Tables of evidence for ambulatory UC

Monitoring and prediction

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Beattie RM, 1996.  1 | Case series | Prospective  n=20  Assess the mucosal inflammatory response to corticosteroid therapy | 18/20 pts improved,  17/20 clinical remission by week 8  Median colitis score  Pancolitis: before treatment: 5  after treatment : 0.5  Distal colitis:  before treatment : 4.5  after treatment: 0.5 | 5/9 |
| Wiernicka A, 2015.  2 | Case series | Retrospective  n=16  Impact of induction with infliximab on mucosal healing | At week 8:  Clinical remission: 68.75%  Endoscopic remission: 12.5%  Histological remission: 75% | 4/9 |
| Turner D, 2009.  3 | Cohort | Retrospective,  Multicenter  n=215  evaluation of PUCAI | Feasibility:  UC vs CD 97.6% vs. 47%  Validity: PUCAI correlated with PGA (*r* =0.90; *P* =0.001).  ICC analysis: excellent test–rest reliability (ICC = 0.89)  Responsiveness judged by the PGA  (*r =* 0.87; Kruskal–Wallis, P= 0.001) | 4/9 |
| Dotson JL, 2015. 4 | Cohort | Retrospective, multicentre  n=2503  Evaluation of PUCAI | Feasibility: 96%  Validity: correlation with PGA  [r = 0.76 (p < 0.001), agreement 77%,  Test-retest reliability: ICC = 0.72 [95% CI 0.70–0.75], p < 0.001). | 4/9 |
| Lee JJ, 2011.  5 | Cohort | Single-centre prospective  n=70  Adult and children  compared patient-and physician-completed PUCAI scores with PGA and laboratory markers | Agreement for 60 (86%) pairs of patient/physician  Patient- and physician-completed PUCAI summary scores were identical 49%  Both patient- and physician-completed PUCAI scores were moderately correlated with CRP (r=0.5) | 5/9 |
| Schechter A, 2015.  6 | Cohort | Multicentre retrospective  n=115  Newly diagnosed UC patients completed at  least 12 months of follow-up. | PUCAI (>10) at 3 months predicts:  Steroid free remission  (AUROC 0.7) NPV 83% PPV 53%  Colectomy by 2 years  (AUROC 0.75)  Need for salvage therapy (p<0.001) | 4/9 |
| Dharmaraj R,  2016.  7 | Case series | Single centre,  Retrospective n=24  Predictive factors for the development of pouchitis after ileal pouch-anal anastomosis (IPAA) | Pouchitis: 24 (56%)  Higher PUCAI at diagnosis was  a significant predictive factor for both pouchitis (P=0.001) and chronic pouchitis (P=0.02). | 4/9 |
| Mack RD, 2007.  8 | Cohort | Multicenter  prospective register  n=124 UC  n=392 CD  Common laboratory tests yield normal results at the time of diagnosis | Normal values for all 4 laboratory tests  54% of mild UC cases (21/39) vs. 21% of mild CD  Mean values of ESR: mild CD> mild UC (*P=*0.026)  Mean platelet counts mild CD > mild UC (*P* =0.001)  Worse in moderate CD than UC:  Mean values ESR (*P* =0026), platelet counts (*P* = 0.021), albumin level (*P* =0.001) | 3/9 |
| Weinstein TA,  2003.  9 | Cohort | Single centre, retrospective  evaluate the differential clinical presentation of young and older children with IBD (routine laboratory test) CD n=82  UC n=71 | Haemoglobin CD: 11.4 ± 1.52 g/dL  UC 12.3 ± 1.58 g/dL  *(P* < 0.01).  Platelet: CD 457 ± 165 × 103/mm3  UC 334 ± 107 × 103/mm3 (*P* < 0.01).  ESR: CD 38.3 ± 27.3 mm/h)  UC 19.2 ± 18.3 mm/h, *P* < 0.01  Albumin: CD 3.5 ± 0.7 g/dL  UC: 4.4 ± 2.2 g/dL (*P* < 0.01) | 4/9 |
| Sidoroff M, 2010.  10 | Case control | Single centre, prospective,  IBD n=39 ,UC n=14  control n=33  Association between hs-CRP and clinical and histological activity in paediatric IBD | Standard CRP  new diagnosis: 0.7 mg/L,  existing diagnosis: 0.2 mg/L  control patients 0.03 mg/L (*P* < 0.01)  hsCRP  active disease 0.2 mg/L (*n* = 17)  quiescent disease 0.1 mg/L, (*n* = 8), *P* = NS). | 5/9 |
| Kelley-Quon LI,  2012.  11 | Cohort | Multicenter, retrospective  n=57  Clinical predictors of surgery in UC | Weight loss Hazard Ratio (HR) 2.55  albumin (<3.5g/dL) HR 6.05,  first-degree relative HR 1.81. | 5/9 |
| Canani RB, 2008.  12 | Cohort | Single centre Prospective  n=64 IBD n=32 UC  Evaluate the accuracy of FC, clinical scores, serum markers and endoscopy in assessment  of intestinal mucosa inflammation. | Optimal cut-off FC level: 143 ug/g  to discriminate between remission and active disease  FC based on histology score:  sensitivity 94, specificity: 64 PPV: 81, NPV: 87  FC based on clinical remission:  sensitivity 100%, specificity 80%, PPV: 67%, NPV: 100%, | 3/9 |
| Borkowska A, 2015.  13 | Case control | Single centre, prospective    IBD n=52 CD: n=24  UC n=28 : control n=41  Usefulness of fecal lactoferrin in the diagnosis and monitoring of IBD | Fecal lactoferrin was significantly higher in IBD pts than in the controls (*p* < 0.001)  The cut-off value of fecal lactoferrin:  13 μg/g sensitivi­ty 80%  specificity 92% PPV 96,8% NPV 63.3%  Moderate UC higher fe­cal lactoferrin than in mild UC (*p* < 0.05). | 4/9 |
| Fagerberg A, 2007  14 | Case control | 2 centres, prospective  IBD n=39; CD n=27  UC n=10; control n=12  Validity of fecal calprotectin based on  microscopic remission | Fecal calprotectin: IBD: 264mg/g  Control group: 16.5mg/g (P<.001).  Clinically active IBD  392mg/g vs. asymptomatic IBD patients 32.9mg/g (P<.001).  Fecal calprotectin (cut-off 50ug/g) and  microscopic colonic inflammation:  Sensitivity 93% Specificity 73%  PPV: 90% NPV: 80% | 3/9 |
| Roszak D, 2015.  15 | Cohort | Retrospective, single centre  IBD n=109; UC n=37  CD n=47; IBD-U n=25  Comparison of several markers fecal makers (M2-PK, calprotectin, lactoferrin) | Disease activity (Truelove and Witt)  M2-PK R= 0.772 p < 0.01;  calprotectin R=0.757 p = 0.004;  lactoferrin R=0.689 p < 0.01). | 3/9 |
| Komraus M, 2012.  16 | Case control | Single centre  Control n=20  CD n=24  UC n=16  Faecal calprotectin to evaluate disease activity | Faecal Calprotectin  Control: 14 ug/k, CD: 436 ug/kg  UC 616 ug/kg  FC positively correlated with Truelove-Witts scale (R=0,74 p<0.001) and Rachmilewitz endoscopic index (R=0,519, p<0.039) | 3/9 |
