Key Literature – BÜHLMANN fecal Calprotectin Citations

Value of fecal Calprotectin in IBD:

• Jensen, M.D. et al., 2011, Fecal calprotectin is equally sensitive in Crohn’s disease affecting the small bowel and colon, *Scandinavian Journal of Gastroenterology*
  
  “The first study to show that fecal calprotectin is equally sensitive in colonic and small bowel CD.”

• Mindemark, M. & Larsson, A. 2012, Ruling out IBD: Estimation of the possible economic effects of pre-endoscopic screening with F-calprotectin, *Clinical Biochemistry*
  
  “The estimated demand for colonoscopies was reduced by 50 % to 67 %. This corresponded to a cost avoidance of approximately up to € 2.13 million.”

Diagnosis of IBD patients:

• Burri, E. et al., 2013, Monoclonal antibody testing for fecal calprotectin is superior to polyclonal testing of fecal calprotectin and lactoferrin to identify organic intestinal disease in patients with abdominal discomfort, *Clinica Chimica Acta*
  
  “…we demonstrated, that the diagnostic accuracy of monoclonal antibody testing of calprotectin is superior to both polyclonal antibody testing…”

  
  “Bühlmann assays were superior with 100 % sensitivity…”

• Labaere, D. et al., 2014, Comparison of six different calprotectin assays for the assessment of inflammatory bowel disease, *United European Gastroenterology Journal*
  
  “The EliA [Phadia] cut off for diagnosis was optimal at a level of 15 mg/g. This is as low as the detection limit of the assay, which is analytically unacceptable.”

• Manz, M. et al., 2012, Value of fecal calprotectin in the evaluation of patients with abdominal discomfort: an observational study, *BMC Gastroenterology*
  
  “All together, those results support the concept that fecal calprotectin is a useful marker in the evaluation of patients with abdominal discomfort…”

• Sydora, M. J. et al., 2012, Validation of a point-of-care desk top device to quantitate fecal calprotectin and distinguish inflammatory bowel disease from irritable bowel syndrome, *Journal of Crohn’s and Colitis*
  
  “Quantum Blue Reader® calprotectin levels were available within 30 min and correlated well with results derived from standard ELISA assays.”

Monitoring of IBD Patients:

• Abej, E. et al., 2016, The Utility of Fecal Calprotectin in the Real-World Clinical Care of Patients with Inflammatory Bowel Disease, *Canadian Journal of Gastroenterology and Hepatology*
  
  “…positive FCAL was significantly associated with abnormal endoscopy, elevated serum CRP, low serum Hg, and low serum albumin.”

• Coorevits, L. et al., 2012, Faecal calprotectin: comparative study of the Quantum Blue rapid test and an established ELISA method, *Clinical Chemistry and Laboratory Medicine: CCLM / FESCC*
  
  “…we may conclude that the POCT can serve as reliable alternative to the time consuming ELISA...”

• Ferreiro-Iglesias, R. et al., 2016, Accuracy of Consecutive Fecal Calprotectin Measurements to Predict Relapse in Inflammatory Bowel Disease Patients Under Maintenance With Anti-TNF Therapy, *J Clin Gastroenterol*
  
  “…time interval to the next FC measurement should be probably shorter than 4 months after a FC result of 130 to 300 mg/g...”
• Ferreiro-Iglesias, R. et al., 2015, Fecal Calprotectin as Predictor of Relapse in Patients With Inflammatory Bowel Disease Under Maintenance Infliximab Therapy, *J Clin Gastroenterol*

> “We found FC to be a very accurate marker to exclude relapse within the following 2 month after administration of Infliximab.”

• Guardiola, J. et al., 2014, Fecal Level of Calprotectin Identifies Histologic Inflammation in Patients with Ulcerative Colitis In Clinical And Endoscopic Remission, *Clinical Gastroenterology and Hepatology*

> “…an FC value less than 155 mg/g is a reliable indicator of the absence of acute inflammatory infiltrate (negative predictive value, 89%).”

• Kostas, A. et al., 2017, Fecal calprotectin measurement is a marker of short-term clinical outcome and presence of mucosal healing in patients with inflammatory bowel disease, *World J Gastroenterol*

> “In our patient cohort, we were able to define an optimal cut-off FC value of 261 µg/g, which had a strong predictive value for the discrimination of future relapses vs maintenance of remission.”

• Lasson, A. et al., 2014, Pharmacological intervention based on fecal calprotectin levels in patients with ulcerative colitis at high risk of relapse: A prospective, randomized, controlled study, *United European Gastroenterology Journal*

> “In patients with UC, FC-guided dosing of the patient’s 5-ASA agent showed significantly lower relapse rates than for patients in the control group.”

• Lobatón, T. et al., 2013, A new rapid test for fecal calprotectin predicts endoscopic remission and postoperative recurrence in Crohn’s disease, *Journal of Crohn’s & colitis*

> “FC determined by rapid quantitative test predicts “endoscopic remission” and endoscopic postoperative recurrence in CD patients.”

