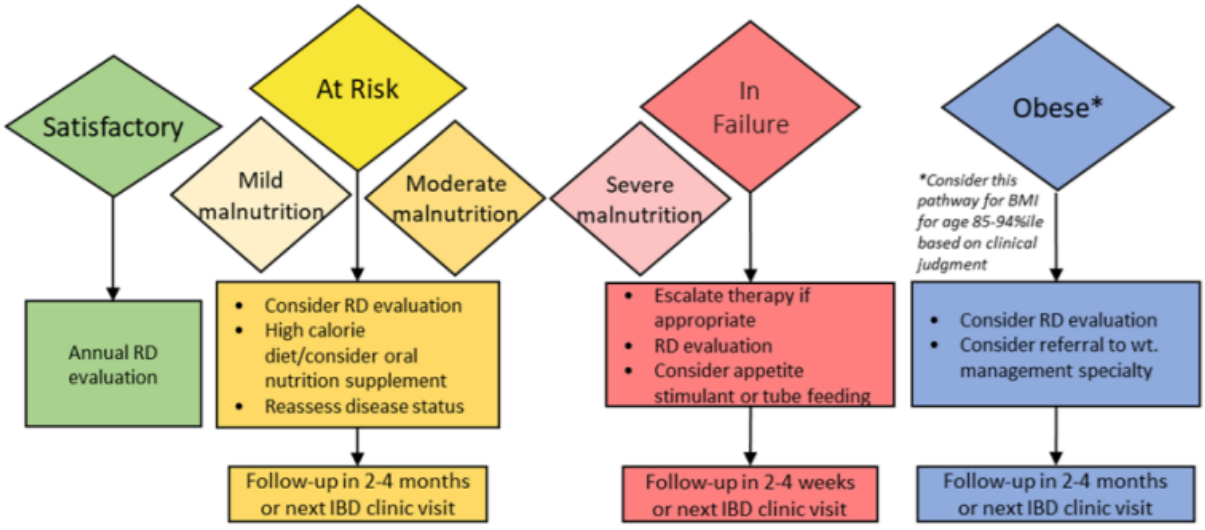
Pediatric IBD Nutritional Status Algorithm

Classify Patients at Every Visit

Nutritional Status	BMI for age z-score	Weight loss	Decline in BMI for age z-score
At Risk Mild Malnutrition	-1.0 to -1.9	5-7.4% usual body weight	Decline of 1 to 1.9
At Risk Mod Malnutrition	-2.0 to -2.9	7.5-9.9% usual body weight	Decline of 2 to 2.9
In Failure Severe Malnutrition	≤-3.0	≥10% usual body weight	Decline of ≥3
Obese	BMI for age ≥95%ile, not at risk or in failure		

Malnutrition = one or more indicators. Pt. with multiple indicators, use clinical judgement to categorize degree of malnutrition.

Table adapted from ASPEN/AND pediatric malnutrition consensus statement[1]



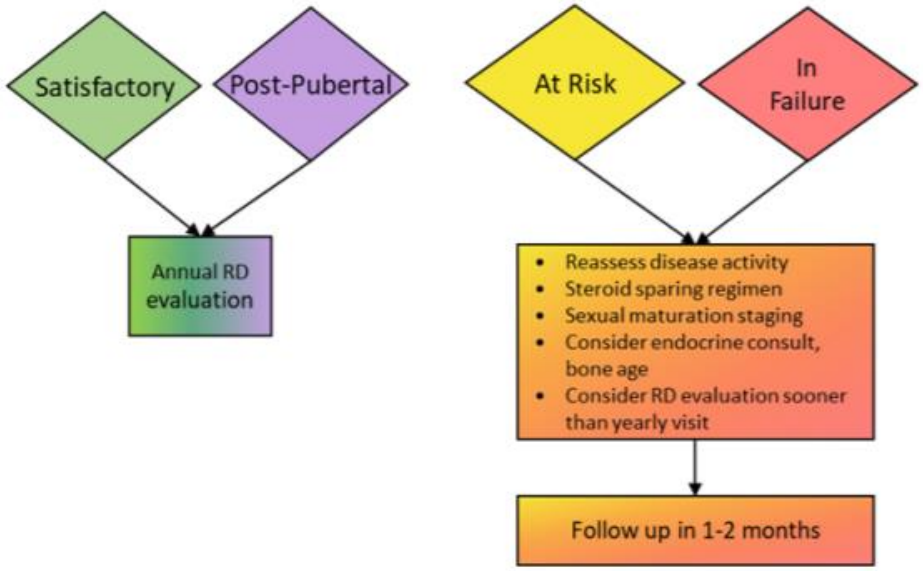
Pediatric IBD Growth Status Algorithm

Classify Patients at Every Visit

Growth Status	Height z-score (adjust for low-mid parental height)	Height velocity Z-score	Decline in height z-score
Post-Pubertal	Growth completed based on clinical judgment*		
At Risk	-1.3 to -1.8	-1 to -1.9	Decline of 1 to 1.9
In Failure	≤-1.9	≤-2	Decline of ≥2

Pt. at risk/in failure if one or more indicators identified. Pt. with multiple indicators, use clinical judgement to categorize degree of risk.

*consider >14-1/2 years (female), >17-1/2 years (male) if no growth delay present



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