What if your child’s doctor could accurately predict how your child’s inflammatory bowel disease (IBD) will behave over time?

Program Overview
We now know that some children diagnosed with Crohn’s disease or ulcerative colitis manifest mild disease course, do well with basic medication, and suffer minimal side effects. However, some children have a more severe disease course with growth failure, pubertal delay, continued active gastrointestinal symptoms, and impaired quality of life. These kids eventually develop complicated disease which may require surgery. It is currently not possible to predict who will develop complicated disease, because disease severity at presentation does not necessarily reflect future disease course.

Medications are able to change the natural history of the disease, and postpone and even avoid the need for surgery, but due to possible side effects and related significant costs, these medications are not used early in all patients who might need them. If we are able to predict the natural course of the disease at the time of diagnosis, doctors and parents can decide to use these medications earlier and reduce the risk of future complicated disease.

To address this need, the Crohn’s & Colitis Foundation supports the RISK Stratification Study.
CCFA’s Pediatric RISK Stratification Study (RISK) Goal
The Crohn’s & Colitis Foundation's RISK stratification study is a multi-center study based on over 1,100 pediatric Crohn’s disease patients. Over the last eight years, the study has collected clinical data and biosamples (DNA/RNA from blood and ileal and rectal biopsies, serum, and stool) with the goal of identifying – at the onset of disease – diagnostic signatures to predict which patients would develop complications that require surgery. Excitingly, the RISK study fulfilled this goal and has yielded biologic signatures that researchers believe can be used as a diagnostic to identify those children most likely to develop strictures and fistulae and those most likely to benefit from treatment with biological therapies.

Why This Matters!
Bowel strictures and fistulae are severe complications in CD patients that dramatically affect their quality of life and ultimately require surgery. Stricturing, known also as fibrostenosis, is characterized by a buildup of fibrotic scar tissue leading to thickening of the intestinal wall and narrowing of the intestinal passage. Fistulae, also referred to as penetrating disease, reflect the impact of inflammation beyond the intestinal wall creating an abnormal connection between the intestine and different organs. Because of the severity of these complications the identification of biologic signatures (biomarkers) that can be used as a diagnostic tool for early prediction of development of complications and response to treatment is critical to guide therapeutic decisions in pediatric patients. RISK is the largest new-onset study ever completed on pediatric Crohn’s disease patients - and eight years after its conception, and the analysis of millions of biological and clinical data points, RISK has generated a predictive risk stratification model based on biologic signatures.

RISK Outcomes: At the Cutting Edge of Precision Medicine
Precision medicine is defined as the tailoring of a medical treatment to the individual characteristics of each patient. The success of personalized medicine fundamentally depends on the successful development of biomarkers and diagnostic tests that can be used to accurately identify which patient will need which tailored medicine.

The RISK predictive model is based on clinical profile, gene expression, microbiome, serological, and genomics data. Remarkably, RISK has identified distinct biologic signatures that can predict whether the patient is at risk of developing stricturing or penetrating complications. RISK also found that early treatment with biologicals was very effective in preventing penetrating complications, while early treatment with biologicals did not seem to have an impact on those likely to develop strictures. These data support the utility of risk stratification of pediatric CD patients at diagnosis, and may guide early tailored use of anti-TNFα therapy. The data also highlight the unmet medical need to find new treatments for children likely to develop strictures.

RISK Looking Ahead: Validation and Development of RISK Diagnostic
In 2017, the CCFA will build upon the findings from the study and work toward developing the RISK predictive model into a diagnostic that would be used clinically to predict complications and therapeutic options for pediatric patients. To accomplish this goal, further validation of the diagnostic is required. This additional work will be critical for the implementation of these signatures as a bona fide clinical diagnostic. This validation will also be crucial to attract the interest of, and partnering with, industry for development of this diagnostic into a routine clinical test.

The CCFA needs to confirm the presence of the biologic signatures in another smaller, well-selected cohort of pediatric Crohn’s disease patients. These studies will require an investment of $5 million over three years to cover the costs of recruitment and follow-up of patients, analysis of samples collected at diagnosis and follow-up, and model validation. Once the model is validated, the CCFA will seek a partnership with industry to advance the diagnostic toward FDA approval.