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Maximising recruitment into randomised controlled trials: The role of multidisciplinary cancer teams ☆

A.G.K. McNair[a,b,c], C.T.P. Choh[b], C. Metcalfe[a], D. Littlejohns[d], C.P. Barham[b], A. Hollowood[b], S.J. Falk[e], J.M. Blazeby[a,b,c,*]

[a]Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Clifton, Bristol BS8 2PR, United Kingdom
[b]Division of Surgery, Head and Neck, University Hospitals Bristol NHS Foundation Trust, Bristol BS2 8HW, United Kingdom
[c]Clinical Sciences at South Bristol, Level 7, Bristol Royal Infirmary, Bristol BS2 8HW, United Kingdom
[d]Faculty of Medicine and Dentistry, University of Bristol, 69 St. Michael's Hill, Bristol BS2 8DZ, United Kingdom
[e]Bristol Haematology and Oncology Centre, University Hospitals Bristol NHS Foundation Trust, Bristol BS2 8HW, United Kingdom

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ABSTRACT

Multidisciplinary cancer teams offer many theoretical benefits, although few have been formally examined. This study evaluated the role of multidisciplinary team (MDT) meetings in recruitment into randomised controlled trials (RCTs). Consecutive MDT patient records were categorised into those with or without a recommendation for a national multicentre RCT. Clinical trial office records identified whether patients were subsequently screened and randomised.

In 125 MDT meetings, 350 new patients were discussed, of whom 103 were potentially suitable for a RCT. The MDT recommended 68 patients for the trial, of whom 58 (85%) were screened for trial eligibility. Of the 35 without an MDT trial recommendation, only 23 (66%) were screened ($p = 0.022$). This difference persisted and resulted in a greater proportion of MDT recommended patients being recruited (65% *versus* 49%; $p = 0.12$). This study demonstrates that trial recommendation by an MDT significantly increases trial screening rates and may improve recruitment.

1. Introduction

Multicentre randomised controlled trials are recognised as the most reliable study design for evaluating interventions in oncology. Recruitment difficulties are frequent, however, and this may delay trials leading to expensive protocol changes or closure if recruitment is poor. In 2001, England was recruiting approximately 4% of patients with a new diagnosis of cancer into clinical trials.[1] Since then, significant national investment has been made through the formation of the National Cancer Research Institute and the National Cancer Research Network, and a rise in trial recruitment and a reduction in the average time taken to complete trials have been reported.[2,3] Many of the cancer initiatives developed by these organisations are implemented through the actions of multidisciplinary teams (MDTs) that coordinate the care of patients with cancer, and it has been suggested that MDTs are an essential tool to help doctors enrol patients in clinical trials.[4]

The multidisciplinary model of cancer care is rapidly becoming the standard in Europe. A recent European Union round-table on improving cancer control has recommended that multidisciplinary care is included in the national cancer

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* *Corresponding author*: Address: Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Clifton, Bristol BS8 2PR, United Kingdom. Tel.: +44 1179287231; fax: +44 1179287325.
E-mail address: J.M.Blazeby@bristol.ac.uk (J.M. Blazeby).
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plans of all European Union member states, and declares that 'A multidisciplinary approach to cancer care is required to make the best decisions about each patient's diagnosis, treatment and support'.[5] In several European countries multidisciplinary cancer teams are already common,[6,7] and in particular, the United Kingdom has adopted MDTs universally across all cancer sites following publication of the National Health Service Cancer Plan in 2000.[8] Worldwide, multidisciplinary team working occurs in a broad range of health services and in a number of forms, such as tumour boards in the United States,[9] multidisciplinary cancer conferences in Canada[10] and MDTs in Australia.[11] Given that there is this widespread and increasing use of multidisciplinary team working, it is essential to examine the potential benefits to patient care.

Multidisciplinary teams bring specialists in relevant disciplines together, aiming to ensure that clinical decisions are fully informed, treatment planning is optimised and there is a coordinated delivery of care.[12] Many potential benefits of MDT working have been suggested: improved cancer staging,[13] prolonged patient survival,[14] improved clinical decision making,[15] as well as increasing recruitment into randomised controlled trials. Although team working has been widely implemented, there is a lack of definitive evidence evaluating the benefits of working in a team.[12] The aim of this study was to investigate whether MDTs can contribute to improved recruitment of eligible patients to the national randomised trials of cancer treatment.

