(pp. 293–295 [5]) may not be typical of that at smaller centres. Interestingly, the only two studies in which survival of cancer patients treated according to standardised protocols was better at a very large centre than elsewhere both related to testicular teratoma [9, 10]. The possibility remains that the higher survival rates at the single large centre in each study were attributable to some characteristic of the centre in question other than its size. Platinum chemotherapy is also effective in ovarian cancer, and it is noteworthy that in a national study of 479 women treated in Scotland during 1987, the mortality rate ratio of 1.4 for women not treated at a multidisciplinary combined clinic was significantly higher ($P<0.01$), even after allowance was made for the effect of platinum therapy on survival, although whether this was given as part of a standard protocol was not analysed [23].

The question whether the survival advantage of protocol treatment for cancer patients is further enhanced by treatment at major centres is unresolved, and the answers may differ according to diagnostic group and type of treatment. The best way of attempting to answer it for testicular germ-cell tumours, as for other cancers, is through large-scale population-based studies covering a wide enough geographical area to include several treatment centres of the most specialised type. Cancer registries have an invaluable role to play in such studies.

1. Moller H, Friis S, Kjaer SK. Survival of Danish cancer patients 1943–1987. Male genital organs. *APMIS 1993*, **33** Suppl. 101, 122–136.
2. Black RJ, Sharp L, Kendrick SW. *Trends in Cancer Survival in Scotland 1968–1990*. Edinburgh, Information and Statistics Division, Directorate of Information Services, National Health Service in Scotland, 1993.
3. Feuer EJ. Testis. In Miller BA, Ries LAG, Hankey BF, Kosary CL, Edwards BK, eds. *Cancer Statistics Review 1973–1989*. NIH Publication No. 92-2789. Bethesda, National Cancer Institute, 1992, XXIV, 1–7.
4. Oliver RTD. Rare cancers and specialist centres. *Br Med J* 1986, **292**, 641–642.
5. Norum J, Nordoy T, Wist E. Testicular cancer treated in a minor general oncology department. *Eur J Cancer* 1995, **31A**, 293–295.
6. Naysmith A, Berry RJ. Treatment of testicular teratoma in general oncology departments. *Lancet* 1985, **1**, 646.
7. Bagshawe KD, Begent RHJ, Newlands ES, Rustin GJS. What sort of oncology team should treat testicular teratoma? *Lancet* 1985, **1**, 930.
8. Thornhill JA, Walsh A, Conroy RM, Fennelly JJ, Kelly DG, Fitzpatrick JM. Physician-dependent prognostic variables in the management of testicular cancer. *Br J Urol* 1988, **61**, 244–249.
9. Klepp O, Olsson AM, Henrikson H, *et al.* Prognostic factors in clinical stage I nonseminomatous germ cell tumors of the testis: multivariate analysis of a prospective multicenter study. *J Clin Oncol* 1990, **8**, 509–518.
10. Aass N, Klepp O, Cavallin-Stahl E, *et al.* Prognostic factors in unselected patients with nonseminomatous metastatic testicular cancer: a multicenter experience. *J Clin Oncol* 1991, **9**, 818–826.
11. Harding MJ, Paul J, Gillis CR, Kaye SB. Management of malignant teratoma: does referral to a specialist unit matter? *Lancet* 1993, **341**, 999–1002.
12. Feuer EJ, Frey CM, Brawley OW *et al.* After a treatment breakthrough: a comparison of trial and population-based data for advanced testicular cancer. *J Clin Oncol* 1994, **12**, 368–377.
13. Stiller CA. Centralised treatment entry to trials and survival. *Br J Cancer* 1994, **70**, 352–362.
14. Begg CB, Carbone PP, Elson PJ, Zelen M. Participation of community hospitals in clinical trials. Analysis of five years experience in the Eastern Cooperative Oncology Group. *New Engl J Med* 1982, **306**, 1076–1080.
15. Gillespie BW, Diamond JJ, Davis LW, Rominger CJ. An outcome study of the RTOG cancer control program. *Int J Radiat Oncol Biol Phys* 1986, **12**, 2157–2163.
16. Stiller CA, Draper GJ. Treatment centre size, entry to trials, and survival in acute lymphoblastic leukaemia. *Arch Dis Child* 1989, **64**, 657–661.
17. Eden OB, Stiller CA, Gerard MP. Improved survival for childhood acute lymphoblastic leukaemia: possible effect of protocol compliance. *Pediatr Hematol Oncol* 1988, **5**, 83–91.
18. Meadows AT, Kramer S, Hopson R, Lustbader E, Jarrett P, Evans AE. Survival in childhood acute lymphocytic leukemia: effect of protocol and place of treatment. *Cancer Invest* 1983, **1**, 49–55.
19. Feuer EJ, Kessler LG, Baker SG, Triolo HE, Green DT. The impact of breakthrough clinical trials on survival in population based tumor registries. *J Clin Epidemiol* 1991, **44**, 141–153.
20. Holzel D, Altwein JE. Hodentumoren: Ist der Ruckgang der Mortalitat in der Bundesrepublik Deutschland zu langsam erfolgt? *Dtsch Artzebl*, 1991, **88B**, 2694–2700.
21. Gerl A. Therapien von Hodentumoren in Spezialistenzentren. *DMW* 1994, **119**, 46–47.
22. Sylvester RJ, Pinedo HM, de Pauw M, *et al.* Quality of institutional participation in multicenter clinical trials. *New Engl J Med* 1981, **305**, 852–855.
23. Junor EJ, Hole DJ, Gillis CR. Management of ovarian cancer: referral to a multidisciplinary team matters. *Br J Cancer* 1994, **70**, 363–370.

