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INTRODUCTION

Randomised clinical trials are the study design least susceptible to bias and remain the gold standard for the evaluation of therapeutic efficacy¹. Several positive outcomes have been associated with clinical trials. These include access to the latest and potentially most effective therapies, access to otherwise unavailable or expensive drugs, greater scrutiny of care and faster acceptance of emerging therapies.

Recruitment of patients into clinical trials remains a significant challenge in clinical research,^{1,2} with adult recruitment rates as low as 2 - 4% commonly seen in North America³. Published data on accrual rates to clinical trials in Australia are scarce. Ellis et al¹ reported that, in one Australian state over a 6 month period in 1990, only 5% of women with breast cancer received adjuvant systemic therapy as part of a clinical trial. While an accrual rate of 2-4% for trials in haematological malignancies in New South Wales (NSW) has been assumed, activity has not been documented.

Despite low accrual rates, approximately one third of surveyed cancer patients in both the USA (38%)³ and Australia (33%)⁴ reported a willingness to participate in clinical trials, illustrating a need to better understand the barriers to efficient and comprehensive recruitment. Documented barriers relate to resources, time, demanding trial designs and regulatory paperwork. Factors reported to positively influence participation in clinical trials^{4,5} include the availability of support staff, entry requirements which are not too restrictive and an active interest in research.

PURPOSE

The purpose of this work, as defined by the New South Wales Oncology Group – Haematology Oncology was to document the number of haematological cancer patients on clinical trials in NSW, establish the barriers to recruitment of patients and examine possible means by which clinical trial participation may be improved.

METHODS

Open Clinical Trials, Participating Centres and Accrual Rates

Quantitative data on clinical trial participation were collected from the records of all 18 sites involved in clinical trials in adult haematological cancers in NSW (Table 1). Data were collected on adults over 17 yrs from 2004 to 2006 and for the first half of 2007 including the number of clinical trials available to patients, new recruitment to trials and staffing levels (2007 only). The accrual rate to clinical trials in haematological cancer for 2004 and 2005 were calculated using NSW cancer incidence data^{6,7} while for 2006 projected data were used.

Barriers and Improvements

Qualitative data were obtained using in-depth, semi-structured interviews with Haematologists or Oncologists (H) and CRAs (Clinical Research Associate including Data Managers, Clinical Trials Nurses, Clinical Trials Co-ordinators and other support staff). A total of 55 professionals (H=25, CRA=30) were interviewed, by a single interviewer, at 18 participating centres.

Data were collected on barriers and opportunities for improvement to the conduct of clinical trials. Responses were directly solicited regarding the establishment of a dedicated haematology oncology clinical trials website and a CRA communication forum.

RESULTS

Open Clinical Trials and Number of Participating Centres

In 2004, a total of 94 trials in haematological cancer were open at centres in NSW, and 11 centres participated in trials. In 2005 there were 140 trials and 13 participating centres, increasing to 164 trials and 16 centres in 2006 and 178 trials and 18 centres by July 2007. In 2007, there were 44.3 full-time equivalent (FTE) CRAs (range = 1–5.6 per site) and 62.7 FTE clinicians (range = 1-8 per site). No records were available for earlier years.

Enrolments to Clinical Trials and Accrual Rates

Enrolments in clinical trials for haematological malignancies increased from 154 in 2004 to 286 in 2005 and 307 in 2006, with patients active on trials rising from 276 to 494 in the same period (Fig 1). The percentage of patients with haematology cancers accrued was 5.8% in 2004, increasing in 2006 to 9.0%. The increase in accrual was not evenly distributed over all sites (2006 range = 0 – 117 increase in accrual), but was concentrated in the large tertiary referral hospitals in major population centres.

There was a positive correlation ($r=0.50$) between the numbers of CRAs per site and recruitment of patients onto clinical trials. There was a similar correlation ($r=0.46$) between the number of clinicians per site and trial recruitment.

Perceived Barriers to the Conduct of Clinical Trials

A total of 44 perceived barriers to the conduct of clinical trials were identified from 121 responses obtained from 55 practitioners involved in clinical trials in haematology oncology in NSW (Fig 2). All 18 participating centres were included. Resource issues were the most common barriers cited, with a total of 44 responses (23 related to human resources and 21 related to physical resources). Insufficient staff in the CRA categories, too few physicians, insufficient physical resources including office space and equipment, and lack of Area Health Service support for clinical research are grouped together in this category.

The HREC submission process and governance issues together scored 16 responses. Communication was cited by 13 respondents and includes poor communication within individual centres, within the Area Health Service (AHS), with pharmaceutical companies and with the general public. It includes poor community awareness of the purpose and methodology of clinical research. Poor or overly complex trial design was cited 11 times. The burden of excessive paperwork was grouped into this category. The spectrum and comparative rarity of haematological cancers was the next most frequently cited barrier. Missing eligible patients had 6 responses. This could conceivably be regarded as a resource issue. With insufficient personnel, there is inevitably higher workload per person.

