The second and more controversial role is inserting the stent at the time of the initial emergency presentation of the patient with obstruction when the resectability of the tumour has not been established; this was examined in a multicentre study of 71 patients.[10] Stent insertion permits rapid symptomatic and radiological resolution of the obstruction, giving time to resuscitate the patient and perform accurate staging.[5–10] Metal stents do not interfere with conventional imaging and permit the use of intracavity endoscopic ultrasound to detect local invasion.[8 10] Patients found to have potentially curable disease may thus be given adequate bowel preparation, increasing their chance of having a primary anastomosis during an elective resection.[8 10] Concerns have been expressed that inflammation or infection around the stent may make this delayed surgery more difficult.

The benefit to patients of avoiding either a permanent or a temporary colostomy must be emphasised. Patients with stomas who have colorectal cancers have more psychological distress, greater sexual dysfunction, and more impairments in social functioning than patients with stomas who do not have colorectal cancer.[11] These problems are compounded among the disproportionately large group of elderly patients who find it difficult to look after their colostomies and who are more prone to complications.[12]

Stent insertion carried out by an experienced interventional radiologist or endoscopist takes 75 minutes on average.[10] Stent delivery using fluoroscopic screening alone seems to be adequate for tumours affecting the distal sigmoid colon and rectum. More proximal lesions may require a joint endoscopic and radiological approach. The stents exert a high radial force, expanding to a diameter of 22 mm, and relieving obstruction in 85% of patients within 24 hours.[6 10]

Enthusiasts report that stent insertion fails to achieve adequate decompression in about 10% of patients.[10] This failure has been attributed to technical difficulty traversing the stricture, poor positioning of the stent, the presence of an undetected proximal synchronous carcinoma, blockage by stool or barium, or mucosal prolapse.[8 9] The risk of blockage increases with the length of the stent used. Stool softeners and a low residue diet are recommended preventive measures. Stent migration, although unusual, is most commonly seen within the first 24 hours after insertion, particularly when the stent has been placed across rectal tumours. Palliative radiotherapy or chemotherapy may increase this risk by causing tumours to shrink.[9] Stents should not be inserted across distal rectal tumours because they can cause severe tenesmus.[6] Experienced operators have reduced the risk of perforation to 1% by avoiding excessive manipulation of guide wires and by using balloon dilatation of strictures.[9 10]

Self expanding metal stents are expensive, costing about £1000 ($1500) each. Only properly conducted trials can establish whether shorter hospitalisation, fewer surgical procedures, and less time spent in intensive care can justify this cost.[8]

Colorectal stenting may prove to be a safe adjunct or alternative to conventional surgery in malignant colorectal obstruction. However, before it is widely adopted prospective multicentre randomised controlled trials are needed to show the potential benefits of self expanding metal stents over traditional surgery in terms of complications, survival, quality of life, and cost effectiveness.