2. Patients and methods

Prospective MDT treatment recommendations from the central upper gastrointestinal cancer MDT of the Avon, Somerset and Wiltshire Cancer Network were retrospectively reviewed. The upper gastrointestinal MDT meets weekly at University Hospitals Bristol NHS Foundation Trust and discusses all relevant details for each patient. At the end of each discussion, the MDT recommendation is documented and projected in the meeting, so all team members have the opportunity to support or dissent the decision. The 'MDT decisions' document is circulated to MDT members, referring clinicians in satellite trusts, and to the three recruiting clinical trials units (the Bristol Haematology and Oncology Centre Clinical Trials Unit, University Hospitals Bristol NHS Foundation Trust, the Oncology and Haematology Research Unit, Royal United Hospital, Bath and the Clinical Trials Unit, Yeovil District Hospital NHS Foundation Trust) based in the referring cancer network, within 24 h of the MDT meeting.

The open national multicentre randomised trial 'OEO5' is comparing cisplatin and 5-flourouracil (5-FU) chemotherapy against epirubicin, cisplatin and capecitabine (ECX) chemotherapy, both followed by resection.[16] From the MDT records, patients with oesophageal adenocarcinoma, without evidence of metastatic disease or immediate evidence of ineligibility for the trial (e.g. history of other cancer, poor general condition), were classified into two groups: (A) where the MDT recommended inclusion into the trial, and (B) where the MDT recommended chemotherapy followed by resection, but there was no explicit trial recommendation. To establish whether patients were formally screened by trial staff and whether they were randomised, the OEO5 trial screening and randomisation logs from each of the three clinical trials units were reviewed. Where patients had not been screened by trial units, the full medical notes were reviewed (AM and JMB) to record the final treatment received. Patient demographics (age, sex) and clinical details (stage of disease and type) were recorded.

Each of the clinical trials units in this study opened to recruitment into the OEO5 trial at different times. The Bristol Haematology and Oncology Centre Clinical Trials Unit, University Hospitals Bristol Foundation NHS Trust opened in January 2005, the Oncology and Haematology Research Unit, Royal United Hospital, Bath opened in September 2005 and the Clinical Trials Unit, Yeovil District Hospital NHS Foundation Trust opened in January 2006. Only relevant MDT records subsequent to these dates and before 25th May 2007 were examined.

2.1. *Statistical analyses*

Comparisons between patients screened and randomised into the trial were made between Groups A and B using Pearson's chi-squared tests, and two-tailed p-values are reported.

3. Results

During the study period, 125 MDT meetings discussed 350 new patients with oesophageal adenocarcinoma, of whom 103 were considered suitable for chemotherapy and resection. The MDT identified and flagged 68 patients for the OEO5 randomised trial, Group A. The 35 patients in Group B, who were not specifically recommended for the trial, had similar age and sex distribution similar to patients in Group A, and the same mix of disease stages (Table 1). There is evidence that MDT recommendation increased the proportion of potentially

Table 1 – Details of potentially eligible patients for the randomised controlled trial

	Recommended by MDT: Group (A) $n = 68$	Not recommended by MDT: Group (B) $n = 35$
Mean age, years (range)	63.4 (37–79)	65.5 (39–81)
Male (%)	60 (88)	28 (80)
Cancer stage[a] (%)		
IIa	5 (7.4)	3 (8.6)
IIb	17 (25.0)	10 (28.6)
III	46 (67.6)	22 (62.8)

a American Joint Committee on Cancer Staging system grouping.[23]

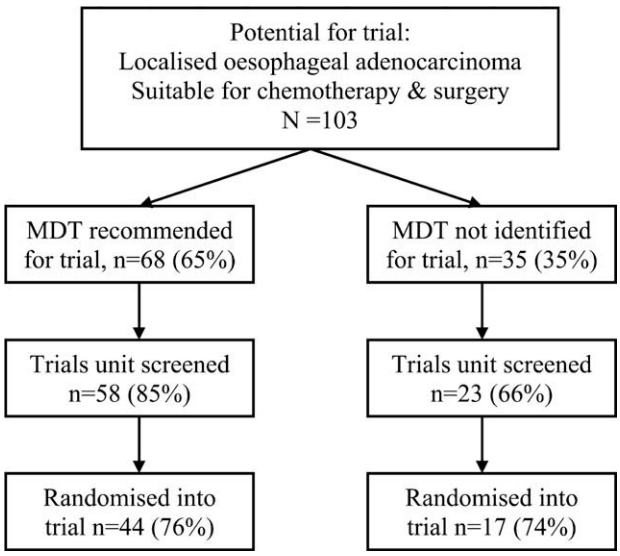

Fig. 1 – Flow diagram to show recruitment into the national randomised controlled trial, OEO5 and the role of the MDT and clinical trials units.

