A randomized controlled trial (RCT) to improve enrollment to cancer clinical trials

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Abstract #6514

Aim

To ascertain if additional funding at a site level would increase recruitment to cancer clinical trials.

Background

The benefits of clinical trials in advancing medical knowledge and patient care are well recognised. A significant challenge of conducting trials is obtaining enough patients to participate in the research to provide a meaningful and statistically significant result. The proportion of adults recruited to oncology clinical trials in the state of Victoria, Australia is approximately 6%[1].

Cancer Council Victoria, a charity based in Melbourne Australia, awards funding to clinical trial sites through its Clinical Trials Management Scheme (CTMS). This scheme aims to improve overall capacity by the funding of onsite data managers at both public hospitals (Government owned and available to all Australians at no direct cost) and private hospitals (privately owned and available to those with insurance and patients purchasing services). All sites submit annual recruitment data for each trial they are conducting.

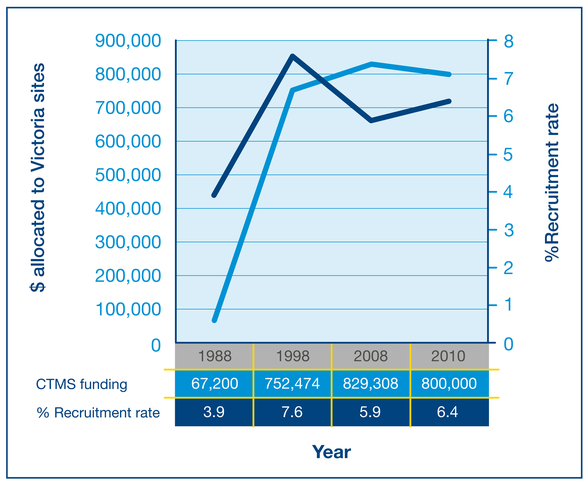
The funding is a mix of government grants and donor dollars, varying over time. There have been periods of increasing funding year on year and periods where funding has not increased.

With the scheme and recruitment data collection, we observed there appeared to be a temporal relationship between growth or stability in funding, and growth or stability in the number of patients recruited. In addition, clinical trial sites have advocated for increased funding for infrastructure support to improve patient accrual to cancer clinical trials (see Figure 1).

We decided to test this idea that providing more money to clinical trials groups would in fact, at the margin, increase patient accrual: we undertook a randomized controlled trial to evaluate this hypothesis that additional funding would improve trial recruitment, with competitive grant funding from the Victorian Cancer Agency.

The study was assessed by the Institutional Research Review Committee has having negligible risk to participants and therefore exempt from ethical review.

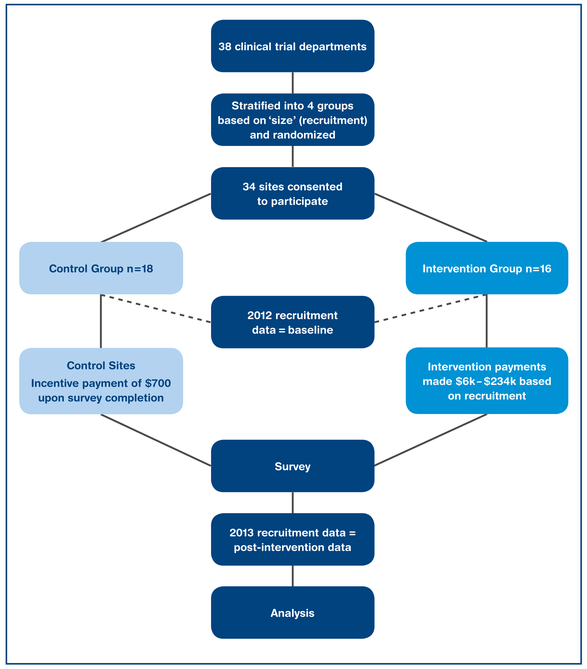
Figure 1: Victorian CTMS allocation & recruitment rate



Methods

Eligible cancer trials were institutional human research ethics committee approved adult treatment intervention trials of chemotherapy, surgical or radiotherapy modalities. There were 40 sites conducting these studies in 2011. Two sites were excluded as one ran only pediatric trials and the other was geographically located on the state border. From the remaining 38 sites, 34 agreed to participate in the study. These sites (n=34) were grouped into four strata based on 2011 recruitment numbers, due to the large variation in recruitment between sites. Control sites (n=18) received usual CTMS funds, while intervention sites (n=16) received usual funds plus additional funds, proportional to the number of patients recruited in 2011 (see Figure 2).

Figure 2: Method schema



The additional funding (in excess of the usual expenditure) was divided by the total number of new participants in eligible trials from participating sites in 2011, to determine a payment amount per new participant, in addition to the quantum they receive through the normal CTMS process. This additional amount was A$1350 per participant (~US$1055). Control sites received their "usual funding" through the CTMS process, and no additional capitated funding, but were paid a single payment of A$700 (~US$540) incentive payment to encourage survey completion.