| Ashorn S, 2009.  17 | Case control | Single centre  Prospective association of fecal calprotectin with serological markers in children and adolescents with IBD CD n= 18,  UC n= 3, IC n=6  non-IBD control n=13 | Fecal calprotectin (≥ 100ug/g): 89% (39/44) of IBD patients vs. 9% of control (1/11, p<0.001 )  The combination of ANCA, FC, anti-I2, Anti-OmpW at the time of diagnosis for UC :Sensitivity 87%, Specificity 36%, PPV 74% NPV 57% | 4/9 |
| Diamanti A, 2008.  18 | Case series | Single centre  Retrospective  CD: n=32 (44%)  UC: n=41 (56%)  Efficacy of calprotectin in histological relapses of pediatric IBD patients. | Histological relapse: 18 (44%)  Histological remission: 23 (56%)  Final FC levels were significantly increased in relapsed UC patients, compared with non-relapsed patients.  Histological relapse + FC<275 ug/g: 1/36 (3%)  Histological relapse + FC>275 ug/g: 31/37 (84%) (*P* < 0.0001) HR: 35.88. | 3/9 |
| Sipponen, T 2010. 19 | Cohort | Cross-sectional study  Single centre  n=72  Faecal calprotectin predicting clinical relapse | Median FC 285 ug/g,  No significant difference between the groups experiencing a clinical relapse (409 ug/g) and those staying in clinical remission 282ug/g; p = 0.440  PPV for relapse: FC >100 ug /g: 0.396;  FC >570 ug/g 0.392; FC >855 ug/g 0.438  FC >1000 ug/g 0.429.  NPV: FC (<100 ug/g): 0.75 | 3/9 |
| Turner D, 2010. 20 | Cohort | Multicenter prospective  n=128  Identify predictors of non response to iv corticosteroids | 37 (29%) children failed iv. corticosteroids  PUCAI (>45) likely to fail intravenous corticosteroids  Sens: 92% Spec. 50%  NPV 94%; PPV 43%; P= 0.001 | 3/9 |
| Zholudev A, 2004.  21 | Case-control | Multicenter  Retrospective  n=54 UC, n=81 CD  n=63 non IBD  disease activity, location and serological markers | 70% of UC cases pANCA pos.  pANCA positive 18% UC vs.  3% non IBD control  No relationship between pANCA and disease activity in UC (Kozarek score) | 4/9 |
| Miele E, 2007  22 | Case series | Single centre, prospective  n=33  Newly diagnosed UC  evaluated at 1,6, 12 months | 10 cases had relapse + 23 no relapse  9/23 pANCA positive.  ANCA status did not change during the follow-up. pANCA was not associated with earlier clinical relapse (P = 0.666). | 3/9 |
| Turner D, 2013. 23 | Cohort | Multicenter prospective  Pediatric UC patients treated with IFX n=51  Post hoc analysis of  ability of the PUCAI, CRP, and mucosal healing to predict steroid-free sustained remission after 1 year of treatment. | 9/17 patients (PUCAI scores <10) sustained remission (53%),  vs. 4/20 pts (PUCAI scores >10)  (20%) (P=.036). | 4/9 |
| Gray FL, 2013.  24 | Cohort | Retrospective  Restorative proctocolectomy and ileal pouch-anal anastomosis.  n=60  Outcomes included pre-operative PUCAI, combined versus staged procedure, and postoperative complications. | 42 (70%) combined proctocolectomy  18 (30%) staged proctocolectomy  Pre-operative PUCAI was lower for combined versus staged patients (p = 0.001).  Higher pre-operative PUCAI strongly correlated with the likelihood of undergoing a staged procedure  (p = 0.001). | 3/9 |
| Teitelbaum JE, 2013.  25 | Cohort | Cross sectional  Prospective  single centre  n=21 | Strong significant correlation between the patient’s perceived symptom burden and that of the parent’s (r 0.59, P < 0.001) and physician (r 0.48, P < 0.001) | 4/9 |
| Hyams J, 2012.  26 | Cohort | Prospective  multicenter  n=60  IFX therapy | Response wk 8 in 73.3%  Overall remission rate at wk 54: 28.6%  The PUCAI determined week 8 remission rate was 33%, identical to the rate of complete mucosal healing found by sigmoidoscopy | 5/9 |
| Romano C, 2010. 27 | Case-control | Open-labelled, randomized  Beclomethasone efficacy vs. 5-ASA  n=30 | Week 4 mean PUCAI score dropped to 26 (P < 0.001)  Week 12 remission:  11 patients (73%) treated with BDP vs  4 pts treated with 5-ASA | 4/9 |
| Civitelli F, 2014. 28 | Case series | Prospective  n=50  US vs. colonoscopy | Endoscopic extent of disease was independently confirmed in 47 patients by US that yielded a 90% concordance with endoscopy (95% CI 0.82-0.96) | /9 |
| Moore JC, 2011. 29 | Cohort | Retrospective  Prediction of colectomy based on clinical variables at diagnosis, n=155 | Colectomy was associated with  WBC (11.6 vs 9.5 p= 0.008),  ANC (7.6 vs 5.7, P =0.006) and  Hematocrit (33.2% vs 36.3%; P=0.02). | 5/9 |
| Birimiberg-Schwartz L, 2016. 30 | Cohort | Multicenter retrospective longitudinal study  n=406 (IBD), n=143 (UC)  Diagnostic utility of serology and to assess whether serology can predict disease severity | UC children with pANCA+/ASCA-  had more often severe disease at diagnosis (36 [62%] vs 22 [38%], P =0.033)  Needed more calcineurin inhibitors, biologics, or colectomy (25 [80%] versus 6 [20%], P = 0.026). | 5/9 |
| Van Rheenen PF, 2012.  31 | Case series | Single centre  n=31 UC, n=31 CD  FC and C-reactive protein (CRP) to predict relapse in teenagers  who report no symptoms | Teenagers with a positive calprotectin test had a 53% (10/19) risk of progressing to symptomatic relapse within 3 months, whereas a negative Calprotectin result gave a 12% (5/43) risk of symptomatic relapse. | 4/9 |
| Kolho KL, 2014. 32 | Case-series | Single-centre  retrospective  n=76  FC levels were measured during the induction  and maintenance phase of infliximab therapy | Pre-treatment FC level  817 ug/g declined to 372 mg/g by week 6  Those who discontinued the therapy within the first period had higher median FC level during induction than the other patients (median 633 mg/g, IQR: 197–819 and median 219 mg/g, IQR: 71–508, respectively; p < 0.025) | 5/9 |

