

Supplementary table 2. Stepwise and comparative-grade endoscopic scoring systems for ulcerative colitis.

Index	Setting	Description of Scale	Extent of Use	Level of Validation
Truelove and Witts sigmoidoscopic assessment ¹ (1955)	Prospective study	Comparative 3-grade scale: (1) <i>Normal or near normal (slight hyperaemia or slight granularity)</i> (2) <i>Improved</i> (3) <i>no change or worse</i>	Some clinical studies	Not validated
Truelove and Richards sigmoidoscopic appearance ² (1956)	Prospective, case-controlled series study	Comparative 3-grade scale: (1) <i>Normal appearances</i> (2) <i>Mild and Moderate Activity: mild hyperaemia, granularity, few petechiae. More advanced changes – well-marked hyperaemia, increased fragility of the mucosa, sometimes ulceration but without features being as marked as severe</i> (3) <i>Intense hyperaemia, marked fragility of the mucosa with oozing blood spontaneously or with very slight trauma, presence of exudate and mucopus. Gross ulceration</i>	Some clinical studies	Not validated
Matts score ³ (1961)	Prospective study	Stepwise 4-grade scale: (1) <i>Normal</i> (2) <i>Mild granularity of the mucosa with mild contact bleeding</i> (3) <i>Marked granularity and oedema of the mucosa, contact bleeding and spontaneous bleeding</i> (4) <i>Severe ulceration of mucosa with haemorrhage</i>	Multiple clinical studies and RCT	Partially validated
Baron score ⁴ (1964)	Prospective study	Stepwise 4-grade scale: (0) <i>Normal</i> (1) <i>Abnormal but not haemorrhagic: appearances between "0" and "2"</i> (2) <i>Moderately haemorrhagic: bleeding to light touch but no spontaneous bleeding</i> (3) <i>Severely haemorrhagic: spontaneous bleeding</i>	Multiple clinical studies and RCT	Not validated
Dick score ⁵ (1966)	Prospective study	Stepwise 5-grade scale: (0) <i>Normal</i> (1) <i>Quiescent</i> <i>A pink finely granular abnormal mucosa, in which the vessels were not visible or only visible in places</i> (2) <i>Slightly active</i>	Some clinical trials	Not validated

		<p><i>A somewhat reddened, oedematous and abnormally friable mucosa</i></p> <p>(3) <i>Very active</i></p> <p><i>A very reddened, oedematous and friable mucosa, often with superficial ulceration and spontaneous bleeding and/or mucopus in the bowel lumen</i></p> <p>(4) <i>Fulminating</i></p> <p><i>The flaming red mucosa, often partly covered with pus, of a fulminating case</i></p>		
Binder ⁶ (1970)	Prospective study	Stepwise 4-grade scale: (1) <i>Normal; smooth, shining mucosa</i> (2) <i>Slightly active: slight granularity and/or fragility</i> (3) <i>Moderately active: pronounced granularity and fragility with pus and/or blood in the lumen</i> (4) <i>Very active: pronounced granularity and fragility together with visible ulcerations</i>	Some clinical studies	Not validated
Powell-Tuck Index ⁷ (1982)	Retrospective study	Stepwise 3-grade scale: (0) <i>Non-hemorrhagic (no bleeding spontaneously or light touch)</i> (1) <i>Hemorrhagic (bleeding on light touch but no spontaneous bleeding ahead of instrument)</i> (2) <i>Hemorrhagic (spontaneous bleeding seen ahead of instrument at initial inspection with bleeding on light touch)</i>	Some clinical studies	Partially validated
Blackstone endoscopic grading activity ⁸ (1984)	Prospective study	8-point scale: a) Quiescent: (1) <i>Distorted or absent mucosal vascular pattern</i> (2) <i>Granularity</i> b) Mildly active: (1) <i>Continuous or focal erythema</i> (2) <i>Friability (touch bleeding)</i> c) Moderately active: (1) <i>Mucopurulent exudate (mucopus)</i> (2) <i>Single or multiple ulcers (<5mm), fewer than 10 per 10-cm segment</i> d) Severe colitis: (1) <i>Large ulcers (>5mm): more than 10 per 10-cm segment</i> (2) <i>Spontaneous bleeding</i>	Some clinical studies	Not validated
Savarymuttu ⁹ (1986)	Prospective study	Stepwise 4 grade scale: (0) <i>Normal appearance</i> (1) <i>Loss of vessel pattern or edema</i> (2) <i>Contact hemorrhage</i>	Some clinical studies	Not validated