Several participants cited workload as a reason that not enough time is spent on trials related activities. Absence of a mechanism for cross-referral was mentioned by four respondents. "Others" encapsulated items which were only cited by a single respondent and did not fit into any of the above categories.

Proposals for Improvement in Clinical Trials Activity

Suggestions for ways in which the conduct of clinical trials can be improved were obtained in the same interviews as described above. A total of 28 proposals for improvement were identified from 105 responses (Fig 3).

Improving resources available to clinical trials units was the most commonly suggested proposal for improvement in the conduct of clinical trials in NSW. There were 38 responses, of which 19 related to human resources and 19 related to physical resources. This is consistent with the identified barriers to clinical trials activity (Fig 2).

The adoption of a strategic approach to the conduct of clinical trials elicited 12 responses. There was support for a centralised approach and cross-referral by respondents. Support for emerging centres had 8 responses, relating directly to the promotion of clinical trials in rural and regional centres. Improving communication was suggested by four respondents. CRA education had three responses. Better trial design with less labour intensive protocols was suggested by two respondents.

CONCLUSIONS

This study documents enrolment in haematological oncology clinical trials in NSW in 2004-2006 and projects an increase in activity. This trend represents a positive outcome for haematological cancer patients in NSW and clinical research, but emphasizes that only a small minority of patients are currently able to be enrolled in clinical trials. Several barriers to clinical trial participation have been identified by health professionals working in the area and opportunities for overcoming these have been proposed.

References

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Table 1

Participating sites in clinical research in haematology oncology in NSW
* Regional sites. + Private clinics

Westmead Hospital	Concord Hospital
Liverpool Hospital	Royal Prince Alfred Hospital
Prince of Wales Hospital	St George Hospital
Sydney Haematology Oncology Clinics*	Border Medical Oncology*
The Tweed Hospital*	Wollongong Hospital*
Calvary Mater Hospital Newcastle*	St Vincent's Hospital
Nepean Hospital	Royal North Shore Hospital
Coffs Harbour Base Hospital*	Port Macquarie Base Hospital*
Lismore Base Hospital*	Gosford Hospital*