Medical treatment

5ASA

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Ferry G, 1993 (33) | RCT | Sulfasalazine vs Olsalazine in mild-moderate UC  (n=56) | Disease activity improvement at 3 months on Sulfasalazine (79%) vs Olsalazine (39%), p=0.006 | 3/6 |
| Quiros J, 2009 (34) | RCT | Balsalazide high versus low dose in mild-moderate UC (n=68) | Non significant Clinical improvement at 8 weeks in 45% (high dose) vs 37% (lower dose) (p>0.05) | 5/6 |
| Romano C, 2010. (27) | RCT | Oral beclomethasone vs mesalazine in mild-moderate UC (n=30) | Clinical remission at week 4 was 80% (beclomethasone) vs 33% (Mesalazine), p<0.025 | 3/6 |
| Winter H, 2014. (35) | RCT | High vs. low dose mesalazine in mild-moderate UC  (n=83) | Remission or partial response in 56% (high dose) and 55% (low dose), p=0.92 | 4/6 |
| Turner D, 2016. (36) | RCT | Once vs. divided daily mesalazine dosing in mild-moderate UC (n=83) | PUCAI response at week 6 was 60% (once daily) vs 63% (twice daily), p=0.78 | 5/6 |
| Zeisler B, 2013(37) | Cohort | Outcome following  5-ASA therapy in UC  (n=213) | Corticosteroid-free remission at 1 year (40%) | 6/8 |
| Gower-Rousseau C, 2009 (38) | Cohort | Clinical outcomes in Paediatric UC cohort | Maintenance 5-ASA monotherapy at maximal follow up [median time of maximal follow up 77months (46-125); 32%] | 6/8 |