eligible patients screened by trials units staff, with 85% of Group A patients screened compared to 66% of Group B patients ($p = 0.022$: Fig. 1). In both groups, around three quarters of those screened were recruited into the trial (76% and 74%, respectively, Fig. 1). There is weak evidence of an association between MDT trial recommendation and trial recruitment rates (65% and 49%, $p = 0.12$). Table 2 shows the final treatment of the patients not screened for the trial. Most patients received standard pre-operative chemotherapy.

4. Discussion

This study shows that trial recommendation by an MDT significantly increases the chances that patients are screened for trial entry, and as a result recruitment rates are improved. It is therefore recommended that during the MDT meeting itself, patients potentially eligible for a national RCT are flagged in the meeting records, as a simple and effective means of increasing trial recruitment.

Many strategies have been suggested to improve recruitment into randomised trials, and these are summarised in several recent systematic reviews.[17–20] Overall these reviews are inconclusive, and no generalisable measures for improving trial recruitment can be identified. All reviews, however, did recommend that further research to understand the recruitment process itself and further examination of factors that maximise trial recruitment are performed. None of these studies have examined the effect of MDT working on recruitment into trials, although the theoretical benefits of MDTs on clinical innovation have been suggested.[12,21] A report published in 2001 provides a snapshot of recruitment rates following the introduction of a lung cancer MDT, with 19% of lung cancer patients randomised into trials. This figure is higher than the national average, but no data are presented to attribute these findings to the MDT meetings itself.[22]

There are at least two reasons why flagging trial patients in MDT meetings may improve trial screening and recruitment; firstly, the process allows clinical trials nurses an easy and quick means to identifying potentially eligible patients, and secondly it serves as a reminder to MDT members to discuss the trial with the patient. Provision of a similar clinical message from all clinicians involved in the patients' cancer journey is likely to enhance patients' final understanding of clinical equipoise and consent to randomisation.

This study was conducted in one MDT and cancer network with an established track record in trial recruitment. Hence interpretation of the results must be cautious. Although it is shown that MDT recommendation can improve the screening and recruitment of potentially eligible patients to trials, it is now necessary to examine the effect of flagging trial patients in studies of other MDTs, including those working in other settings, to obtain evidence that the effect of MDT recommendation on trial recruitment is both reliable and widespread.

This study provides evidence to support the benefits of working in teams to improve entry into national clinical trials. By simply flagging patients potentially eligible for a trial in the MDT meeting itself, it was found that patients were significantly more likely to be formally screened for trial entry. The whole team can see the recommendation and subsequently discuss it with patients. It is therefore possible that team working in oncology represents a potentially powerful tool to systematically identify trial patients and maximise recruitment. In many countries, the organisational structure is already in place to make use of these findings, and it is recommended that MDTs have sufficient administrative support for this role.[12] It is also recommended that further research into the role of MDTs in trial recruitment is undertaken with potential benefits of enhancing clinical trials, and therefore evidence-based medicine in oncology.

Conflict of interest statement

None declared.

Table 2 – Final treatments received by patients not screened by the trial units

	Patients not screened, Group A, $n = 10$	Patients not screened, Group B, $n = 12$
Pre-operative chemotherapy, cisplatin and 5-fluorouracil	6	6
Pre-operative chemotherapy, epirubicin, cisplatin, 5-fluorouracil	0	4
Definitive chemoradiotherapy	4	0
Palliative chemotherapy	0	1
Palliative radiotherapy	0	1