Tariq Ahmad *research fellow*

Department of Gastroenterology, Radcliffe Infirmary, Oxford OX2 6HE

Anthony S Mee *consultant gastroenterologist*

Department of Gastroenterology, Royal Berkshire Hospital, Reading RG1 5AN

1 Boyle P. Some recent developments in the epidemiology of colorectal cancer. In: Bleiberg H, Rougier P, Wilke H-J, eds. *Management of colorectal cancer*. London: Martin Dunitz, 1998:19-34.
2 Ohman U. Prognosis in patients with obstructing colorectal carcinoma. *Am J Surg* 1982;143:742-7.
3 Grandrup P, Lund L, Balslev I. Surgical treatment of acute malignant large bowel obstruction. *Eur J Surg* 1992;158:427-30.
4 Wong R, Rappaport W, Witze D, Putnam W, Hunter G. Factors influencing the safety of colostomy closure in the elderly. *J Surg Res* 1994;57:289-92.
5 Dohmoto M. New method—endoscopic implantation of metal stent in palliative treatment of malignant stenosis. *Endoscopy* 1991;3:1502-12.
6 Turegano-Fuentes F, Echenagusia-Belda A, Simo-Muerza G, Camunez F, Munoz-Jimenez F, del Valle Hernandez E, et al. Transanal self-expanding metal stents as an alternative to palliative colostomy in selected patients with malignant obstruction of the left colon. *Br J Surg* 1998;85:232-5.
7 Wallis F, Campbell K, Eremin O, Hussey J. Self-expanding metal stents in the management of colorectal carcinoma—a preliminary report. *Clin Radiol* 1998;53:251-4.
8 Binkert C, Ledermann H, Jost R, Sauenmann P, Decurtins M, Zollikofer C. Acute colonic obstruction: clinical aspects of preoperative and palliative treatment with self-expanding metallic stents—a preliminary report. *Radiology* 1998;206:199-204.
9 Baron T, Dean P, Yates M, Canon C, Koehler R. Expandable metal stents for the treatment of colonic obstruction: techniques and outcomes. *Gastrointest Endosc* 1998;47:277-85.
10 Mainar A, Ariza M, Tejero E, Tobio R, Alfonso E, Pinto I. Acute colorectal obstruction: treatment with self-expandable metal stents before scheduled surgery—results of a multicenter study. *Radiology* 1999;210:65-9.
11 Sprangers M, Taal B, Aaronson N, Velde AT. Quality of life in colorectal cancer. *Dis Colon Rectum* 1995;38:361-9.
12 Londono-Schimmer E, Leong A, Phillips R. Life table analysis of stoma complications following colostomy. *Dis Colon Rectum* 1994;37:916-20.

Why we need a broad perspective on meta-analysis

It may be crucially important for patients

In the world of clinical trials and meta-analyses there is an important debate between the "lumpers" and the "splitters." This relates to whether the overall findings of clinical trials and meta-analyses are the appropriate outcome to apply to individuals (lumping) or whether it is better to try to match the characteristics of particular patients to characteristics of subgroups within trials or meta-analyses (splitting). Although the splitters' view seems intuitively correct, there are usually substantial clinical and methodological advantages to lumping.

The generalisability and usefulness of meta-analyses are increased considerably if the individual trials cover different patient populations, settings, and concomitant routine care. For example, when a meta-analysis showed that the use of human albumin increased mortality[1] this result applied to all three groups of critically ill patients studied. For patients with hypovolaemia the difference

BMJ 2000;321:585–6

was not conventionally significant (95% confidence interval for the odds ratio 0.99 to 3.15), but it would be wrong to interpret this result as meaning that clinicians should continue to give these patients albumin. Most significant results will disappear because of lack of power if trials in a meta-analysis are split up into a large enough number of subgroups. It is more relevant that the point estimates were similar in the three subgroups studied and that the combined estimate was homogeneous. It is therefore reasonable to assume that albumin is harmful also in hypovolaemia.

Abandoning inappropriate treatments is difficult, even when they are harmful. For albumin—and many other harmful interventions—the typical argument is that if everything else fails, it should be tried as a last resort. However, albumin is likely to be harmful even in such cases. Some critically ill patients take longer to recover than others, and those are the ones now being given albumin. This is not logical. As the ultimate test, one should ask what good evidence there is that albumin is beneficial in these patients. Alternatively, one could ask whether a drug regulatory agency would be likely to approve albumin today if it were a new drug. The answers to these questions indicate that the use of albumin should be stopped altogether.

As another example, the continuous presence and support of a caregiver during childbirth (compared with usual care) has been shown to reduce the likelihood of medication for pain relief, operative vaginal delivery, caesarean delivery, and a 5 minute Apgar score of less than 7 and to improve mothers' views of their childbirth experiences.[2] The 14 trials included in the meta-analysis that showed these outcomes were performed under quite different circumstances—for example, the caregiver could be a professional, a specially trained laywoman, or a friend and the hospitals included a teaching hospital in Canada and public hospitals in Africa and Guatemala serving low income women. It strengthens the credibility of a systematic review when the results are consistent across such a varied range of settings, and it would be difficult to sustain the view that "it probably doesn't apply here"—although such arguments are sometimes heard.