Steroids

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Beattie M, 1996  6 | Cohort | 20 children with active UC  assessed before and after 8 weeks of medical therapy with 5-ASA derivatives and corticosteroids -  CRP elevated initially 10/20 | 18 clinical improvement  complete remission at 8 - 17 (85%).  Improved endoscopic appearance in 15 and complete remission in eight (40%). | 6/8 |
| Bossa F, 2013.  21 | RCT | Efficacy of erythrocyte-mediated delivery of dexamethasone 21-phosphate in patients with steroid-dependent UC.  37 patients with steroid-dependent UC | 37 patients with steroid-dependent UC were randomized dexamethasone 21-phosphate encapsulated into autologous erythrocytes (n = 19) or to sham infusions (n = 18).  6-month therapy allowed the withdrawal of oral steroids and the reversal of steroid-related adverse events in 95% of patients. | 6/6 |
| Cakir M, 2011.  2 | Cohort | 28 children with moderate/severe UC. who were graded as having moderate/severe UC and received corticosteroids as first-line therapy. | At day 30, 15 (53.5%) in remission, partial remission in 2 (7.1%), and no response in 11 (39.2%).  Short-term follow-up overall remission in 17 (60.7%).  Predictors for steroid non-response were analyzed and only PUCAI at the initial admission was found to be associated with non-response to steroids (51.4 ± 11.4 vs. 65.4 ± 6.8, P<0.05. | 6/8 |
| Tripathi 1992  (Tripathi, Kirschner et al. 1992) | Cohort | [Twenty patients with UC in therapy with methylprednisolone](https://www.ncbi.nlm.nih.gov/pubmed/1587414) | [Corticosteroid treatment for inflammatory bowel disease in pediatric patients increases intraocular pressure.](https://www.ncbi.nlm.nih.gov/pubmed/1587414) | 6/8 |
| Hyams J, 2006.  3 | Cohort | Clinical outcome using PGA after methylprednisolone therapy in newly diagnosed UC  97 with minimum of 1 year follow up | 77 (79%) received corticosteroids (62 within 30 days of diagnosis [early] and 15 between 31 days and 6 months [late])  1 year, 31 of 62 (50%) of the early patients were corticosteroid responsive and 28 (45%) were corticosteroid dependent. 4 patients (5%) required colectomy in the first year. | 6/8 |
| Kolho KL, 2006.  23 | Cohort | To asess whether the changes in fecal calprotectin levels reflect therapeutic responses in 57 patients after oral prednisolone  . | Fecal calprotectin was <100 microg/g in 70% of the children with normal findings on colonoscopy or a non-IBD disease. Fecal calprotectin was >100 microg/g in all but one child with active IBD and in 13/15 of those children who were introduced to glucocorticoids by the clinicians. Fecal calprotectin values decreased within 4 weeks in line with clinical improvement in 7 children and normalized in 4/15 children during the follow-up ( < 100 microg/g) | 6/8 |
| Kudo T, 2011.  24 | Cohort | Retrospectively compared induction therapy using pulse steroids (glucocorticoids) with conventional steroid treatment for children and adolescents with moderate-to-severe UC. | Pulse steroid therapy successfully induced rapid remission in UC patients with moderate-to-severe disease compared with conventional treatment (13.2 days vs. 25.1 days; P < 0.05).  PUCAI score before pulse steroid therapy was 36.8 +/- 4.2 points, which was not significantly different to conventional therapy. PUCAI score was significantly improved 1 week after (12.6 +/- 3.9 points). | 6/8 |
| Jakobsen 2011  (Jakobsen, Bartek et al. 2011) | Cohorts, | Two population-based cohorts comprising paediatric (2001-2006) 20 children and adult (2003-2004) patients (n=106) from Copenhagen County and City were studied. | Children with UC had more extensive disease compared to adult patients [14 (70%) vs. 20 (19%), P<0.001]. The risks of starting systemic steroid treatment and AZA/MP were higher for paediatric UC patients compared to adult UC patients; hazard ratio (HR): 3.1 (95% CI: 1.8-5.3) and HR: 2.5 (1.3-5-9), respectively. Steroid dependency was more frequent in paediatric than in adult UC patients [9 (45%) vs. 9 (8%), P<0.001]. | 5/8 |
| Mrakotsky C, 2013  25 | Cohort | The study investigated acute effects of corticosteroids on memory, executive functions, emotion, and behaviour in children and adolescents with inflammatory bowel disease (IBD) | Patients 8-17 years with IBD (Crohn's disease, CD; ulcerative colitis, UC) on high-dose prednisone (n = 33) and IBD patients in remission off steroids (n = 33) completed standardized neuropsychological tests and behavior rating scales. Corticosteroid therapy can have acute effects on cognition, emotion, and behavior in chronically ill children. | 6/8 |
| Sidoroff and Kolho 2014  (Sidoroff and Kolho 2014) | Case series | Retrospective case series of 57 paed IBD patients about to stop oral prednisolone. | Morning cortisol was below the reference range in 20% of the patients and undetectable in 10%.  Low cortisol levels associated with higher daily glucocorticoid doses (median 7.2 mg/m(2) vs. 3.0 mg/m(2) in patients with normal cortisol levels, p < 0.05) and long duration of the treatment (median 11 months vs. 4 months, p < 0.05). Patients with undetectable cortisol levels recovered within few weeks (median 5.6 weeks). | 6/8 |
| Romano C, 2010.  9 | Cohort | Evaluate the clinical efficacy of oral beclomethasone diproprionate (BDP) in inducing clinical and endoscopic remission in children with mild to moderate active ulcerative colitis (UC). | BDP showed a significant reduced clinical activity within 4 weeks (P < 0.001 vs pretreatment values) with 80% achieving clinical remission compared with 33% treated with only 5-ASA (P < 0.025).  A significant reduction in clinical activity was achieved by 5-ASA after 8 weeks.). Erythrocyte sedimentation rate was significantly reduced (P < 0.025 or less) with both treatments, whereas C-reactive protein dropped significantly (P < 0.02) only in BDP. | 6/8 |
| Sylvester FA, 2011.  26 | Cohort | 83 children with UC intravenous methylprednisolone treatment classified as responders/nonresponder based on the need for therapy escalation.  Fecal OPG results were compared with those of four other fecal markers. | 22 children failed corticosteroid therapy and required infliximab (n = 20) or colectomy (n = 2).  Day 3 fecal OPG may guide the decision to institute second-line therapy in children with severe UC. The role of OPG in the inflammatory response in pediatric UC deserves further study. | 6/8 |
| Tung J, 2006.  1 | Cohort | UC (n = 36) < 19 years of age  Outcomes at 30 days and 1 year after the initial course of corticosteroids were recorded. | Thirty-day outcomes for UC were complete remission in 7 (50%), partial remission in 4 (29%), and no response in 3 (21%). One-year outcomes for UC disease were prolonged response in 11 (42%) and corticosteroid dependence in 8 (31%), whereas 7 (27%) were postsurgical. | 6/8 |
| Turner D, 2010.  27 | Prospective cohort study | multicenter prospective study, to evaluate CS bioavailability plays a role in prednisolone refractoriness in 128 patients with severe pediatric UC | 28% (95% CI, 23 to 34%) required admission for intravenous corticosteroid therapy, of whom 53 (53%; 95% CI, 44 to 63%) responded.  multivariable modelling only C-reactive protein [OR = 3.5 (1.4 to 8.4)] and number of nocturnal stools [OR = 3.2 (1.6 to 6.6)] remained significant at both days 3 and 5. | 6/8 |
| Uchida 2006  (Uchida, Araki et al. 2006) | Case control | Steroid side effects in 28 paeds  57 adults with UC pre op | Higher rates of glaucoma (36%), osteoporosis (322%), cataract (25%) in children C/W adults on similar total doses of steroids.  Growth failure in 50% of the children. | 4/8 |
| Hawthorne AB  1993  28 | Cohort | Fluticasone propionate compared with prednisolone in the management of active left sided or total ulcerative colitis  205 patients were studied in the multicentre four week double blind study  Prednisolone was given in a dose of 40 mg daily orally, reducing over four weeks to 10 or 20 mg. Fluticasone propionate was given in an oral daily dose of 20 mg. | Using the primary outcome measure (investigators assessment of response) improvement was signficantly better in the prednisolone group at 2 weeks but although still better this was no signficant at 4 weeks.  Unlike the prednisolone group fluticasone did not cause suppression of early morning cortisol. | 6/8 |
| Campieri M  2003  8 | RCT | Beclometasone dipropionate (BDP) in an oral controlled release formulation in the treatment of extensive or left-sided ulcerative colitis  177 patients were enrolled and randomly treated with BDP (n = 90) or 5-ASA (n = 87). | Mean DAI score decreased in both treatments groups (35 vs 15 , P < 0.0001 vs. baseline for both groups).  Clinical remission was achieved in 63.0% of patients in the BDP group vs. 62.5% in the 5-ASA group.  A significant DAI score improvement (P < 0.05) in favour of BDP was observed in patients with extensive disease. . | 6/6 |
| Gionchetti P  2005  29 | RCT | A total of 217 patients were enrolled and treated with BDP (n = 111) or 5-ASA (n = 106). | A significant decrease in the DAI score (P < 0.05) was observed in both treatment groups, with a clinical remission rate of 36.7% in the BDP group and of 29.2% in the 5-ASA group. | 6/8 |
| Sandborn WJ  2012  30 | RCT | Budesonide vs. Budesonide MMX® in 509 patients with active, mild to moderate ulcerative colitis  . | The rates of remission at week 8 among subjects given 9 mg or 6 mg budesonide MMX or mesalamine were 17.9%, 13.2%, and 12.1%, respectively, compared with 7.4% for placebo (P = .0143, P = .1393, and P = .2200). The rates of clinical improvement at week 8 among patients given 9 mg or 6 mg budesonide MMX or mesalamine were 33.3%, 30.6%, and 33.9%, respectively, compared with 24.8% for placebo (P = .1420, P = .3146, and P = .1189) | 6/8 |
| Travis SP  2014  11 | RCT | Budesonide MMX with placebo in patients with active, mild-to-moderate ulcerative colitis (UC). Patients were randomised 1:1:1:1 to receive budesonide MMX 9 mg or 6 mg, or Entocort EC 9 mg (budesonide controlled ileal-release capsules; reference arm) or placebo once daily for 8 weeks. The primary endpoint was combined clinical and endoscopic remission, defined as UC Disease Activity Index score </=1 with a score of 0 for rectal bleeding and stool frequency, no mucosal friability on colonoscopy, and a >/=1-point reduction in endoscopic index score from baseline. | 410 patients were evaluated for efficacy Combined clinical/endoscopic remission rates with budesonide MMX 9 mg or 6 mg, Entocort EC and placebo were 17.4%, 8.3%, 12.6% and 4.5%, respectively. budesonide MMX 9 mg and placebo was significant (OR 4.49; 95% CI 1.47 to 13.72; p=0.0047). and higher rates of clinical (42.2% vs 33.7%) and endoscopic improvement (42.2% vs 31.5%) versus placebo. | 6/8 |