Figure 1

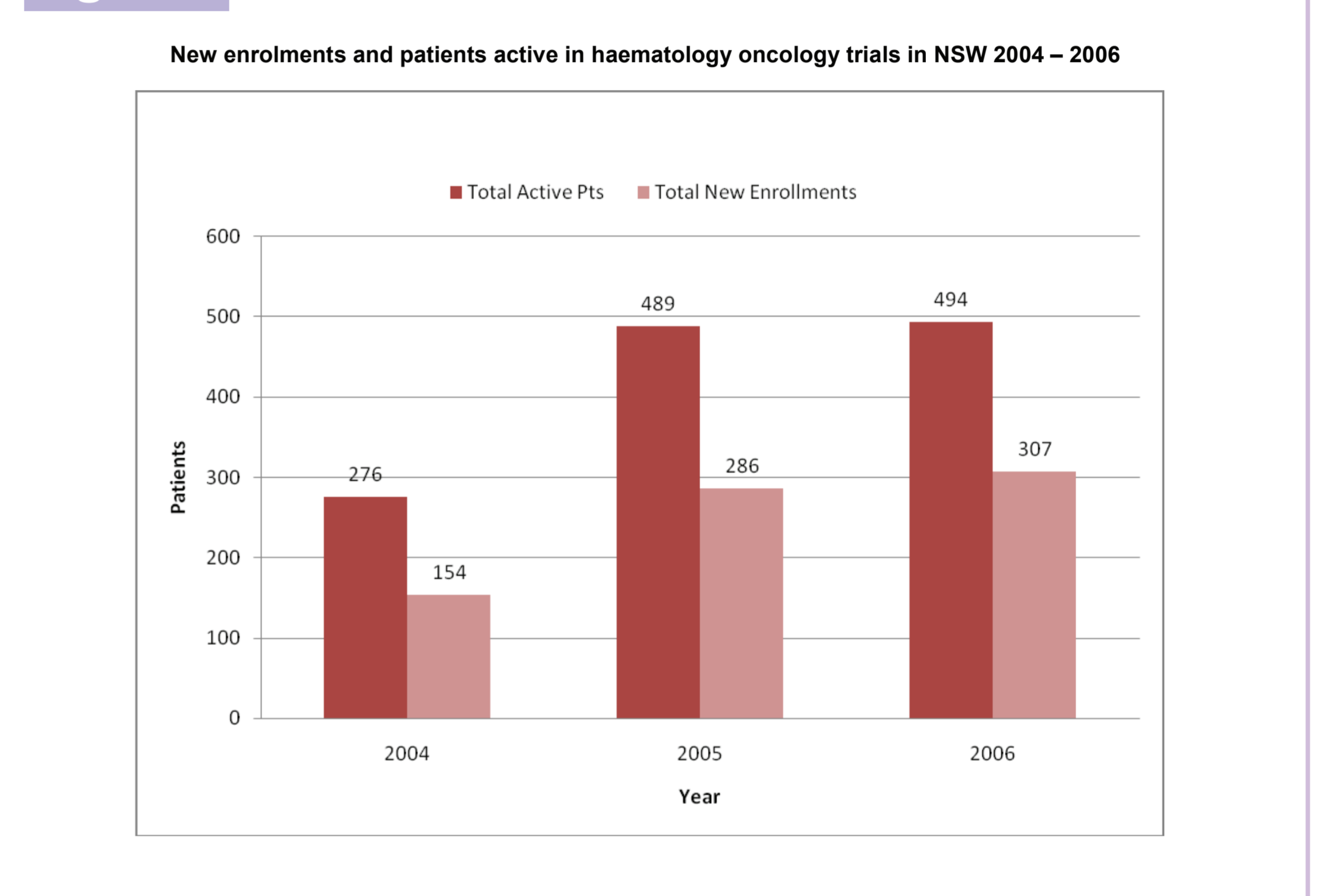


Figure 2

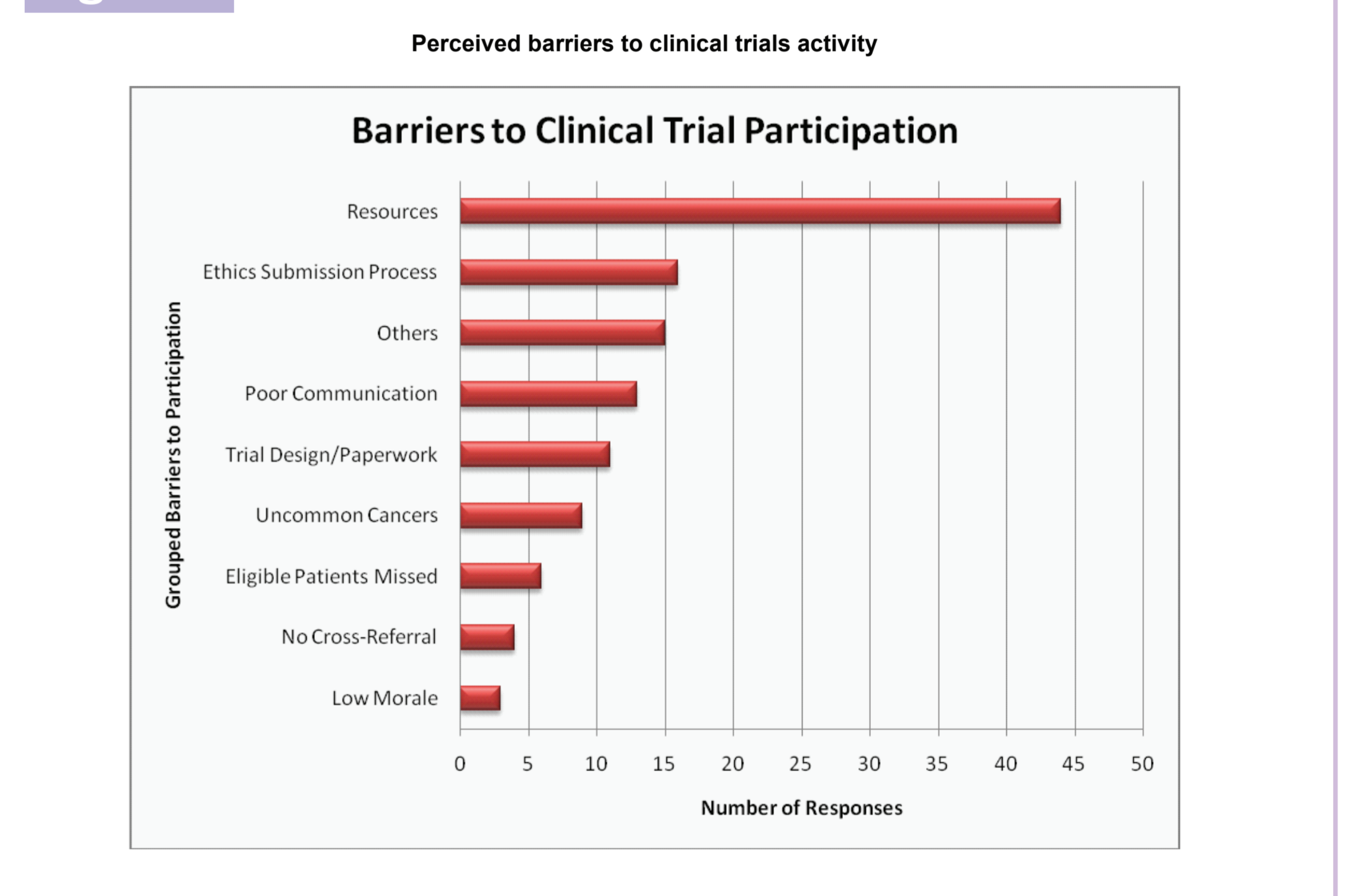


Figure 3