		(3) Ulceration or surface mucopurulence		
Friedmann Score ¹⁰ (1986)	Randomized controlled study	Stepwise 5-grade scale: (0) Normal (1) Erythema (2) Friability (contact bleeding) (3) Spontaneous bleeding and exudate (4) Frank ulceration	Some clinical studies	Not validated
Sutherland index (DAI or UCDAI) ¹¹ (1987)	Randomized-controlled study	Stepwise 4-grade scale: (0) Normal (1) Mild friability (2) Moderate friability (3) Exudation, spontaneous hemorrhage	Multiple clinical studies and RCT	Not validated
McPhee proctoscopic grading scale ¹² (1987)	Prospective study	Stepwise 4-grade scale: (0) Normal; chronic changes may be present, ie, patchy erythema; no friability (1) Erythema; edema (loss of vascular pattern); minimal friability (2) Marked edema and erythema; friability; small amount of exudate or pus (3) Spontaneous bleeding; ulceration; gross pus and mucus	Some clinical studies	Not validated
Danielsson-Löfberg score ^{13, 14} (1987)	Prospective RCT and Randomized, double-blind, prospective, pilot study	Mean scoring system (0-3) generated by averaging the scores of each colonic segment assessed (ascending, transverse, descending, sigmoid and rectum): (0) Normal/non-inflamed mucosa (1) Granularity, edema and lack of normal vascular pattern (2) Hyperemia, friability and petechiae (and all of score 1) (3) Ulcerations (and all of score 1 and 2)	Some clinical studies	Not validated
Maier ¹⁵ (1988)	Prospective study	Stepwise 4-grade scale: (0) No visible pathological change (1) hyperemia, lack of the typical vascular pattern (2) contact bleeding (3) Mucous, plaques of fibrin, blood, ulcers	Some clinical studies	Not validated
Carbonnel score ¹⁶ (1994)	Retrospective study	Stepwise 2-grade scale: Moderate: Erythematous/swollen mucosa, superficial ulcerations, deep/non-extensive ulcerations Severe: Deep extensive ulcerations, well-like ulcerations, large mucosal abrasions, mucosal detachment	Some clinical studies	Not validated
Sigmoidoscopic Inflammation	Randomized, double-blind,	Stepwise 4-grade scale: (0) Normal mucosa	Some clinical trials	Not validated

Grade Score ¹⁷ (Lemann) (1995)	comparative, single centre study	(1) <i>Granularity, oedema, lack of normal vascular pattern</i> (2) <i>Hyperaemia, friability, petechiae</i> (3) <i>Ulceration</i>		
Lindgren score ^{18,} ¹⁹ (2001)*	Randomized, double-blind, prospective study	Stepwise 4-grade scale: (0) <i>No visible signs of inflammation</i> (1) <i>Granularity, edema, lack of normal vascular pattern</i> (2) <i>Hyperaemia, friability, petechie and all of score 1</i> (3) <i>Ulcerations and all of score 2</i>	Some clinical studies	Not validated
Sigmoidoscopic grade (Levine) ²⁰ (2002)	Randomized, double-blind, prospective study	Stepwise 4-grade scale: (0) <i>Normal – normal mucosa</i> (1) <i>Mild – edema, loss of vascular pattern, fine granularity without ulceration</i> (2) <i>Moderate – friability, petechiae, coarse granularity with pinpoint ulceration</i> (3) <i>Severe – Visible ulcers, spontaneous bleeding</i>	Some clinical trials	Not validated
Simple 5-point score (Rutter) ²¹ (2004)	Retrospective study	Stepwise 5-grade scale: (0) <i>Entirely normal appearance</i> (1) <i>Quiescent disease (mild edema or chronic features, but no active inflammation)</i> (2) <i>Mild active inflammation</i> (3) <i>Moderate active inflammation</i> (4) <i>Severe active inflammation</i>	Some clinical trials	Not validated
Modified Baron score (Feagan) ²² (2005)	Prospective study	Stepwise 5-grade scale: (0) <i>Normal, smooth, glistening mucosa, with vascular pattern visible; not friable</i> (1) <i>Granular mucosa; vascular pattern not visible; not friable; hyperaemia</i> (2) <i>As 1, with a friable mucosa, but not spontaneously bleeding</i> (3) <i>As 2, but mucosa spontaneously bleeding</i> (4) <i>As 3, but clear ulceration; denuded mucosa</i>	Multiple clinical studies and RCT	Partially validated
Froslie endoscopic score ²³ (2007)	Prospective study	Stepwise 3-grade scale: (0) <i>Normal</i> (1) <i>Light erythema or granularity</i> (2) <i>Granularity, friability and bleeding, with or without the addition of ulceration</i>	Some clinical studies	Not validated
Osada Modified 6-point Activity Index ²⁴	Retrospective study	Stepwise 6-grade scale: (1) <i>Normal or inactive disease. ramifying vascular pattern clearly visible</i> (2) <i>Mild erythema, decreased vascular</i>	Some clinical studies	Partially validated