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| Hymes 2011 | Cohort | Prospective TP efficacy 1y, n=133 | 49% steroid remission at 1y | 5/9 |
| Aloi 2016 | Cohort | Prospective TP efficacy 2y, n=121 | 72% steroid free remission at 2y | 5/9 |
| Chhaya 2015 | Cohort | Retrospective  Colectomy rate, n=1175 | TP did not reduce colectomy rate | 6/9 |
| Fuentes 2003 | Cohort | Retrospective TP withdrawal rate | TP withdrawal rate -18% | 4/9 |
| Kirschner 1998 | Cohort | Retrospective TP withdrawal rate | TP withdrawal rate -30% | 4/9 |
| Gazouli 2012 | Cohort | Prospective  TPMT and myelosuppression, n=108 | 15% myelosuppression in the abnormal TPMP group | 5/9 |
| DeRidder 2006 | Cohort | Prospective  TPMT and myelosuppression, n=72 | No benefit for TPMP measurement | 5/9 |
| Nguyen 2013 | Cohort | Retrospective  TP metabolites and benefit, n=86 | Higher rate of clinical remission, OR 4.1 if 6TGN higher than 250 | 5/9 |
| Armstrong L, 2011. | Cohort | Retrospective  TP metabolites and benefit, n=70 | 68% of patients not in therapeutic window | 4/9 |
| Nguyen 2013 | Cohort | Retrospective  TP metabolites and benefit, n=78 | OR=11 for TP failure if level higher than 405 and symptoms | 5/9 |
| Aloi M, 2010. | Cohort | Retrospective  MTX efficacy in TP intolerant children, n=32 | 50% response/remission at 1y | 4/9 |

Immunomodulators

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| --- | --- | --- | --- | --- |
| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Conrad, M A, (2016) | Cohort | Prospective Study  Twenty-one subjects (5 with ulcerative colitis) received vedolizumab | Clinical response was observed in 6/19 (31.6%) of the evaluatated subjects at week 6 and in 11/19 (57.9%) by week 22.  Steroid-free remission was seen in 1/20 (5.0%) subjects at 6 weeks, 3/20 (15.0%) at 14 weeks, and 4/20 (20.0%) at 22 weeks. | 5/8 |
| Hyams, J. (2012) | Cohort | 332 pediatric patients with UC  Response by PGA | Corticosteroid-free inactive disease in 27%, 38% and 21% at 6, 12, and 24 months, respectively  Colectomy free after treatment with infliximab was 75% at 6 months, 72% at 12 months, and 61% at 2 years | 6/8 |
| Hyams, J, (2012) | RCT | Sixty patients (6-17 years old) active UC given 5 mg/kg infliximab (weeks 0, 2, 6). At week 8, responders were randomly assigned to q8w or q12w and followed through week 54 | At week 8, response in 73.3%  Among responders, twice as many were in remission at week 54 after q8w (8 of 21, 38.1%) than q12w (4 of 22, 18.2%; P = .146) therapy.  Assuming the q8w remission rate for responders, the overall remission rate at week 54 would be 28.6% | 6/6 |
| Jacobstein DA (2005) | cohort | Retrospective  243 patients in 6 (1652 infusions). Thirty-three received premedication before the first infusion reaction (IR) (group 1). Two hundred ten patients did not receive premedication until the development of IRs, if at all (group 2 | 60 infusion reactions were recorded in 40 patients (3.6% of infusions, 16.5% of patients). ). IRs were more common among patients in group 1 than in group 2 (12/33 versus 28/210, P < 0.01). Two of 10 who began receiving premedication had a subsequent IR versus 6 of 12 who did not receive premedication (P = 0.15). remedication does not seem to prevent the development of IRs; however, once an IR has occurred, premedication may be indicated to prevent subsequent IRs | 5/8 |
| Lahdenne, P (2010) | cohort | Prospective  64 pediatric patients (16 IBD) were give premedication oral acetaminophen and cetirizine | Twelve infusion reactions, 4 mild and 8 severe, were observed in 8 (12.5%) of the 64 subjects, and in 1 subject 4 times.In pediatric patients, acute infusion reactions could not be prevented with premedication. | 5/8 |
| Larsen, M. D. (2016) | Cohort | Retrospective  Pediatric patients included in the Danish National Patient Registry who had received IFX within 5 years from diagnosis and the proportion of surgery in that cohort | 19% of UC children had been treated within 5 years. In 1468 UC patients, the cumulative proportion of surgery suggested a decline in patients diagnosed after mid 2005, and the hazard ratio of surgery was 0.64 [95% CI: 0.47-0.86] after the introduction of anti-TNFalpha agents compared with before. For UC patients diagnosed in 2009-2013, the 5 year cumulative proportion of surgery was 7.6% [95% CI: 5.2-11.2]. | 5/8 |
| Singh, N. (2016) | cohort study | Retrospective  Fifty-two patients, (42% UC) initiated vedolizumab | Week 14 remission rates for UC was 76% respectively  80% of anti-TNF-naive experienced week 14 remission.  week 22, anti-TNF-naive higher remission rates than exposed patients (100% versus 45%, P = 0.04).  UC patients experiencing earlier and higher rates of remission than CD patients. | 5/8 |
| Turner, D. (2011) | Systematic review | 291 children from five studies | Infliximab effective (75% pooled short-term response (95% CI: 67%-83%); n = 126, six studies) with a pooled 1-year response of 64% (95% CI: 56%-72%) | Systematic review |
| Vahabnezhad, E. (2014) | cohort study | Retrospective  188 patients initiating IFX at <21 years of age with 1-year minimum follow-up | 29% of patients with UC achieved sustained durable remission.  70% avoided colectomy at 1 year.  Of IFX failures, 11% developed ATI.  IFX dose intensification can optimize durability and overcome loss of response. | 5/8 |
| Volonaki, E., (2015) | Cohort study | Retrospective  11 patients received adalimumab.  All previously treated with infliximab | 6 achieved and maintained clinical remission, with a median duration of treatment of 25 months.  1 weaned off adalimumab after 26 months  Treatment unsuccessful in 4/ 11 (36%) who underwent colectomy 4-13 months (median 7 months) from the first adalimumab dose. The remaining patient developed extensive rash and was switched to alternative therapy | 5/8 |