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Should We Still Advocate Referral to Specialist Centres for Teratoma?

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WHO SHOULD be treating patients with malignant teratoma? In particular, is there evidence that referral of such cases to a "specialist" centre influences outcome? In many solid tumours the data on this controversial topic are rather sparse, but in malignant teratoma there are two separate large scale population based studies which support the notion that referral does confer

a survival benefit. Aass and associates [1] reviewed the treatment of 200 testicular teratoma patients (at least 90% of all patients with this disease) during 1981–1986 in Scandinavia. They showed that the survival rate of the 46% of patients treated at the Norwegian Radium Hospital in Oslo was significantly better, especially for those with large volume disease ($P=0.01$).

Harding and colleagues [2] examined 97% of testicular teratoma patients presenting in the West of Scotland over 1975–1989 (440 patients in total). They found that referral to a specialist centre, treating 53% of cases, had a statistically significant beneficial effect on overall survival (87% compared to 73% elsewhere). This could not be ascribed to differences in tumour stage as the specialist centre treated a higher proportion of poorer prognostic patients. Even when allowance was made for the fact that more of the specialist centre patients were treated by protocol (97% versus 61% elsewhere), there was still a lower relative mortality rate (0.35, 95% confidence interval 0.19–0.65).

Stiller [3] in his recent review of centralised treatment, entry to trials and survival, points out some of the sources of bias that may lead to errors in such studies. Bias can arise if there are more patients of a poorer prognosis in any one group. For instance, patients may not be referred to a specialist centre if they are too ill to travel. Patients may be assigned to different prognostic groups if staging procedures are different between centres. Differing areas and hospitals may have differing groups of patients in terms of socio-economic status and may have differing local screening programme initiatives leading to varying delays in diagnosis. In the above two studies account was taken of poor prognostic factors, and the centre of referral was still found to be an independent factor in survival. Indeed the data from Harding and colleagues [2] suggest that there is a tendency for poorer prognostic patients to be referred to the specialist centre.