(2010)		<i>pattern</i> (3) <i>Marked erythema, absent vascular pattern. Edema, friability or granularity of mucosa.</i> (4) <i>Erosions, small ulcer with regenerating epithelium (<4 mm)</i> (5) <i>Active ulcers, fewer than 10 per 10-cm segment</i> (6) <i>Multiple and deep ulcers, more than 10 per 10-cm segment (>5 mm)</i>		
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*Modification of the Danielsson-Löfberg score.

Reference:

1. Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955 Oct 29;2(4947):1041-8. 1981500 1981500.
2. Truelove SC, Richards WC. Biopsy studies in ulcerative colitis. Br Med J. 1956 Jun 9;1(4979):1315-8. 1980058 1980058.
3. Matts SG. The value of rectal biopsy in the diagnosis of ulcerative colitis. Q J Med. 1961 Oct;30:393-407.
4. Baron JH, Connell AM, Lennard-Jones JE. Variation between Observers in Describing Mucosal Appearances in Proctocolitis. Br Med J. 1964 Jan 11;1(5375):89-92. 1812908 1812908.
5. Dick AP, Holt LP, Dalton ER. Persistence of mucosal abnormality in ulcerative colitis. Gut. 1966 Aug;7(4):355-60. PMC1552432 PMC1552432. Epub 1966/08/01. eng.
6. Binder V. A comparison between clinical state, macroscopic and microscopic appearances of rectal mucosa, and cytologic picture of mucosal exudate in ulcerative colitis. Scand J Gastroenterol. 1970;5(7):627-32.
7. Powell-Tuck J, Day DW, Buckell NA, Wadsworth J, Lennard-Jones JE. Correlations between defined sigmoidoscopic appearances and other measures of disease activity in ulcerative colitis. Dig Dis Sci. 1982 Jun;27(6):533-7. Epub 1982/06/01. eng.

