



# Communicating the benefits and risks of inflammatory bowel disease therapy to patients and families

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## Purpose of review

Treatment options for inflammatory bowel disease (IBD) have rapidly expanded as the treatment paradigm has shifted from controlling symptoms to reducing lifetime inflammatory burden. Families are confronted with the actual and perceived risks of this ever-expanding array of choices. We aim to review the shared decision-making process in pediatric IBD to ensure an optimal therapeutic plan for the child and their family.

## Recent findings

Mucosal healing is a critical treatment target in pediatric IBD but it may not coincide with clinical symptoms. Evidence-based therapies carry important risks, some of which may be less severe than previously suspected, and a family's understanding of these risks plays a crucial role in how they make health decisions. To form an effective shared therapeutic plan, the physician must incorporate an understanding of the values of both the child and family along with their lived experience of illness.

## Summary

To limit harm and promote health in pediatric IBD, the physician must communicate collaboratively with the child and their family to form mutually understood goals of care – both subjective experiential and objective biological – and appreciate actual and perceived risks of treatment options to effectively educate families and navigate toward the best treatment choices.

## Video abstract

<http://links.lww.com/MOP/A27>

## Keywords

Crohn's disease, inflammatory bowel disease, pediatrics, shared decision-making, ulcerative colitis

## INTRODUCTION

Treatment options for inflammatory bowel disease (IBD) have rapidly expanded over the past decade along with increasing knowledge of how to optimize therapy. With these improved treatment options, the goals of therapy have moved from symptom relief, or clinical remission, to control of the underlying inflammatory response, thereby preventing bowel damage and positively altering the natural history of the disease. Making treatment decisions with families, while integrating actual and perceived risks, demands open, direct and unbiased dialogue. We aim to provide a framework for this decision-making process, outline the natural history of IBD, delineate current treatment paradigms, and provide guidance on the utilization of available therapies.

## MAKING DECISIONS

Decisions that involve the well-being of children inherently carry substantial gravity. IBD, comprised of Crohn's disease and ulcerative colitis, is life-long, uncommonly life-threatening, invariably burdensome on quality of life, and, in the pediatric patient, potentially detrimental to growth and

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## KEY POINTS

- The shift in the treatment paradigm in pediatric IBD from minimizing clinical symptoms to reducing lifetime inflammatory burden and bowel damage by targeting mucosal healing necessitates the effective communication of the benefits and risks of treatment options to address both patient-centered goals and biological targets.
- Risk education in pediatric IBD, including actual and perceived risks of therapies and risks of inaction and progression of disease, must incorporate a child's and family's prior understanding of risk and their worldview.
- When there is clinical equipoise, shared decision-making, a process of discriminating benefits, and risks of treatment options in the context of a family's value system to make a mutual choice, will ensure the successful pursuit of therapeutic plans for children and adolescents with IBD.

development. IBD treatment is best implemented through a team approach maximizing the available medical and surgical options, each of which has their own potential benefits and risks.

### Understanding risk and numeracy

The Hippocratic tradition guides us to accurately determine therapeutic risk. To facilitate clinical decision-making, the physician's role is to explain the balance between risk and benefit, garner agreement, and proceed with the clear choice. To make an informed and shared decision with a family, all participants require an understanding of risk. Numeracy is the ability to interpret numbers and the real world meaning of ratios. The level to which patients are competent in numeracy has been shown to affect their decision-making about medical risk. For instance, it has recently been shown that patients with lower levels of numeracy were less likely to present to an emergency room at the appropriate time for evaluation of acute coronary syndrome [1]. This applies to parents too; lower parental numeracy, as it applies to food labels, has been associated with childhood underweight and overweight [2<sup>¶</sup>]. An early assessment of a family's level of numeracy, with targeted education when necessary, may aid the decision-making process.

In general, when people are uncertain on how to fully interpret data, there is a proven tendency to make the facts conform to one's worldview, a concept known as 'motivated reasoning' [3<sup>¶</sup>]. An exploration of this worldview may clarify for the physician the family's thought process and provide

the opportunity to mitigate misinterpretation. Cultural influences and community norms can also impact perceived risk, as evidenced in parental vaccine acceptance and other health-related decisions [4,5]. Recognition of these influences is essential to preventing negative impacts and promoting reassurance of a given choice. Broadly, we can improve our parents' and children's understanding of risk through visual aids [6] and instructional videos [7,8].