• Lobatón Ortega, T. et al., 2013, A New Rapid Quantitative Test for fecal Calprotectin Predicts Endoscopic Activity in Ulcerative Colitis, *Inflammatory bowel diseases*

> “FC determined by QPOCT was an accurate surrogate marker of “endoscopic remission” in UC presented a good correlation with the FC-ELISA test.”

• Louis Edouard, 2015, Fecal calprotectin: towards a standardized use for inflammatory bowel disease management in routine practice, *Journal of Crohn’s and Colitis*

> “…fecal calprotectin as a unique first line test would be sufficient to decide in which patient to perform further endoscopic or medical imaging explorations.”

• Naismith, G. D. et al., 2014, A prospective evaluation of the predictive value of faecal calprotectin in quiescent Crohn’s disease, *Journal of Crohn’s and Colitis*

> “The FC result, obtained by non-invasive means, can provide prognostic information for both the patient and clinician alike.”

• Pavlidis, P. et al., 2016, Early change in faecal calprotectin predicts primary non-response to anti-TNFα therapy in Crohn’s disease, *Scandinavian Journal of Gastroenterology*

> “The ΔFCAL could act as an ‘early warning’ to consider alternatives such as dose optimisation or another biologic with a different mode of action, rather than persisting for several months.”

• Roblin, X. et al., 2017, Development and Internal Validation of a Model Using Fecal Calprotectin in Combination with Infliximab Trough Levels to Predict Clinical Relapse in Crohn’s Disease, *Inflamm Bowel Dis*

> “In IFX-treated patients with CD in clinical remission, a combination of TLI (<2 µg/mL) and fecal calprotectin (>250 µg/g of stools) is a good model for predicting loss of response.”

• Rosenfeld, G. et al., 2016, Focus: Future of fecal calprotectin utility in inflammatory bowel disease, *World J Gastroenterol*

> “…FC is a simple, non-invasive test that is gaining widespread use in the diagnosis and management of IBD.”

• Theede, K. et al., 2016, Fecal Calprotectin Predicts Relapse and Histological Mucosal Healing in Ulcerative Colitis, *Inflamm Bowel Dis*

> “Two consecutive measurements of a 1-month interval with FC >300 mg/kg were most predictive of relapse.”
• Turvill, J. et al., 2017, Validation of a care pathway for use of faecal calprotectin in monitoring patients with Crohn’s disease, *Frontline Gastroenterology*
  
  “…the PPV of 0.85 and a NPV of 0.97 of this clinical validation are compelling…”

• Voiosu, T. et al., 2014, Rapid Fecal Calprotectin Level Assessment and the SIBDQ Score Can Accurately Detect Active Mucosal Inflammation in IBD Patients in Clinical Remission: a Prospective Study, *J Gastrointestin Liver Dis*
  
  “FC levels appears to be a practical method for monitoring disease activity in these patients, possibly reducing the need for repeat endoscopic examinations.”

• Wright, E. K. et al., 2016, Comparison of Fecal Inflammatory Markers in Crohn’s Disease, *Inflamm Bowel Dis*
  
  “This study shows that FC is the optimal marker for diagnosing and monitoring endoscopic postoperative recurrence.”

• Wright, E. K. et al., 2015, Measurement of Fecal Calprotectin Improves Monitoring and Detection of Recurrence of Crohn’s Disease After Surgery, *Gastroenterology*
  
  “The present study has shown that FC concentration is sufficiently sensitive to monitor for recurrence of Crohn’s disease.”

• Zhulina, Y. et al., 2016, The prognostic significance of faecal calprotectin in patients with inactive inflammatory bowel disease, *Aliment Pharmacol Ther*
  
  “Our data suggest that longitudinal monitoring of faecal calprotectin is informative in predicting relapse in IBD.”

**Special Focus on Cut-off:**

• Pavlidis, P. et al., 2013, Diagnostic accuracy and clinical application of faecal calprotectin in adult patients presenting with gastrointestinal primary care, *Scandinavian Journal of Gastroenterology*
  
  “This study provides the first evidence on the use of fCal [BÜHLMANN fCAL® ELISA] testing in primary care…..to be used as part of the pathway for management of patients with suspected IBS.”

• Seenan, JP. et al., 2015, Are we exposing patients with a mildly elevated faecal calprotectin to unnecessary investigations?, *Gastroenterology*
  
  “we propose an alternative diagnostic approach of repeating the FC after 6-8 weeks in patients with values of 100-200 µg/g.”

• Walsham and Sherwood, 2016, Fecal calprotectin in inflammatory bowel disease, *Clinical and Experimental Gastroenterology*
  
  “The choice of a cutoff will depend on whether sensitivity or specificity is considered to be the most important and needs to be made taking into consideration the clinical features of an individual patient.”

**The use of fecal Calprotectin in Pediatrics:**

• Prell, C. et al., 2014, Comparison of three tests for faecal calprotectin in children and young adults: a retrospective monocentric study, *BMJ Open*
  
  “In conclusion, measurement of FC in paediatric patients with unspecific symptoms is very helpful in order to avoid invasive procedure.”