Additional funding was a median increase of 300% (IQR: 112.5%, 459%) relative to usual CTMS funds and was an average 11.8% (IQR: 8%, 12.3%) increase in the site's total budget. Additional funds were provided in early 2013. Sites were required to use the funds with the aim of increasing recruitment.

The primary study endpoint was the number of new participants recruited to clinical trials in 2013 relative to recruitment in 2012.

Negative binomial regression analysis was used to model the endpoint, adjusting for any imbalance in randomized groups' features and historical recruitment. An online survey assessed strategies employed to increase recruitment.

Results

A comparison of the control and intervention sites at baseline is given in Table 1 based on their recruitment numbers, the type of institution (public/private) and the amount of intervention funding. The number of sites per stratification group is also shown.

Table 1: Baseline characteristics of sites, by treatment group. Values are given as number (percentage) or median (interquartile range – IQR)

Characteristic	Level	Control	Intervention	p-value
Number of sites		18	16	
2012 New recruits, median (IQR)		17.5 (10.0, 51.0)	17.0 (6.5, 41.5)	0.63
Intervention funding (A$), median (IQR)		0	22275 (16200, 67500)	
Private/Public organisations	Private	2 (11%)	6 (38%)	0.11
	Public	16 (89%)	10 (63%)	
Stratification group (based on 2011 new recruitment numbers)	<15	7 (39%)	7 (44%)	
	15-34	5 (28%)	4 (25%)	
	35-99	4 (22%)	4 (25%)	
	100+	2 (11%)	1 (6%)	

Descriptive statistics for the recruitment outcomes, along with change in recruitment numbers from baseline are given in Table 2. The median number of new trial recruits in 2013 was 21 (IQR: 5, 39) in the control arm and 12.5 (IQR: 3.5, 44.5) in the intervention arm. These results indicate there is no difference between the groups, but there is no ability to adjust for baseline values. Regression models were used to do this.

Table 2: Numbers of new recruits and total recruits in 2013 and the changes in these recruitment numbers from 2012 to 2013. Values are given as median (interquartile range – IQR)

Outcome	Control	Intervention	p-value
N	18	16	
2013 New recruits, median (IQR)	21.0 (5.0, 39.0)	12.5 (3.5, 44.5)	0.70
Change in new recruits (2013 minus 2012), median (IQR)	-2.5 (-10.0, 3.0)	-2.0 (-5.0, 3.5)	0.39

Table 3 shows the ratio of the annual recruitment rate of new trial recruits at the intervention sites compared to control sites in 2013 adjusting for 2012 numbers and institution type was 0.99 (95%CI: 0.69, 1.43, p=0.96) which is consistent with the null effect of no difference between the two groups. We found no evidence of a differential intervention effect across strata of higher pre-trial recruitment (χ^2_3=2.27, p=0.5).

Table 3: Negative binomial regression results for number of new recruits and total recruits: Rate Ratios, 95% confidence intervals (CIs) and p-values are presented

MODEL OUTCOME: Recruits 2013	NEW RECRUITS	
	Rate Ratio (95% CI)	p-value
Adjusting for baseline only		
Group (intervention/control)	0.99 (0.69 – 1.43)	0.96
Ln (recruits 2012)		<0.001
Adjusting for baseline and institution		
Group (intervention/control)	1.03 (0.72 – 1.45)	0.89
Ln (recruits 2012)		<0.001
Institution (public/private)	1.51 (0.95 – 2.38)	0.08

All of the trial managers at both the control and intervention sites responded to the survey. Sixteen of the control site clinical leads responded (89%) and 15 intervention site clinical leads responded (94%). The survey revealed most intervention sites utilised funding for increased staffing.

Discussion and Conclusions

We acknowledge that the short-term nature of the funding may have affected how intervention sites spent their additional funding. The unsustained nature of the funding may have also impacted our results. We assumed that sites were in the best position to know how to increase accrual at their individual sites, but further research is needed to determine if more targeted funding would have made a difference.

In conclusion additional funding at a site level did not lead to a contemporaneous increase in trial recruitment. A lag-effect may become apparent. In our setting, simply providing more funding without targeting and managing its use does not immediately increase trial accrual. We encourage other jurisdictions to replicate our study design to ascertain if our results are widely applicable.

1. Parker, Catriona on behalf of Cancer Council Victoria's Clinical Network: Celebrating 25 years of the Clinical Trials Management Scheme (CTMS): Victorian clinical trial activity, 1988-2013. Presented at the Clinical Oncology Society of Australia's 40th Annual Scientific Meeting, Adelaide, SA, November 12-14, 2013.

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