Granulocyte apheresis

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Ikeda H, 200653. | Case Series | Three males and 1 female ranging 11 - 17 years  treated with GCAP once per week for 5 consecutive weeks/course | In 2 patient’s clinical, laboratory and endoscopic improvement. In 1 patient, GCAP improved laboratory and endoscopic markers, but no remission. Ineffective in the fourth patient | 3/8 |
| Martin de Carpi J. 200854. | Case Series | 9 patients with a mild to moderate disease (6 boys, 3 girls; 5 UC and 4 CD.  GMA apheresis - 5 consecutive weekly sessions  Steroids could be tapered after 2nd apheresis | 4 /5 UC and 1/ CD achieved remission. Remission maintained 2 / 4 UC 1/4 CD.  3 / 5 steroid-free at study end  GMA apheresis was well tolerated and no severe side effects | 4/8 |
| Mori K, 200455. | Case Series | 3 UC patients (different disease severity, location, disease duration and therapy). | All patients were under mesalamine or steroids at baseline, and GCAP was started after therapy failure. In all 3 patients improvement of symptoms became apparent | 2/8 |
| Ruuska T, 200956. | Cohort | Retrospective study of 37 children who had received GMA treatment and followed at least one year afterwards. 13 had CD, 22 UC and 2 IC.  Efficacy was evaluated by PUCAI, PCDAI. | PUCAI and PCDAI decreased significantly after 3 months (P 0.0007, P 0.025).  Steroid dosage significantly reduced in the UC group by the end of GMA (P 0.004) and this response continued after 3 months. Relapse was seen in 2 patients with UC and 3 patients with CD after 3 months follow-up. | 5/8 |
| Tanaka T, 201357. | Cohort | 17 patients who relapsed on mesalamine received GMA, 2 sessions in week 1, then weekly, up to 11 sessions.  A decrease of ≥5 in the clinical activity index (CAI) continued with GMA, while non-responders got steroids plus GMA similar to responder cases. | At entry and week 12, patients were clinically and endoscopically evaluated.  5 (29%) did not respond to the first 5 GMA sessions and received steroids plus GMA, while 12 (71%) responded to the first 5 sessions and got additional sessions.  At entry, the average CAI was 12.7 ± 2.5, range 8–17, and the average endoscopic index was 8.5 ± 1.5, range 7–11. The corresponding values at week 12 were 2.1 ± 0.2, range 1–4 (P < 0.001) and 2.4 ± 0.2, range 1–4 (P < 0.001). | 5/8 |
| Tomomasa T, 200358. | Case series | Retrospective study. Twelve steroid-refractory children  treated with GCAP, one session/week for 5–10 consecutive weeks | 8 patients (67%), clinical symptoms improved after two sessions.  The endoscopic grade improved from 2.6 to 0.4. The dose of tapered during GCAP therapy by 50%. No serious adverse effects. 4/ 8 cases relapsed 3.5±2.2 months after the last GCAP | 3/8 |
| Ruuska T,200956 | Case Series | Retrospective study of 38 children who had received GMA treatment and followed at least one year afterwards.  12 had CD, 24 UC and 2 IC. All with moderate or severe disease and were corticosteroid- dependent or corticosteroid-resistant. | 20/24 (83%) UC patients, 9/12 (75%) CD patients and 2 IC patients responded initially. During the 1 year follow-up 16/20 UC patients (80%) relapsed in an average of 25 (range 4–52) weeks. In the CD group all the patients relapsed, in an average of 17(range 5–26) weeks. In the IC group both relapsed after 12 weeks. | 4/8 |
| Tomomasa T, 201159. | Cohort | Multicenter open label study. 23 patients ages 8 to 16 years with moderate (19) to severe (4) steroid-resistant UC were enrolled  LCAP once per week for 5 consecutive weeks. Primary endpoint - decreased stool frequency/hematochezia score,  Secondary endpoints - clinical, laboratory, and endoscopic improvements. | Clinical parameters significantly improved. Stool frequency/hematochezia score decreased from 4.5 ± 1.2 to 1.6 ± 1.9  Remission rate 9/23 (39%)  Clinical improvement 19/23 (83%) patients.  Fecal calprotectin decreased significantly. [6636 ±13667 microg/g before treatment vs 2568±3564 after 6 weeks (p<0.05)]  Endoscopic findings evaluated using Matts score also improved (P<0.01).  Adverse effects was 61%, (none serious). | 6/8 |
| Ruuska T, 201660. | Cohort | Prospective Open-label, multicenter study in 25 children with moderate, active ulcerative colitis with PUCAI of 35-64.  One weekly apheresis with Adacolumn granulocyte, monocyte/macrophage adsorptive (GMA) apheresis over 5 consecutive weeks, optionally followed by up to 3 additional apheresis treatments over 3 consecutive weeks | primary endpoint - mean PUCAI change between baseline and week 12; secondary endpoint - improvement in PUCAI  Intention-to-treat (ITT), mean PUCAI improvement was 22.3 [95%CI: 12.9-31.6; n = 21].  Per-protocol (PP) mean improvement was 36.3 [95%CI: 31.4-41.1; n = 8].  Significant Improvement was recorded for 9 out of 20 patients (45%); 5 out of 20 patients (25%) had Moderate Improvement and one patient (5%) had No Change in PUCAI score at week 12.  The endoscopic activity index (EAI) decreased by 3 points on average. Seven (7) out of 21 (33%) patients in ITT and 4 out of 8 (50%) patients in PP have used steroids during the clinical investigation. | 6/8 |

There were case reports which not included in the evidence table

61Dittrich K. Inflamm Bowel Dis. 2008 Oct;14(10):1466-7.

62Kawasaki Y. J pediatr Gastroenterol Nutr. 2004 Oct;39(4):422-5.

63Martín-Carpi J. Journal of Crohn's and Colitis (2009) 3:3 (216-217). Date of Publication62: September 2009

64Ruuska T. Scand J Gastroenterol. 2007 Nov;42(11):1390-1.

Faecal Microbiota transplant

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Suskind DL, 201561. | Cohort | Four patients with moderate symptoms defined by the PUCAI were enrolled in a prospective, open-label study of FMT via nasogastric tube in pediatric UC. | None of the patients clinically improved with FMT, nor were there any significant changes in stool calprotectin or laboratory values, including C-reactive protein, albumin, and hematocrit. | 4/8 |
| Kunde S, 201362. | Case Series | Ten children, 7 to 21 years of age, with mild-to-moderate UC (pediatric UC activity index [PUCAI] between 15 and 65) received freshly prepared fecal enemas daily for 5 days. | Clinical response/remission was defined by PUCAI.  7 of the 9 (78%) subjects showed clinical response within 1 week, 6 of the 9 (67%) subjects maintained clinical response at 1 month, and 3 of the 9 (33%) subjects achieved clinical remission at 1 week after FMT. | 4/8 |

Four cases reports were excluded from inclusion in the table.

67Kellermayer R. Am J Gastroenterol 2015;110:604–6.