### Prognostic disclosure and informed consent

In pediatric practice, parents provide 'informed permission' for treatment to be delivered to their children in conjunction with developmentally appropriate assent from the child/adolescent. It is the healthcare provider's duty to explain the treatment benefits and risks, assess the parents' and child's understanding of these benefits and risks and capacity to judge the balance, and obtain consent for any given therapy [9]. Incorporating the developmental level of the child in these conversations and decisions lies within the fabric of pediatrics. There has been an evolution of prognostic disclosure from a 'protective' approach (the possibility of bad outcomes may adversely impact a child's psychosocial well-being) through an 'open' approach (information is empowering and necessary to psychosocial growth) to a nuanced recognition that the developmental stage of a child must be factored into the degree to which potential and expected long-term outcomes are communicated [10].

### Shared decision-making and preference-sensitive decisions

Many decisions in pediatric IBD are now preference sensitive, in which multiple acceptable treatment options are available for a given clinical scenario. Until there is an increased ability to assess a given patient's risk for disease progression [11], the indefinite and unpredictable nature of IBD paired with the risks of IBD therapies often result in clinical equipoise and at these times, the healthcare provider should engage in collaborative communication to foster shared decision-making. Shared decision-making is a process in which a physician applies expertise in the evidence to guide a patient through multiple acceptable treatment options to arrive at the one that best fits their value system. The process should be deliberate and open and may be facilitated by decision-making aids, which, when validated, have been shown to improve patient knowledge and confidence in the ultimate choice. Education

of the benefits and risks of the treatment options, along with the risk of disease progression and complications, are critical to this process.

When parents foresee substantial treatment benefit they may be willing to live with the known risks of IBD therapies [12,13<sup>11</sup>,14]. Parents whose children started biologic therapy for IBD or juvenile idiopathic arthritis reported less decision regret when the decision-making process was perceived as shared between physician–parent as opposed to primarily by the parents [15<sup>12</sup>]. Ultimately, the healthcare team should strive to instill confidence in making the right choices together with the family while relieving the burden of the decision.

## NATURAL HISTORY

### Risks of inaction

IBD, although historically characterized as an auto-inflammatory disease with relapses, remissions, and flares, is, more accurately, a disease of progressive inflammatory burden and bowel damage, complicated by periods of clinical decline. Untreated IBD in children carries enough risk that an expert panel determined that the use of placebo in pediatric IBD clinical trials was unethical when the study agent had already demonstrated efficacy in adults [16].

### Progression of disease

Both Crohn's disease and ulcerative colitis have the potential for disease progression and complications. A subset of children with Crohn's disease will progress to – or may even present with – internally penetrating or stricturing behavior. These phenotypes can lead to significant morbidity, such as abdominal sepsis, hospitalization, surgical intervention, and growth failure. Children with ulcerative colitis may have extension of their disease, develop acute severe colitis, or the urgent need for colectomy. The clearest risk for progression of disease in either Crohn's or ulcerative colitis is lack of effective control of the inflammatory process [17].

## TAILOR TREATMENT TO TARGET

Although it is the physician's first duty to avert undue harm, their ultimate duty is to promote health. Given the chronic, currently incurable nature of IBD, the goal of any given therapy must be well defined and incorporate the values of the child/family along with objective clinical endpoints. Originating from the rheumatoid arthritis literature, the goals of therapy in IBD have entered the era of 'treat-to-target', with mucosal healing –

the endoscopic appearance of a normal intestine – becoming a primary biological target [18].

