TABLES OF EVIDENCE FOR ASC

**Pain management**

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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  0-9 for cohort and case control studies (see methods) |
| Benchimol, E.I. et al. AJG 2008 | CASE-CONTROL STUDY | Retrospective  n=10  Toxic megacolon in children with IBD: clinical and radiographic characteristics | 10 children with TMC were matched with 20 controls  2/10 TMC received low doses of narcotics  Fever (P = 0.005), tachycardia (P = 0.0001), dehydration (P = 0.01), and electrolyte abnormalities (P = 0.0002) were more common in children with TMC than controls.  0/10 children with TCM died  7/10 children with TCM required colectomy during admission.  2/3 children with TCM without colectomy required second line therapy | 6/9 |

**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) |
| Turner, D., et al. Gastroenterology, 2010. 138(7): p. 2282-91. | PROSPECTIVE COHORT STUDY. | Assessment of outcomes and predictors of nonresponse in children hospitalized for ASC (N=128) | Predictors associated with IVCS failure : number of stools (OR 1.9; 95% CI, 1.1–3.5)   * amount of blood ( OR, 2.5; 95% CI, 1.3–4.6) * age (OR, 1.2; 95% CI, 1.04–1.36) * new-onset disease (OR, 0.27; 95% CI, 0.1–0.7) * Day 5 PUCAI > 70 optimally guided implementation of salvage therapy (PPV 100%; NPV 79%; P<.001).   overall cumulative colectomy rate   * discharge: 9% * 1 year: 19%.   Day 3 PUCAI predicted response up to 1 year postdischarge (P<.001; time to salvage therapy). | 8/9 |
| Turner, D., et al. Gut, 2008. 57(3): p. 331-8. | RETROSPECTIVE COHORT STUDY | Retrospective review of rates and predictors (at day 3 and 5) of response to IVCS in ASC from a single-centre cohort (N=99). | admission for IVCS: 28 children with 53% response  Predictors of IVCS failure at D3, D5:   * CRP [OR=3.5 (1.4 to 8.4)] * number of nocturnal stools [OR=3.2 (1.6 to 6.6)] * PUCAI, Travis and Lindgren’s indices strongly predicted non-response   Cumulative colectomy rates   * discharge: 42%, * 1 year 58% * 6 years 61% | 8/9 |
| Cakir, M., et al. World J Pediatr, 2011. 7(1): p. 50-3. | RETROSPECTIVE COHORT STUDY | Steroid response in moderate to severe pediatric ulcerative colitis (mean PUCAI 57, pancolitis in 68%): a single center's experience (N=28) | CS as first-line therapy (2mg/kg/day max. 60 mg po or iv)  At day 30   * Complete remission**:** 15 patients (53.5%), * partial remission: 2 (7.1%) * no response: 11 (39.2%, 8 received cyclosporine, 2 infliximab and 1 tacrolimus; 3 indicated to colectomy with a median interval of 5 mo after the diagnosis).   predictors of non response to Cs   * PUCAI at the initial admission (51.4 +/- 11.4 vs 65.4 +/- 6.8, P<0.05). | 6/9 |
| Choshen, S., et al. J Pediatr Gastroenterol Nutr, 2016. 63(1): p. 58-64. | RETROSPECTIVE ANALYSIS FROM PROSPECTIVE + RETROSPECTIVE LONGITUDINAL COHORT | Corticosteroid Dosing in Pediatric Acute Severe Ulcerative Colitis: A Propensity Score Analysis  n=283 | optimal dosing of IVCS  3 cutoffs   * 1 mg/kg methylprednisolone to 40 mg/day (N=94) * 1.25 mg/kg to 50 mg/day (N=218) * 2 mg/kg to 80 mg/day (N=86) * no statistical differences in the outcomes of the two lower cutoffs. * High doses were not associated with better outcome | 9/9 |
| Kudo, T., et al. Pediatrics International, 2011. 53(6): p. 974-979. | RETROSPECTIVE CASE-CONTROL | Pulse steroids as induction therapy for children with moderate-to-severe ulcerative colitis.  n=37 | induction of remission : 13.2 days vs 25.1 days; P < 0.05) after   * methylprednisolone pulse (iv 20–30 mg/kg/day, max. 1000mg/day for 3 days;) vs. * prednisolone 1–1.5 mg/kg/day * No serious adverse effects of pulse therapy were observed. * relapse rate during 12 months after pulse therapy was not significantly different from that after conventional treatment. | 5/9 |
| Vora, R., et al. J Pediatr Gastroenterol Nutr, 2016. 63(1): p. 51-7. | RETROSPECTIVE CASE-CONTROL | Clinical Experience of Use of High-dose Intravenous Methylprednisolone in Children With Acute Moderate to Severe Colitis (n=34) | efficacy of standard (2 mg/kg/day) IVCS vs high dose (10-30 mg/kg/day) IVCS.   * Day 5 PUCAI significantly lower in high-dose (15, IQR 8.5–20) vs standard-dose IVCS (30, IQR 20–30). * IVCS side effects were minor and reversible. * medical salvage therapy was required in 5.8% (2 children) before discharge, and in 17% (6 children) at follow-up after 1 year. The colectomy rate * During admission: 0% * 1 year; 11% (4 children) after 1 year, * trend of less colectomies in high-dose (4.8%—1 child) than in standard-dose (23%—3 children) | 7/9 |
| Faure, C., et al. Eur J Clin Pharmacol, 1998. 54(7): p. 555-60. | RCT | Pharmacokinetics of intravenous methylprednisolone and oral prednisone in paediatric patients with inflammatory bowel disease during the acute phase and in remission  (n=12) | 8CD, 3UC, 1undefined colitis  Acute phase: iv MP (2 mg/kg) versus oral prednisone (2 mg/kg)  Remission: oral prednisone (2mg/kg)  Elimination half-life  MP: 1.67h (acute phase)  PL 3.51h (acute phase) and 2.42h (remission). | 2/6 |