68Vandenplas Y. J Pediatr Gastroenterol Nutr 2015;61:e12–4

69Kumagai H Pediatr Gastroenterol Hepatol Nutr. 2016 Sep;19(3):214-220

70Shimizu H, Pediatr Int. 2016 Aug;58(8):781-5

Probiotics and Antibiotics

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Henker J, 200863 | RCT | 34 patients with UC in remission aged 11 -18 years allocated to Escherichia coli Nissle 1917 (EcN) (2 capsules o. d., n = 24) or 5-ASA (median 1.5 g/d, n = 10) and observed over a year. | The relapse rate was 25 % (6 / 24) in the EcN group and 30 % (3 / 10) in the 5-ASA group. | 2/6 |
| Huynh HQ, 200964. | Cohort | 18 patients (3-17 YEARS) mild to moderate UC received open-label VSL#3 daily in 2 divided doses for 8 weeks.  Disease activity assessed by simple clinical colitis activity index (SCCAI); Mayo ulcerative colitis endoscopic score; inflammatory markers: erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP); serum cytokine profiling; and rectal tissue microbial profiling done at baseline and at week 8. | Thirteen patients completed 8 weeks of VSL#3 treatment and 5 patients were withdrawn due to lack of improvement. Remission (defined as SCCAI <or=3) was achieved in 56% of children (n = 10); response (decrease in SCCAI >or=2, but final score <or=5) in 6% (n = 1); and no change or worsening in 39% (n = 7).  Post-VSL#3 treatments demonstrated a bacterial taxonomy change in rectal biopsy. The VSL#3 was well tolerated in clinical trials and no biochemical and clinical adverse effects attributed to VSL#3 were identified. | 6/8 |
| Miele E, 200965. | RCT | 29 consecutive patients with newly diagnosed UC randomized to receive VSL#3 or an identical placebo (n=15) in conjunction with concomitant steroid induction and mesalamine maintenance treatment.  Children were prospectively evaluated at four time points: within 1, 2, 6 months, and 1 year after diagnosis or at the time of relapse. Lichtiger activity index and PGA were used to measure disease activity | Remission was achieved in 13 patients (92.8%) treated with VSL#3 and in 4 patients (36.4%) treated with placebo and IBD therapy (P<0.001).  3 of 14 (21.4%) patients treated with VSL#3 and 11 of 15 (73.3%) patients treated with placebo and IBD therapy relapsed within 1 year of follow-up (P=0.014; RR=0.32; CI=0.025-0.773; NNT=2).  All 3 patients treated with VSL#3 and 6 of 11 (54.5%) patients treated with placebo relapsed within 6 months of diagnosis. Relapse significantly lower in the VSL#3 group than in the placebo group (P<0.05). There were no biochemical or clinical adverse events related to VSL#3. | 4/6 |
| Oliva S, 201266. | RCT | 40 patients with mild to moderate UC (E1) prospective, randomised, placebo-controlled study. They received an enema solution containing 10(10) CFU of L. reuteri ATCC 55730 or placebo for 8 weeks, in addition to oral mesalazine. | 31 patients completed the trial  Mayo score (including clinical and endoscopic features) decreased significantly in the L. reuteri group (3.2 ± 1.3 vs. 8.6 ± 0.8, P < 0.01) compared with placebo (7.1 ± 1.1 vs. 8.7 ± 0.7, NS); Histological score significantly decrease only in the L. reuteri group (0.6 ± 0.5 vs. 4.5 ± 0.6, P < 0.01) (placebo: 2.9 ± 0.8 vs. 4.6 ± 0.6, N | 4/6 |

Complementary Medicine

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Suskind DL, 201367. | Case Series | 11 patients (6 CD, 5 UC) in remission or with mild disease in a tolerability study.  All patients received curcumin in addition to their standard therapy (6 mesalamine, 5 anti-TNF).  Patients initially received 500 mg twice per day for 3 weeks. Using the forced-dose titration design, doses were increased up to 1 g twice per day at week 3 for a total of 3 weeks and then titrated again to 2 g twice per day at week 6 for 3 weeks. | Nine patients completed the study. All tolerated curcumin well at all study doses. Two patients reported increase gassiness during three visits. Laboratory studies remained within normal range during the study. Three patients had lowering of PUCAI or PCDAI scores. Two patients with ulcerative colitis had PUCAI scores decrease 20 points indicating remission (scores dropped from 30 to 10 and 25 to 5, respectively). The Crohn’s patients score dropped from 5 to 0 suggesting improvement. No participants experienced a relapse or worsening of symptoms while on the study medication. | 3/8 |

Other considerations

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Broide 2011 | Cohort | Retrospective study  Acute pancreatitis preceding IBD diagnosis  (n=3960) in retrospective study | Acute pancreatitis precedes IBD in 2,17% in children and 0.06% in adults | 8 /9 |
| Felekis 2009 | Cohort | Prospective study Ophthalmological examination in IBD adolescents and adults  (n=60) | 43% of IBD patients have ophthalmological manifestations | 7/9 |
| Furlano 2015 | Cohort | Prospective study  Transfer capacity of carbon monoxide in IBD paediatric patients (n=48) | Transfer capacity of carbon monoxide is decreased in IBD | 7/9 |
| Frid  1986 | Cohort | Retrospective study  Cardiac manifestations in IBD in retrospective study  (n=106) | Myocarditis in 2/106 both in IBD remission | 3 /9 |
| Tabibian JH | Cohort | Prospective study  Vancomycin 125 mg or 250 mg four times/day, or metronidazole  250 mg or 500 mg three times/day for 12 weeks | The primary endpoint was decrease  in alkaline phosphatase (ALK) at 12 weeks.  Only patients in the vancomycin groups reached the primary endpoint, and with  less adverse effects. | 8/9 |
| Mason 2015 | Cohort | Prospective study  Puberty and growth in children/adolescents with IBD (n=63) | Puberty and growth and abnormal IGF-1 more frequent in boys | 8/9 |
| Schmidt  2012 | Cohort | Prospective study  Bone mineral density (BMD) in IBD  n=144 | Low BMD in IBD and more pronounced in boys. BMD in IBD is mostly temporarily decreased | 8/9 |
| Bollegala  2013 | Cohort | Prospective study  Characterizing transfer of care and health resources in transition of IBD care  (n=95) by questionnaire | In transferred adolescents fewer clinic visits but more non-compliance | 5/9 |
| Benchimol  2011 | Cohort | Prospective study  Assessment of health care resources in transition  (n=78) using “My Health passport for IBD” | Patients and parents equally understand the disease but not equally use the health services and resources | 6/9 |
| Cerveci  2013 | Cohort | Prospective study  Health care concerns among physicians and patients (n=15) paediatricians, 11 paediatric residents,28 patients by questionnaire | Differences in health care concerns among physicians and patients | 7 /9 |
| Bennett  2016 | Cohort | Retrospective study  Psychosocial survey  n=81 (46 transition and 35 non-transition patients) | Need for better psychosocial preparations and transition plans to improve on previous model used | 7/9 |
| Whitfield 2015 | Prospective cohort | Prospective study  Survey on self management skills  I pad survey in IBD n = 67 | Self-management skills in IBD improves with age but not with disease duration | 6/9 |

