APPENDIX 1

Predefined questions that the subgroups addressed.

- 1. What are the red flags upon admission that suggest a particularly severe course in children?
- 2. How to dose intravenous corticosteroids in severe pediatric UC?
- 3. What are the recommendations regarding antibiotic therapy?
- 4. What are the recommendations regarding other medical therapies (e.g., enemas, 5-ASA, heparin)?
- 5. Should children with severe colitis undergo active evaluation for CMV and C. difficile infections? If so, what is the preferred way?
- 6. How and when should children with severe attacks be monitored for change in disease activity? When should endoscopic evaluation of the colonic mucosa be evaluated?
- 7. When and on what grounds to introduce second-line therapy?
- 8. Which second-line therapy should be preferred (colectomy, infliximab, cyclosporine, or tacrolimus)?
- 9. What are the prescription recommendations of cyclosporine, tacrolimus, and infliximab (route, dose, monitoring levels and toxicity, and duration of treatment)?
- 10. How to determine success/failure of second-line therapy?
- 11. When second-line therapy fails, should salvage (i.e., third line) medical therapy be administered or is it an absolute indication for colectomy?
- 12. What should be the recommendations regarding dietary restriction and parenteral nutrition?
- 13. How to manage severe abdominal pain in children?
- 14. How should toxic megacolon be defined in children (including interpretation of abdominal radiography) and how should it be managed?
- 15. When can a child with severe colitis be discharged and when to introduce maintenance therapy?
- 16. Is there a preferred surgery in children?
- 17. What are the ways, before the surgery, to minimize surgical complications?

APPENDIX 2

Levels of evidence and grades of recommendation based on the Oxford Centre for Evidence-Based Medicine (for details see http://www. cebm.net/levels_of_evidence.asp#refs)

| Level | Diagnostic study | Therapeutic study | |
|-------|---|---|--|
| 1a | Systematic review (SR) with homogeneity of level 1 diagnostic studies | SR with homogeneity of randomized controlled trials (RCTs) | |
| 1b | Validating cohort study with good reference standard | Individual RCT (with narrow confidence interval) | |
| 1c | Specificity or sensitivity are so high that a positive or a negative result rules out or in the diagnosis | All or none | |
| 2a | SR with homogeneity of level >2 diagnostic studies | SR (with homogeneity) of cohort studies | |
| 2b | Exploratory cohort study with good reference standards | Individual cohort study (including low-quality RCT; e.g., <80% follow-up) | |
| 2c | | "Outcomes" research; ecological studies | |
| За | SR with homogeneity of 3b and better studies | SR with homogeneity of case-control studies | |
| Зb | Nonconsecutive study; or without consistently applied reference standards | Individual case–control study | |
| 4 | Case–control study, poor, or nonindependent reference standard | Case series (and poor-quality cohort and case–control studies) | |
| 5 | Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles" | Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles" | |
| | Grading of recommendation A, Consistent level 1 studies | | |

B, Consistent level 2 or 3 studies or extrapolations from level 1 studies

C, Level 4 studies or extrapolations from level 2 or 3 studies

D, Level 5 evidence or troublingly inconsistent or inconclusive studies of any level