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REFERENCES

1. Corrie P, Shaw J, Harris R. Rate limiting factors in recruitment of patients to clinical trials in cancer research: descriptive study. *BMJ* 2003;**327**(7410):320–1.
2. National Cancer Research Institute. National Cancer Research Institute Operating report 2006/2007. <http://www.ncri.org.uk/includes/Publications/reports/Operating_Report_07.pdf>.
3. Vale C, Stewart L, Tierney J. Trends in UK cancer trials: results from the UK Coordinating Committee for Cancer Research National Register of Cancer Trials. *Br J Cancer* 2005;**92**(5):811–4.
4. Castel P, Negrier S, Boissel JP. Why don't cancer patients enter clinical trials? A review. *Eur J Cancer* 2006;**42**(12):1744–8.
5. Gouveia J, Coleman MP, Haward R, et al. Improving cancer control in the European Union: conclusions from the Lisbon round-table under the Portuguese EU Presidency, 2007. *Eur J Cancer* 2008;**44**(10):1457–62.
6. Lutterbach J, Pagenstecher A, Spreer J, et al. The brain tumor board: lessons to be learned from an interdisciplinary conference. *Onkologie* 2005;**28**(1):22–6.
7. Schopper D, Obrist R. National Cancer Programme Switzerland 2005–2010. Bern: Oncosuisse. <http://www.oncosuisse.ch/frontpage/downloads/krebsprogramm_e.pdf>.
8. UK Department of Health. The NHS Cancer Plan. London: Department of Health, 2000. <http://www.dh.gov.uk/assetRoot/04/01/45/13/04014513.pdf>.
9. Petty JK, Vetto JT. Beyond doughnuts: tumor board recommendations influence patient care. *J Cancer Educ* 2002;**17**(2):97–100.
10. Wright FC, De VC, Langer B, Hunter A. Multidisciplinary cancer conferences: a systematic review and development of practice standards. *Eur J Cancer* 2007;**43**(6):1002–10.
11. New South Wales Department of Health. A clinical service framework for optimising cancer care in NSW. New South Wales Department of Health; 2003. <http://www.health.nsw.gov.au/pubs/2003/pdf/cancercare_sum_a4.pdf>.
12. Fleissig A, Jenkins V, Catt S, Fallowfield L. Multidisciplinary teams in cancer care: are they effective in the UK? *Lancet Oncol* 2006;**7**(11):935–43.
13. Stephens MR, Lewis WG, Brewster AE, et al. Multidisciplinary team management is associated with improved outcomes after surgery for esophageal cancer. *Dis Esophagus* 2006;**19**(3):164–71.
14. Junor EJ, Hole DJ, Gillis CR. Management of ovarian cancer: referral to a multidisciplinary team matters. *Br J Cancer* 1994;**70**(2):363–70.
15. Ruhstaller T, Roe H, Thurlimann B, Nicoll JJ. The multidisciplinary meeting: an indispensable aid to communication between different specialities. *Eur J Cancer* 2006;**42**(15):2459–62.
16. Medical Research Council. A randomised controlled trial comparing standard chemotherapy followed by resection versus ECX chemotherapy followed by resection in patients with resectable adenocarcinoma of the oesophagus. ISRCTN01852072, 2005.
17. Watson JM, Torgerson DJ. Increasing recruitment to randomised trials: a review of randomised controlled trials. *BMC Med Res Method* 2006;**6**:34.
18. Mapstone J, Elbourne D, Roberts I. Strategies to Improve recruitment to research studies. *The Cochrane Database Syst Rev* 2004;**1**:MR000013.
19. Campbell MK, Snowdon C, Francis D, et al. Recruitment to randomised trials: strategies for trial enrollment and participation study. The STEPS study. *Health Technol Assess* 2007;**11**(48).
20. Fayter D, McDaid C, Ritchie G, Stirk L, Eastwood A. Systematic review of barriers, modifiers and benefits involved in participation in cancer clinical trials. centre for reviews and dissemination (CRD), University of York; 2006. Report No.: 31.
21. Haward R, Amir Z, Borrill C, et al. Breast cancer teams: the impact of constitution, new cancer workload, and methods of operation on their effectiveness. *Br J Cancer* 2003;**89**(1):15–22.
22. Magee LR, Laroche CM, Gilligan D. Clinical trials in lung cancer: evidence that a programmed investigation unit and a multidisciplinary clinic may improve recruitment. *Clin Oncol (R Coll Radiol)* 2001;**13**(4):310–1.
23. Greene FL, Page DL, Fleming ID, et al. *AJCC cancer staging manual*. 6th ed. New York, NY: Springer-Verlag; 2002.