Prospective analysis of quality of life and survival following mesorectal excision for rectal cancer (*Br J Surg* 2001; 88: 1617–22)

Sir

Quality of life impairment in patients with advanced colorectal cancer, particularly depression, correlates significantly with T lymphocyte activation as defined by increased serum levels of interleukin 2 soluble receptor α[1]. In addition, increased serum interleukin 2 soluble receptor α also predicts weight loss in such patients that is detrimental to survival[2]. The precise mechanism for the association between depression and interleukin 2 soluble receptor α is not clear. Tumour-initiated circulating products of immunological activation may cause depression by depleting serum tryptophan concentration, which results in the reduction of the neurotransmitter serotonin in the central nervous system[3]. We agree with the authors' conclusion that quality of life measurements should be performed in this setting and suggest that there is biochemical evidence for the use of selective serotonin reuptake inhibitors in patients with impairment of quality of life, particularly depression.

A. A. Huang
K. S. Hindle*
Academic Department of Surgery
St Bartholomew's and The London Hospital
London E1 1BB
**Department of Surgery*
Mayday University Hospital
Croydon CR7 7YE
UK

1 Allen-Mersh TG, Glover C, Fordy C, Henderson DC, Davies M. Relation between depression and circulating immune products in patients with advanced colorectal cancer. *J R Soc Med* 1998; **91:** 408–13.
2 Fordy C, Glover C, Henderson DC, Summerbell C, Wharton RQ, Allen-Mersh TG. Contribution of diet, tumour volume and patient-related factors to weight loss in patients with colorectal liver metastases. *Br J Surg* 1999; **86:** 639–44.
3 Huang A, Fuchs D, Widner B, Tsavellas G, Henderson DC, Allen-Mersh TG. Immune activation in advanced bowel cancer is associated with tryptophan depletion and reduced quality of life. *Br J Surg* 2001; **88**(Suppl 1): 56–7.

Stoma-related complications are more frequent after transverse colostomy than loop ileostomy: a prospective randomized clinical trial (*Br J Surg* 2001; 88: 360–3)

Sir

We are concerned about the incomplete description of the randomized controlled trial (RCT) reported in this paper. A checklist for such reporting is available[1] and was revised last year[2,3]. Edwards *et al*. have not detailed the randomization process (in particular sequence generation and allocation concealment), how the sample size was obtained and do not clearly define outcome measures. The χ^2 test with Yates' correction is unreliable for such small numbers.

S. Bhalerao
M. W. Scriven
A. da Silva
Department of General Surgery
Wrexham Maelor Hospital
Wrexham LL13 7TD
UK

1 Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I *et al.* Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *JAMA* 1996; **276:** 637–9.
2 Moher D, Schulz K, Altman D, Lepage L. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet* 2001; **357:** 1191–4.
3 Bossuyt PM. Better standards for better reporting of RCTs. *BMJ* 2001; **322:** 1317–18.

The authors of this article chose not to reply to the above letter.

Effect of multimodality therapy on circulating vascular endothelial growth factor levels in patients with oesophageal cancer (*Br J Surg* 2001; 88: 1105–9)

Sir

We agree that vascular endothelial growth factor (VEGF) detected in serum may not be derived solely from tumour cells and agree that macrophages could be an additional source. The authors do not discuss another recognized source, the platelet. The megakaryocyte constitutively produces VEGF[1] and platelets release it when activated *ex vivo* in the formation of serum[2]. This has obvious consequences for use of serum VEGF as a marker of tumour angiogenesis and it has been hypothesized that measurement of VEGF in plasma might be more appropriate[2]. The fact that serum VEGF levels did not fall following neoadjuvant chemoradiotherapy despite a favourable pathological response and the lack of correlation demonstrated with tumour stage tend to support the hypothesis that serum VEGF may not be a useful surrogate marker of the angiogenic status of the primary tumour. Alteration in serum VEGF levels may be influenced more by changes in platelet number than by tumour effects, and measurement of plasma VEGF should be more specific.