Norum and associates pp. 293–295 in this issue provide us with impressive evidence from their department of oncology that a unit, seeing on average just over 12 cases of germ cell tumour per year, is capable of producing survival data comparable with much larger centres. They argue that this may help patients psychologically, and in a sparsely populated area it may be the most cost-effective way of providing care, reducing patient travelling, without compromising on patient survival.

To an extent, Norum and associates miss the point. The data they describe refer to treatment in a regional cancer centre, albeit relatively small in terms of the population served (500 000). They expect to see 10–15 cases of testicular cancer per year. This is a level of referral which is indeed compatible with optimal treatment results, although it is probably at the lower limits in this respect [2].

In most walks of life, experience with a given procedure leads to improved performance, and it seems reasonable to apply this general principle to the treatment of a particular cancer. Frequent experience of treatment of the condition leads to optimal results through reduced morbidity (care with hydration schedules, treatment of emesis and sepsis, psychological support), as well as through expert surgery (post chemotherapy excision of residual masses).

It is important that smaller oncology centres, such as those in Tromso, perform regular audits and are prepared to publish survival data. The Tromso data were not directly compared with data from a specialist unit as in the previous studies and, therefore, are not as statistically significant. Whether treatment in a regional compared to a national centre reduces the psychosocial problems associated with cancer treatment, as claimed by Naysmith and Berry [5], has not been subjected to study. Given the increase in specialist nurses and psychologists working in the field of cancer care, it would be interesting to know which patients find more beneficial; the accessibility of the local centre or the "emotional security of the specialist team of doctors and nurses" claimed by Bagshawe and associates [6]. This is an area worthy of study.

Given the high survival rates, especially of the good prognosis patients, perhaps we should be looking for any differences between centres other than survival alone. It has become increasingly recognised that an important objective in teratoma management is to reduce the short and long term toxicity of chemotherapy. Unfortunately, we have not yet reached the happy scenario of curing all patients with no morbidity. New trials looking not only at survival but also at morbidity and quality of life are required. To continue to improve the situation for teratoma patients, it is important that there is a close liaison between specialist centres regarding accrual into trials and protocol treatments. Although the data from Norum and associates show no deficiencies in terms of survival, we would like to see more evidence that there is the same "treatment related morbidity and mortality".

Stiller's exhaustive review of 51 articles relating to this issue of centralised treatment and survival in all cancers concludes that "referral to a specialist centre or to a hospital treating many patients with the disease, or inclusion in a clinical trial, is often linked with a higher survival rate for the cancers which have been studied" [3]. The results from Tromso may well be comparable with larger cancer centres, although the numbers are small, particularly of patients with advanced disease on whom the impact of post chemotherapy surgery may be most evident. It would be most unfortunate, however, if the reader were to misconstrue this report as a vindication of the attitude, fortunately now rare, of individual clinicians who may see only 1 or 2 cases of testicular cancer per year but still consider themselves to have the necessary expertise to treat this highly curable condition.

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1. Aass N, Klepp O, Cavallin-Stahl E, Dahl O, *et al.* Prognostic factors in unselected patients with nonseminomatous metastatic testicular cancer: a multicenter experience. *J Clin Oncol* 1991, **9**, 818–826.
2. Harding MJ, Paul J, Gillis CR, Kaye SB. Management of malignant teratoma: does referral to a specialist unit matter? *Lancet* 1993, **341**, 999–1002.
3. Stiller CA. Centralised treatment, entry to trials and survival. *Br J Cancer* 1994, **70**, 352–362.
4. Norum J, Norday T, Wist E. Testicular cancer treated in a minor general oncology department. *Eur J Cancer* 1995, **31A**, pp. 293–295.
5. Naysmith A, Berry RJ. Treatment of testicular teratoma in general oncology departments. *Lancet* 1985, i, 646.
6. Bagshawe KD, Begent RHJ, Newlands ES, Rustin GJS. What sort of oncology team should treat teratoma? *Lancet* 1985, i, 930.