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| Study author, year (reference) | Study type | Description and study numbers | Summary results of primary outcome or main finding (OR/RR with CI or other summary format) | Quality score  0-6 for RCT  0-8 for cohort and case control studies (see methods) |
| Fonkalsrud 2001 | Cohort | Outcome in 168 patients who underwent IPAA. 131with U , 26 FAP, 9 Hirschsprung Disease and 2 colonic inertia.  *Mean Follow up 2 years* | 16% pouchitis, was most exclusively of UC patients and 3 times more frequent in lateral pouch than J pouch (no info regarding differentiation between the groups) | 6/9 |
| Gray 2012 | Cohort | Comparison of 50 UC patients who had IPAA, 22 with and 28 without diverting ileostomy  *Mean Follow up 2 years* | No significant difference in short and long term outcome between the 2 groups | 7/9 |
| Lillehei 2009 | Cohort | Outcome in 100 patients who underwent IPAA, 75 UC and 25 FAP  *Mean Follow up 2 years* | Pouchitis in 35/75 (47%) UC patients and 1/25 FAP patients. In both groups excellent results on fecal continence 93/100 and stool frequency average 5.43/day | 6/9 |
| Ozdemir 2014 | Cohort | Functional outcome and complications in 433 patients who underwent IPAA, 339 UC, 68 FAP, 22CD, 4 other  Mean Follow up 9 years | 35% pouchitis in UC patients (121/339), more frequent compared to CD and FAP group, (p=0.02).  Pouch failure and wound infection significantly more frequent in CD patients (p=0.02 and p= 0.004 respectively).  No significant difference in functional outcome | 8/9 |
| Pakarinen 2010 | Cohort | Fecal calprotectin in pouchitis cohort study in 32 UC patients post IPAA  *Mean Follow up 11 years* | Calprotectin higher in recurrent pouchitis vs. no pouchitis (Median 365,IQR 61.5-1580 vs Median 66.5, IQR 24-102, p=0.01) | 6/9 |
| Pakarinen 2009 | Case control | 52 UC patients with IPAA and 117 controls filled out questionnaires on QOL and long term health outcomes  *Mean Follow up 10 years* | Pouchitis reported in 73% (37 of 51 patients).  Overall QOL (scale1-7) was similar between patients and controls (5.7+1.1 in patients vs 5.8+1.2 in controls). Overall QOL was related to stool frequency (R=.42, p=0.002) | 7/9 |
| Durno 1998 | Cohort | 73 UC Patients after IPAA | Pouchitis in 41 (44%) with J-pouch. 12/18 required prolonged antibiotics. 2 patients (11% of those with pouchitis) required pouch excision. | 7/9 |
| Chew 2003 | Case-control | 19 pediatric patients (12 UC) and 19 (15 UC) adult patients after IPAA  *Mean Follow up of 8.6 years for pediatric group and 6.0 years for adult group* | Pouchitis 5 (31%) in pediatric group and 2 (13%) in adult.  Morbidity and mortality, functional outcome and quality of life after IPAA are similar in both pediatric and adult groups. | 7/9 |
| Koivusalo 2007 | Cohort | Surgical complications in relation to functional outcome in 47 UC patients with IAA, 37 J pouch and 10 straight  *Mean follow up 10 years* | 49% pouchitis (23/47)  Among surgical complications only pelvic sepsis and ultimate diagnosis of CD significantly worsen functional outcome, p=<0.05 | 6/9 |
| Rintala 2002 | Cohort | 40 patients after IPAA with J pouch, 29 with UC | 9/29 (31%) of UC patients had pouchitis, 2 had recurrent or chronic symptoms | 6/9 |
| Alexander 2003 | Cohort | 151patients <21 yrs of age following IPAA  *Mean follow-up of 7 years* | 73 patients (48%) had acute pouchitis, 11 (7%) had chronic pouchitis, 13 patients (9%) pouch failure. Perianal disease, prolonged symptom duration, CD on biopsy, long-term complications, and pouch fistulae were associated with poor outcome. | 7/9 |
| Dharmaraj 2016 | Cohort | 60 patients (43 UC, 17 FAP)after IPAA  *Mean follow up 3 years* | Pouchitis in 24 UC patients (56%) and 2 patients (12%) with FAP. 15 (35%) UC patients had chronic pouchitis. Multivariable showed higher PUCAI at diagnosis more likely to develop pouchitis (p=0.001) and chronic pouchitis (p=0.002). | 7/9 |
| Knod 2016 | Cohort | 26 UC patients <11 yrs old compared to 38 patients>11 yrs following IPAA  *Mean follow up not indicated* | Most common post-op complication was pouchitis.  Rate was similar between young (23.8%) and adolescent (28.6%) patients. | 5/9 |
| Wu 2014 | Cohort | Pouch outcomes in 104 pediatric patients compared with 1135 adults  *Mean follow up 10 years* | Time from IBD diagnosis to colectomy shorter in pediatric group (4(2.4-6) vs 8(4-15) yrs, p<0.001). Pediatric patients higher rate of procedure-related complications after IPAA than adults (20.2% vs 13.3%, P 1⁄4 .052).  Pediatric and adult patients had a similar long-term pouch retention rate (log rank test, p=0.26). | 7/9 |
| Seetharamaiah 2009 | Cohort | 168 UC cases and 35 FAP cases comparison between straight and J pouch IAA  *Mean follow up 3 years* | Mean number of bowel movements at 24 months for SIAA patients was 8.4+3.9 vs 6.2+2.8 per day in JPAA (p=0.003). Pouchitis/enteritis more frequent in the UC patients, and the odds of symptomatic pouchitis were higher in JPAA (OR 4.5, CI 2,32-8.72). | 7/9 |
| Shannon 2016 | Cohort | 176 children/adolesc. With IPAA from prev. reported cohorts, 74 of whom were reached by telephone for long-term followup | Median follow up 20 years, pouchitis in 33 patients (45%), fistulae in 22 (30%). 10(14%) had pouch failure, change of diagnosis to Crohn’s in 20 (28%). | 4/9 |
| Sarigol 1999 | Case series | 76/176 UC patients with IPAA were reviewed for dysplasia and mucosal adaptation in the pouch  *Mean Follow up 5 years* | No dysplasia was identified even in 5 patients who had dysplasia in resected colon. 3 types of mucosal adaptation were identified and outcomes compared, screening for dysplasia yearly or every other year were recommended based on mucosal type. | 6/9 |
| Ryan 2011 | Cohort | 83 pediatric patients with UC and 7 with polyposis syndromes, 68 underwent IPAA without diverting ileostomy  *Mean follow up not indicated* | Severe chronic pouchitis in 8/19 colitis patients with diverting ileostomy and 12/64 patients without a stoma (p=0.063). | 5/9 |
| Polites 2015 | Cohort | 175/202 patients with UC who underwent IPAA returned at least 1 questionnaire re long term function and qol  *Mean length of Follow up questionnaire 15 years* | Most patients reported qol unaffected or improved postop.  Chronic pouchitis in 22 patients and change in diagnosis to Crohn in 33 patients. | 6/9 |