8. Blackstone MO. Endoscopic interpretation: normal and pathological appearances of the gastrointestinal tract. New York: Raven press; 1984.
9. Saverymuttu SH, Camilleri M, Rees H, Lavender JP, Hodgson HJ, Chadwick VS. Indium 111-granulocyte scanning in the assessment of disease extent and disease activity in inflammatory bowel disease. A comparison with colonoscopy, histology, and fecal indium 111-granulocyte excretion. *Gastroenterology*. 1986 May;90(5 Pt 1):1121-8. Epub 1986/05/01. eng.
10. Friedman LS, Richter JM, Kirkham SE, DeMonaco HJ, May RJ. 5-Aminosalicylic acid enemas in refractory distal ulcerative colitis: a randomized, controlled trial. *The American journal of gastroenterology* [Internet]. 1986; 81(6):[412-8 pp.]. Available at: <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/745/CN-00042745/frame.html>.
11. Sutherland LR, Martin F, Greer S, Robinson M, Greenberger N, Saibil F, et al. 5-Aminosalicylic acid enema in the treatment of distal ulcerative colitis, proctosigmoiditis, and proctitis. *Gastroenterology*. 1987 Jun;92(6):1894-8. Epub 1987/06/01. eng.
12. McPhee MS, Swan JT, Biddle WL, Greenberger NJ. Proctocolitis unresponsive to conventional therapy. Response to 5-aminosalicylic acid enemas. *Dig Dis Sci*. 1987 Dec;32(12 Suppl):76S-81S.
13. Danielsson A, Hellers G, Lyrenas E, Lofberg R, Nilsson A, Olsson O, et al. A controlled randomized trial of budesonide versus prednisolone retention enemas in active distal ulcerative colitis. *Scand J Gastroenterol*. 1987 Oct;22(8):987-92.
14. Löfberg R, Ostergaard Thomsen O, Langholz E, Schiöler R, Danielsson A, Suhr O, et al. Budesonide versus prednisolone retention enemas in active distal ulcerative colitis. *Alimentary pharmacology & therapeutics* [Internet]. 1994; 8(6):[623-9 pp.]. Available at: <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/355/CN-00112355/frame.html>.
15. Maier K, von Gaisberg U, Kraus B. [Ulcerative colitis. Activity index for the clinical and histological classification of inflammatory activity]. *Schweiz Med Wochenschr*. 1988 May

21;118(20):763-6. Epub 1988/05/21. Colitis ulcerosa. Aktivitatsindex zur klinischen und histologischen Klassifikation der Entzundungsaktivitat. ger.

16. Carbonnel F, Lavergne A, Lemann M, Bitoun A, Valleur P, Hautefeuille P, et al. Colonoscopy of acute colitis. A safe and reliable tool for assessment of severity. *Dig Dis Sci.* 1994 Jul;39(7):1550-7. Epub 1994/07/01. eng.
17. Lemann M, Galian A, Rutgeerts P, Van Heuverzwijn R, Cortot A, Viteau JM, et al. Comparison of budesonide and 5-aminosalicylic acid enemas in active distal ulcerative colitis. *Aliment Pharmacol Ther.* 1995 Oct;9(5):557-62.
18. Lindgren S, Löfberg R, Bergholm L, Hellblom M, Carling L, Ung KA, et al. Effect of budesonide enema on remission and relapse rate in distal ulcerative colitis and proctitis. *Scandinavian journal of gastroenterology [Internet].* 2002; 37(6):[705-10 pp.]. Available at: <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/181/CN-00409181/frame.html>.
19. Lindgren S, Suhr OB, Persson T. Budesonide enema once daily shows similar efficacy as budesonide enema twice daily for treatment of active distal ulcerative colitis. *Gastroenterology.* 2001;120(5 Suppl 1):A-748.
20. Levine DS, Riff DS, Pruitt R, Wruble L, Koval G, Sales D, et al. A randomized, double blind, dose-response comparison of balsalazide (6.75 g), balsalazide (2.25 g), and mesalamine (2.4 g) in the treatment of active, mild-to-moderate ulcerative colitis. *The American journal of gastroenterology [Internet].* 2002; 97(6):[1398-407 pp.]. Available at: <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/977/CN-00389977/frame.html>.
21. Rutter M, Saunders B, Wilkinson K, Rumbles S, Schofield G, Kamm M, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. *Gastroenterology.* 2004 Feb;126(2):451-9.

22. Feagan BG, Greenberg GR, Wild G, Fedorak RN, Pare P, McDonald JW, et al. Treatment of ulcerative colitis with a humanized antibody to the alpha4beta7 integrin. *N Engl J Med.* 2005 Jun 16;352(24):2499-507.
23. Froslie KF, JahnSEN J, Moum BA, Vatn MH, Group I. Mucosal healing in inflammatory bowel disease: results from a Norwegian population-based cohort. *Gastroenterology.* 2007 Aug;133(2):412-22.
24. Osada T, Ohkusa T, Yokoyama T, Shibuya T, Sakamoto N, Beppu K, et al. Comparison of several activity indices for the evaluation of endoscopic activity in UC: inter- and intraobserver consistency. *Inflamm Bowel Dis.* 2010 Feb;16(2):192-7. Epub 2009/07/04. eng.