### Framing goals

Most patients experience a disease through an illness narrative and their treatment decisions are guided by their quality of life. This takes on multiple dimensions in the setting of the family experience of disease. Pediatricians, however, must recognize important prognostic targets and guide therapy to achieve them. Normalizing growth and development along with clinical wellness through the induction and then maintenance of a durable remission should be paramount goals. Increasingly, durable remission is tied to 'deep remission' which includes not only the relief of clinical symptoms but the control of inflammation and prevention of bowel damage as evidenced by mucosal healing [19]. Vexingly, clinical symptoms often do not correlate with mucosal healing. It is therefore necessary to educate children and families about the value of biological targets in treatment. The prior treatment model of treating flares and aiming for clinical remission may fit with a patient's perspective of pursuing treatment when they feel ill. The concept of bowel healing may not coincide with a child or family's motivation to continue treatments when they feel well. It is imperative to frame the risks of untreated disease alongside the benefits and risks of treatment in order arrive at mutual long-term goals that satisfy both known biological benefit and the family's perceived benefit (Table 1).

### Following through

Adherence to a given treatment is optimized when patients understand the time to onset of action, side-effects and safety, route of administration, efficacy, and cost of the therapy. As the decision process unfolds, it is advantageous to incorporate an assessment of self-management skills and to foster their development in the child and family. Problem-solving skills, a trusting patient–provider relationship and a strong social support network all enhance self-management and adherence to therapy [20].

## TREATMENT OPTIONS

### Corticosteroids

Corticosteroids reduce inflammation and may help with symptom control but carry a plethora of side-effects—adrenal suppression, growth failure, decreased bone mineral density, increased risk of infection, behavioral changes, among others.

**Table 1.** Goals of treatment in pediatric inflammatory bowel disease

Disease process	Subjective experiential	Objective biological
Short term		
General inflammation	Relieve pain, feel better	Normal ESR, CRP, calprotectin
Intestinal inflammation	Stop diarrhea, stop blood in stool	Normal endoscopic appearance
Growth	Same height as peers, family	Normal height velocity, on target to midparental height
Malnutrition	Improve energy	Weight gain, micronutrient sufficiency
Long term		
Inflammatory burden	Avoid repeat hospitalizations	Extend time in endoscopic remission
Bowel damage	Avoid unnecessary surgery	No strictures, fistulas, abscesses, or other internally penetrating complication
Treatment effect	Owing to therapy	Owing to disease
Infections	Minimize increased risk of respiratory and GI infections	Prevent intraabdominal abscess, <i>Clostridium difficile</i>
Cancer	Minimize increased risk of lymphoma	Prevent IBD-related lymphomas and colon cancer

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; IBD, inflammatory bowel disease.

Budesonide preparations limit these side-effects by regional enteral release and can be effective inductive agents in mild-to-moderate active Crohn's disease involving the ileum and/or the ascending colon (Entocort) [21] and adult ulcerative colitis (Uceris). Systemic corticosteroids are used to induce remission in more active or extensive Crohn's and ulcerative colitis; however, corticosteroids are only used as short-term induction agents. They do not achieve mucosal healing and are not effective in maintenance.

### Immunomodulators

The thiopurines (6-mercaptopurine and azathioprine) and methotrexate (MTX) have been mainstays in the armamentarium against autoimmune diseases and both are effective maintenance therapies for IBD [22,23]. Thiopurines, however, have shown an increasingly clear signal for increased risk of non-Hodgkins lymphoma, especially in Epstein-Barr virus-naïve children [24,25<sup>22</sup>]. Hepatosplenic T-cell lymphoma is of particular concern because of its primarily fatal course. MTX has not yet shown this increased risk in its extensive use in rheumatic diseases, but its cancer risk in IBD is still to be determined. Owing to the renewed interest in MTX, evidence is building of its efficacy in both Crohn's [26] and ulcerative colitis [27]. Both thiopurines and MTX are administered orally – although parenteral administration of MTX may be more effective – and both agents carry the risks of neutropenia and liver toxicity. Nausea limits use of MTX, although this can be overcome with antiemetics. MTX is teratogenic and should be

used with extreme caution in girls of childbearing potential.