**Heparin, Antibiotics, 5ASA**

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| Turner D, 2014  (14) | Retrospective cohort study  n=15 | Combination of 3–4 antibiotics MADoV (metronidazole, amoxicillin, doxycycline, and if hospitalized, vancomycin) in children with moderate-severe  refractory UC and IBD-unclassified  (n=15) | Complete remission in 47% (7/15) | 5/9 |
| Lazzerini M, 2011  (31) | Systematic review | Review of Thromboembolisms in pediatric IBD: Two historical  cohort studies, 5 retrospective analysis of single  hospital databases, 8 case series, and 36  case-reports were included | TE occurred in children with IBD in all age ranges,   * 82.8% during active disease, and more frequently in children with UC (OR 3.7, 95% CI 1.8–7.6). * At least 1 specific risk factor for TE was recognized in 50% of cases; * 2 risk factors were present in 24%. * 92 published cases of TE in children with IBD   + 54.3% occurred in cerebral site,   + 26% in the limbs,   + 13% in the abdominal vessels,   + remaining in the retina and lungs. * 11,4 % early recurrence * 10% late recurrence in 10%. * 5,7% overall mortality mostly associated with cerebral TE. | n.a. |

**Radiography, toxic megacolon and monitoring**

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| Travis 1996 (2) | Cohort study  Prospective | 51 consecutive episodes of  ASC (Truelove and Witts criteria)  n= 49 adult UC patients | A stool frequency > 12/day on day 2 was associated with 55% colectomy while a stool frequency of 8/day or 3-8/day and CRP > 45 mg/L predicted colectomy in the 85% of 49 patients with severe ulcerative colitis | 4/8 |
| Lindgren 1998 (3) | Cohort study  Retrospective | n=97 adult patients with ASC treated with steroids | Sustained elevation of body temperature, persistent bloody diarrhoea and continued CRP elevation on day 3 of intravenous GCS treatment strongly predict clinical steroid resistance in severe acute ulcerative colitis | 4/8 |
| Jarnerot 2005 (4) | RCT | n=45 adult patients with ASC and Sweden Index ≥ 8 on day 3 were randomized to infliximab or placebo group. | A Sweden index ≥ 8 (stool frequency + 0.14xCRP > 8 mg/L) on day 3 predicted colectomy in 46% in both groups. | 4/6 |
| Seo 2002 (5) | Cohort study  Retrospective | n=127 adult patients with ASC | A Seo index > 200 after 2 weeks of medical treatment was predictive for colectomy | 5/8 |
| Ho 2004 (6) | Cohort study  Retrospective | n=167 consecutive patients with ASC | A risk score ≥4 had a sensitivity of 85% and specificity of 75% in predicting non-response | 5/8 |
| Corte 2015 (7) | Cohort study  Retrospective | n=89 patients with ASC | The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) at admission was useful to predict the need for second line therapy or colectomy | 5/8 |