G. M. Spence
I. McAllister
A. N. J. Graham
J. A. McGuigan
Department of Thoracic Surgery
Royal Victoria Hospital
Grosvenor Road
Belfast BT12 6BA
UK

1 Mohle R, Green D, Moore MA, Nachman RL, Rafii S. Constitutive production and thrombin-induced release of vascular endothelial growth factor by human megakaryocytes and platelets. *Proc Natl Acad Sci U S A* 1997; **94:** 663–8.
2 Banks RE, Forbes MA, Kinsey SE, Stanley A, Ingham E, Walters C *et al.* Release of the angiogenic cytokine vascular endothelial growth factor (VEGF) from platelets: significance for VEGF measurements and cancer biology. *Br J Cancer* 1998; **77:** 956–64.

Authors' reply

Sir

We readily acknowledge the role of the platelet as a source of vascular endothelial growth factor (VEGF)[1]. In our series controls and patients with cancer had serum prepared in a similar manner and there can be no doubt that, regardless of source, circulating VEGF levels are raised in patients with oesophageal cancer.

The majority of patients who die from oesophageal cancer do so as a result of local recurrence or distant metastases. It seems, therefore, that the important issue is not the angiogenic status of the primary tumour but rather the ability of residual occult deposits to develop following resection. Over 80 per cent of patients undergoing apparently 'curative' surgery for gastro-oesophageal cancer have rib bone marrow micrometastases[2]. If these cells are exposed to a potently pro-angiogenic fluid, their capability to develop into detectable disease is greatly enhanced.

We do not dispute that generating plasma can induce platelet activation with consequent VEGF release[3], but platelets are often activated in the tumour vasculature of patients with cancer[4]. An assessment of the total amount of VEGF present in the circulation, while not necessarily a direct reflection of tumour angiogenesis, may be a more appropriate measure of the potential for residual micrometastases to develop into clinically significant recurrent or metastatic disease.

C. O. McDonnell
T. N. Walsh
James Connolly Memorial Hospital
Blanchardstown
Dublin 15
Ireland

1 Verheul HM, Hoekman K, Luykx-de Bakker S, Eekman CA, Folman CC, Broxterman HJ *et al.* Platelet: transporter of vascular endothelial growth factor. *Clin Cancer Res* 1997; **3:** 2187–90.
2 O'Sullivan GC, Sheehan D, Clarke A, Stuart R, Kelly J, Kiely MD *et al.* Micrometastases in esophagogastric cancer: high detection rate in resected rib segments. *Gastroenterology* 1999; **116:** 543–8.
3 Wynendaele W, Derua R, Hoylaerts MF, Pawinski A, Waelkens E, de Bruijn EA *et al.* Vascular endothelial growth factor measured in platelet poor plasma allows optimal separation between cancer patients and volunteers: a key to study an angiogenic marker *in vivo*? *Ann Oncol* 1999; **10:** 965–71.
4 Verheul HM, Hoekman K, Lupu F, Broxterman H, van der Valk P, Kakkar AK *et al.* Platelet and coagulation activation with vascular endothelial growth factor generation in soft tissue sarcomas. *Clin Cancer Res* 2000; **6:** 166–71.

Estimating the benefits of adjuvant systemic therapy for women with early breast cancer (*Br J Surg* 2001; 88: 1513–18)

Sir

The authors have clearly pointed out that 70–95 per cent of women with node-negative disease are disease-free 10 years after local therapy. It is a dilemma, therefore, whether to subject a woman to the toxicities of systemic therapy if she has an up to 95 per cent chance of survival at 10 years. Surely it is even more of a dilemma if the woman is 40 as opposed to 74 years old?

It came to our attention that the 10-year cause-specific survival statistics analysed for all women aged 40–74 years (range 99·2–76·6 per cent) could not then be applied to two separate age groups of under and over 50 years in order to determine the survival benefit of adjuvant systemic therapy. Although the Swedish breast cancer detection results[1] implied that mortality was similar for women under and over 50 years, it appears that the absolute survival benefits (per cent) may well be inaccurate when taking into account the different mortalities for women of different ages.

K. McCarthy
J. Hewitt*
R. Carpenter
Breast Unit
St Bartholomew's Hospital
West Smithfield
London EC1A 7BE
**London School of Hygiene and Tropical Medicine*
Keppel Street
London WC1E 7HT
UK

1 Tabar L, Duffy SW, Burhenne LW. New Swedish breast cancer detection results for women aged 40–49. *Cancer* 1993; **72**(Suppl 4): 1437–48.

