

## Key Literature – BÜHLMANN fecal Calprotectin Citations

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### 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.”

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- 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.”

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### 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...”

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- De Sloovere, M. *et al.* 2017, Analytical and diagnostic performance of two automated fecal calprotectin immunoassays for detection of inflammatory bowel disease, *Clin Chem Lab Med*

“Bühlmann assays were superior with 100 % sensitivity...”

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- 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.”

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- 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...”

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- 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.”

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### 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...”

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- 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...”

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- 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.”

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- **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 %).”

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- **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 mg/g, which had a strong predictive value for the discrimination of future relapses vs maintenance of remission.”

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- **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.”

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- **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.”

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- **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.”

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- **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.”

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- **Magro, F. et al., 2018, Comparison of different histological indexes in the assessment of UC activity and their accuracy regarding endoscopic outcomes and faecal calprotectin levels, *Inflamm bowel dis***

“...81 %, 93 % and 88% of the patients that have an FC level below 150µg/g (using the QB method) are in histological remission according to NI, RHI and GS (using 3.1 as the cut-off).”

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- **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.”

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- **Nakov, R. V. et al., 2018, Fecal Calprotectin for Assessment of Inflammatory Bowel Disease Activity, *Clin Res Immunology***

“The ROC analysis found that a cutoff FCP level of 315 µg/g differentiates quiescent CD from active ileal disease with 94% sensitivity, 98% specificity, and area under the curve (AUC) 0.984.”

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- **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.”

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- **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.”

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- **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.”

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- **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.”

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- 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..."

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- 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."

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- 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."

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- 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."

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- 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."

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#### Special Focus on Cut-off:

- Pavlidis, P. *et al.*, 2013, Diagnostic accuracy and clinical application of faecal calprotectin in adult patients presenting with gastrointestinal symptoms in 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."

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- 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."

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- 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."

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

- Meglicka, M. *et al.*, 2017, Can we predict mucosal inflammation in children with ulcerative colitis without colonoscopy? Own experience in assessing faecal calprotectin, *Post N Med*

"The area under the curve (AUC) for discrimination between subgroup of patients in remission vs moderate disease was 0.90 with cut-off level of 300 µg/g and sensitivity 0.89, specificity 0.82."

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- 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."

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- Rodriguez, A. *et al.*, 2017, Correlation of rapid point-of-care vs send-out fecal calprotectin monitoring in pediatric inflammatory bowel disease, *World Journal of Gastrointestinal Pharmacology and Therapeutics*

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

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- 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."

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### Further Literature citing the BÜHLMANN fecal Calprotectin Assays:

- Bin-Nun, A. *et al.*, 2015, Rapid Fecal Calprotectin (FC) Analysis: Point of Care Testing for Diagnosing Early Necrotizing Enterocolitis, *Am J Perinatal*
- 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*
- Ferreira-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*
- Hessels, J. *et al.*, 2012, Evaluation of Prevent ID and Quantum Blue rapid tests for fecal calprotectin, *Clin Chem Lab Med*
- 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, *JPGN*
- 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*
- Noebauer, B. *et al.*, 2017, Analytical evaluation of a fully automated immunoassay for faecal calprotectin in a paediatric setting, *Biochem Med (Zagreb)*
- Oord, T. and Hornung, N., 2014, Fecal calprotectin in healthy children, *Scandinavian Journal of Clinical & Laboratory Investigation*
- Oyaert, M. *et al.*, 2017, Analytical performance and diagnostic accuracy of six different faecal calprotectin assays in inflammatory bowel disease, *Clin Chem Lab Med*
- 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*
- Shentova, R. *et al.*, 2016, Diagnostic Value of Fecal Calprotectin Point of Care Testing in the Pediatric Practice, *Merit Res. J. Med. Med. Sci.*
- Wang, S. *et al.*, 2014, Faecal calprotectin concentrations in gastrointestinal diseases, *Journal of International Medical Research*
- Whitehead, S.J. *et al.*, 2012, Between-assay variability of faecal calprotectin enzyme-linked immunosorbent assay kits, *Ann Clin Biochem*
- Wright, E.K. *et al.*, 2016, Cost-effectiveness of Crohn's disease post-operative care, *World J Gastroenterol*
- Yamamoto, T., 2015, The clinical value of fecal calprotectin and lactoferrin measurement in postoperative Crohn's disease, *United European Gastroenterology Journal*