### Antitumor necrosis- $\alpha$ therapies

Monoclonal antibodies directed against tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), have revolutionized the care of children with IBD. Infliximab and adalimumab are both effective for induction and maintenance in pediatric Crohn's [28,29] and infliximab is effective for induction and maintenance in pediatric ulcerative colitis [30]. Both have shown durable remission [31,32] and both are associated with improvement in growth [33,34]. The use of anti-TNF therapy does not appear to increase risk of surgical complications in children [35,36].

Inherent to its modulation of T-cell effects, the risk of tuberculosis (TB) reactivation is increased and all children must be screened for TB. Infections in general are increased, but the risk of serious infections is lower than with corticosteroids. Cancer risk has been a central focus of anti-TNF therapy; however, emerging evidence in prospective cohorts show that this risk is not increased in comparison with other IBD therapies and may not be increased if used as monotherapy [25<sup>22</sup>].

### Enteral nutritional therapy

Enteral nutrition characterizes the use of formula or specific diet as a treatment for pediatric IBD. Enteral nutrition in the form of exclusive enteral nutrition, which entails consuming 100% of one's calories by formula, is an effective induction therapy for pediatric Crohn's disease, may impart a durable



steroid-free remission, and is the standard induction therapy for mild-to-moderate pediatric Crohn's disease in Europe [37]. Exclusive enteral nutrition in the appropriately selected patient may be as effective as anti-TNF therapy [38]. Enteral nutrition does not carry the risks of infection or cancer and may be more effective in ameliorating malnutrition and promoting growth.

Enteral nutrition requires a substantial lifestyle change and often involves the entire family. In some centers, because of the logistical challenge of drinking sufficient calories by mouth, overnight nasogastric feedings are utilized to achieve the necessary amount. This requires a dedicated medical team and dedicated family working together. Not surprisingly, children prefer eating real food [39]. Exclusion diets have had mixed success [40] and although studies are ongoing, no definitive evidence supports their standard use.

### 5-aminosalicylates

The 5-aminosalicylates (5-ASAs) remain a mainstay in the treatment of ulcerative colitis offering steroid-free remission in 40% of pediatric ulcerative colitis patients [41]. Several preparations have been developed to improve targeted efficacy and adherence (daily dosing, fewer pills). 5-ASAs can be administered orally and rectally as suppository or enema. Side-effects are few, including paradoxical colitis, pancreatitis, and interstitial nephritis.

### Surgery

Complications of IBD – for example, intestinal perforation or obstruction in Crohn's disease – can necessitate surgical intervention, and families often perceive the specter of surgery lurking over their child. In adults with ulcerative colitis, patients were more concerned with the possibility of an ileostomy rather than the side-effects of medications [42<sup>\*\*\*</sup>]. Surgery, however, is an instrumental therapy in the care of children with IBD and its use should be framed as a tool to be utilized for the right indication at the right time, and not as an unfortunate outcome or indication of 'treatment failure' [43–45].

Proctocolectomy with ileal pouch–anal anastomosis has become the standard surgery in severe ulcerative colitis unresponsive to medical therapy. It can achieve durable acceptable bowel function and quality of life [46], even in younger children [47]. There may be a temptation to characterize colectomy as a 'cure' of ulcerative colitis, but complications including pouchitis, which are not uncommon [46], need to be remembered and appropriately project surgery as a potential cure.

## COURSE MODIFICATIONS

The rapidly evolving therapeutic armamentarium, driven by ongoing research, provides the prospect of more treatment options at every horizon. It is important that the pediatric IBD patient and their family know that the choices will continue to expand, as well the ability to better personalize and optimize therapy.

## CONCLUSION

Goals of therapy in pediatric IBD continue to evolve as emerging treatment options diversify opportunities to alter the disease course, with a paradigm shift toward deep remission, consisting of control of inflammation and prevention of bowel damage. The communication of the benefits and risks of these IBD therapies plays a pivotal role in the long-term success of a shared therapeutic plan. A family's understanding of risk and their value system must be incorporated into the determination of goals mutual to the child, family, and healthcare team. An effective shared decision-making process that integrates illness-experience oriented goals of well-being into objective-biological oriented goals of reducing inflammatory burden will provide the best opportunity for treatment success in the pediatric patient with IBD.

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### Conflicts of interest

*There are no conflicts of interest.*

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