| Turner 2008 (8) | Cohort study  Retrospective | n=99 children admitted with ASC | The PUCAI, calculated on days 3 and 5 of steroid therapy, can identify patients requiring salvage therapy. | 5/8 |
| Turner 2010 (9) | Prospective multicentre cohort study | n=128 children admitted with ASC | Higher rate of clinical remission, OR 4.1 if 6TGN higher than 250 | 5/8 |
| Kowlowsky 2014 (10) | Cohort study  Retrospective  Multicenter | n=153 adults with ASC | 68% of patients not in therapeutic window | 5/8 |
| Soon 2012 (11) | Population-based cohort study | n=30 children with UC who underwent colectomy | Prolonged steroid treatment before colectomy may increase the risk of post-operative complications | 4/8 |
| Randall 2010 (12) | Cohort study  Prospective | n= 80 adults with ASC who underwent urgent colectomy and ileostomy for ASUC | 50% response/remission at 1y | 5/8 |

**Second line medical therapy**

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| Turner, D., et al. Gastroenterology, 2010. 138(7): p. 2282-91. | RETROSPECTIVE COHORT STUDY | Retrospective review of rates and predictors (at day 3 and 5) of response to IVCS in ASC from a single-centre cohort (N=99). | 37 (children failed IVCS and received, within 10.5 +/- 6.4 days,   * cyclosporine (n=1; 3%), * colectomy (n=3; 8%), * infliximab (n=33; 89%). * 25/33 children treated with infliximab responded.   overall cumulative colectomy rate:   * 9% by discharge * 19% by 1-year. | 8/9 |
| Turner, D., et al. Gut, 2008. 57(3): p. 331-8. | RETROSPECTIVE COHORT STUDY | Steroid response in moderate to severe pediatric ulcerative colitis (mean PUCAI 57, pancolitis in 68%): a single center's experience (N=28) | 28 % (95% CI, 23 to 34%) required admission for IVCS, of those **53% responded to IVCS.**  Cumulative colectomy rates   * discharge: 42%, * 1 year 58% * 6 years 61% | 8/9 |
| Cakir, M., et al. World J Pediatr, 2011. 7(1): p. 50-3. | PROSPECTIVE COHORT STUDY. | Assessment of outcomes and predictors of nonresponse in children hospitalized for ASC (N=128) | CS as first-line therapy (2mg/kg/day max. 60 mg po or iv)  At day 30   * Complete remission**:** 15 patients (53.5%), * partial remission: 2 (7.1%) * no response: 11 (39.2%, 8 received cyclosporine, 2 infliximab and 1 tacrolimus; 3 indicated to colectomy with a median interval of 5 mo after the diagnosis).   predictors of non response to Cs  PUCAI at the initial admission (51.4 +/- 11.4 vs 65.4 +/- 6.8, P<0.05). | 6/9 |

**Sequential therapy**

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| Narula N 2015 | Systematic review | sequential therapy in adult ASUC to May 2014 (n=10 studies: one prospective cohort, 9 retrospective cohorts, and RCT, all studies of poor methodological quality | risk of sequential therapy seems lower than initially reported, so no decision for or against; only experienced IBD centers should consider patients for sequential therapy | na. |
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