As the examples illustrate, patients may be harmed or deprived of treatment benefits if the results of meta-analysis are interpreted too narrowly. Clinicians therefore need to think more broadly than they are used to by their training in subjects such as pathophysiology, pharmacology, and biochemistry. Clinical researchers often adopt unnecessarily narrow entry criteria when they write protocols for clinical trials, and the splitting approach is also prevalent in the drug industry, because it is profitable to make clinicians believe that minor differences between similar drugs are important. Meta-analyses have shown repeatedly, however, that such differences can often be ignored. It is far more important to address methodological issues, such as publication bias[3 4] and the disturbing finding that reports of trials in which the method of randomisation is not described exaggerate the treatment effect (measured as the odds ratio) by about 30% on average.[5 6]

A broad meta-analysis increases power, reduces the risk of erroneous conclusions, and facilitates exploratory analyses which can generate hypotheses for future research. If the results are not homogeneous, the reasons for this could be explored. The lumping approach should therefore be preferred unless there are good reasons to the contrary. Such reasons should be empirically based and not just speculative. For example, there is no good reason to suspect that pain in osteoarthritis of the knee should respond differently to an analgesic from pain in osteoarthritis of the hip. On the other hand, adopting a broad approach in general should, of course, not prevent us from looking at subgroups when there is a good reason why a treatment may work differently in different subgroups. Thus, carotid endarterectomy is beneficial in patients with severe stenosis but harmful in those with the lowest degrees of stenosis.[7]

A recent meta-analysis of homoeopathy has been criticised for including all kinds of homoeopathic treatments and diseases.[8] Yet this broadness of approach makes a lot of sense. There is no sound empirical basis for believing that homoeopathy should be effective for some conditions and not for others. Furthermore, the theory behind homoeopathy is speculative and far fetched, so it is important to study biasing factors carefully. The summary estimate indicated that homoeopathy was effective but the analyses revealed important biases[8 9] and the authors concluded that their study had "no major implications for clinical practice."[8]

If the authors had used a narrow approach and had published several small meta-analyses, each reporting the effect of homoeopathy in just one disease and including only about two to five trials, then clinicians and patients might have been misled. Many of these meta-analyses would have been positive, but it would have been impossible to detect bias.

Bias in medical research is common,[3–10] and this fact is probably the strongest single argument in favour of broad meta-analyses. The homoeopathy example can be generalised. Patients and clinicians alike are better served by a reliable answer that there is no convincing evidence that a therapeutic principle, or a class of treatments, is effective, than by an unreliable answer that a particular example of that class of treatment is effective for a particular disease.

Peter C Gøtzsche *director*

Nordic Cochrane Centre, Rigshospitalet, DK-2100 Copenhagen ø, Denmark (p.c.gotzsche@cochrane.dk)

1 Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. *BMJ* 1998;317:235-40.
2 Hodnett ED. Caregiver support for women during childbirth (Cochrane Review). In: *Cochrane Library*, Issue 4, 1999. Oxford: Update Software, 1999.
3 Dickersin K. The existence of publication bias and risk factors for its occurrence. *JAMA* 1990;263:1385-9.
4 Stern JM, Simes JR. Publication bias: evidence of delayed publication in a cohort study of clinical research projects. *BMJ* 1997;315:640-5.
5 Schulz KF, Chalmers I, Hayes RJ, Altman D. Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;273:408-12.
6 Moher D, Pham B, Jones A, Cook DJ, Jadad A, Moher M, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet* 1998;352:609-13.
7 Cina CS, Clase CM, Haynes RB. Refining the indications for carotid endarterectomy in patients with symptomatic carotid stenosis: a systematic review. *J Vasc Surg* 1999;30:606-17.
8 Linde K, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges L, et al. Are the clinical effects of homoeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet* 1997;350:834-43.
9 Linde K, Scholz M, Ramirez G, Clausius N, Melchart D, Jonas WB. Impact of study quality on outcome in placebo-controlled trials of homeopathy. *J Clin Epidemiol* 1999;52:631-6.
10 Gøtzsche PC. Bias in double-blind trials. *Dan Med Bull* 1990;37:329-36.

We ask all editorial writers to sign a declaration of competing interests (bmj.com/guides/confli.shtml#aut). We print the interests only when there are some. When none are shown, the authors have ticked the "None declared" box.