  
  “…we present the first correlation study of rapid POC calprotectin testing in a pediatric IBD cohort in the United States.”

• Zhu, Q. et al., 2016, Fecal Calprotectin in Healthy Children Aged 1-4 Years, *PLOS ONE*
  
  “Children aged from 1 to 4 years old have lower FC concentrations compared with healthy infants (<1 years), and higher FC concentrations when comparing with children older than 4 years and adults.”
Further Literature citing the BÜHLMANN fecal Calprotectin Assays:

- Brandse, J.F. et al., 2016, Performance of Common Disease Activity Markers as a Reflection of Inflammatory Burden in Ulcerative Colitis, *Inflamm Bowel Dis*
- Burri, E. et al., 2014, Diagnostic yield of endoscopy in patients with abdominal complaints: incremental value of faecal calprotectin on guidelines of appropriateness, *BMC Gastroenterology*
- Calafat, M. et al., 2015, High Within-day Variability of Fecal Calprotectin Levels in Patients with Active Ulcerative Colitis: What Is the Best Timing for Stool Sampling? *Inflamm Bowel Dis*
- Chang, M. et al., 2014, Faecal calprotectin as a novel biomarker for differentiating between inflammatory bowel disease and irritable bowel syndrome, *Molecular Medicine Reports*
- Delefortrie, Q. et al., 2015, Comparison of the Liaison® Calprotectin kit with a well-established point of care test (Quantum Blue — Bühlmann-Alere®) in terms of analytical performances and ability to detect relapses amongst a Crohn population in follow-up, *Clinical Biochemistry*
- Dhaliwal, A. et al., 2014, Utility of faecal calprotectin in inflammatory bowel disease (IBD): what cut-offs should we apply? *Frontline Gastroenterology*
- Du, L. et al., 2016, Within-Stool and Within-Day Sample Variability of Fecal Calprotectin in Patients With Inflammatory Bowel Disease, *J Clin Gastroenterol*
- Ferreiro-Iglesias, R. et al., 2015, Usefulness of a rapid faecal calprotectin test to predict relapse in Crohn’s disease patients on maintenance treatment with adalimumab, *Scandinavian Journal of Gastroenterology*
- Frin, A-C. et al., 2016, Accuracies of fecal calprotectin, lactoferrin, M2-pyruvate kinase, neopterin and zonulin to predict the response to infliximab in ulcerative colitis, *Digestive and Liver Disease*
- Gauss, A. et al., 2016, Quality of Life Is Related to Fecal Calprotectin Concentrations in Colonic Crohn Disease and Ulcerative Colitis, but not in Ileal Crohn Disease, *Medicine*
- Halfvarson, J. et al., 2017, Dynamics of the human gut microbiome in inflammatory bowel disease, *Nature Microbiology*
- Kok, L. et al., 2012, Diagnostic Accuracy of Point-of-Care Fecal Calprotectin and Immunochemical Occult Blood Tests for Diagnosis of Organic Bowel Disease in Primary Care: The Cost-Effectiveness of a Decision Rule for Abdominal Complaints in Primary Care (CEDAR) Study, *Clinical Chemistry*
- Kolho, K. et al., 2012, Rapid Test for Fecal Calprotectin Levels in Children With Crohn Disease, *JPEN*
- Kristensen, V. et al., 2015, Prediction of Endoscopic Disease Activity in Ulcerative Colitis by Two Different Assays for Fecal Calprotectin, *Journal of Crohn’s and Colitis*
- Lasson, A. et al., 2015, The Intra-Individual Variability of Faecal Calprotectin: A Prospective Study In Patients With Active Ulcerative Colitis, *Journal of Crohn’s and Colitis*
- Levine, A. et al., 2014, Comparison of Outcomes Parameters for Induction of Remission in New Onset Pediatric Crohn’s Disease: Evaluation of the Porto IBD Group “Growth Relapse and Outcomes with Therapy”, *Inflamm Bowel Dis*
- Li, F. et al., 2014, Comparison of the different kinds of feeding on the level of fecal calprotectin, *Early Human Development*
- Lin, Wei-Chen et al., 2015, Fecal calprotectin correlated with endoscopic remission for Asian inflammatory bowel disease patients, *World J Gastroenterol*
- Oyaert, M. et al., 2013, Comparison of two immunoassays for measurement of faecal calprotectin in detection of inflammatory bowel disease: (pre)-analytical and diagnostic performance characteristics, *Clin Chem Lab Med*
- Paul, S. et al., 2013, Therapeutic Drug Monitoring of Infliximab and Mucosal Healing in Inflammatory Bowel Disease: A Prospective Study, *Inflamm Bowel Dis*
- Rogler, G. et al., 2013, Concept for a rapid point-of-care calprotectin diagnostic test for diagnosis and disease activity monitoring in patients with inflammatory bowel disease: Expert clinical opinion, *Journal of Crohn’s and Colitis*
- Wang, S. et al., 2014, Faecal calprotectin concentrations in gastrointestinal diseases, *Journal of International Medical Research*