

Cancer Trials Management Scheme
incorporating Victorian Cancer Trials Link

Report on 2009 Clinical Trial Activity in Victoria



helping to bring patients and new treatments together

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Clinical Trials Office, Cancer Council Victoria

1 Rathdowne Street

Carlton Vic 3053 Australia

trialslink@cancervic.org.au

www.cancervic.org.au/trials

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Executive summary																	
Background	The Cancer Trials Management Scheme (CTMS) was established in 1988 by the Victorian Cooperative Oncology Group (VCOG) as a funding mechanism to increase participation in clinical trials, through the funding of on-site dedicated clinical trial coordinators. The CTMS has grown substantially, in both the size of the annual grant available and the number of participating sites. In return for the grant monies, sites submit data regarding the trials they are conducting, including the type of trials and the number of patients recruited and followed-up. The CTMS remains the only source of comprehensive data on cancer clinical trial activity in Victoria.																
Objective	This report aims to summarise clinical trial activity in Victoria during 2009, as submitted by sites participating in the CTMS grant scheme for that year.																
Methods	Site-specific lists of cancer clinical trials were exported from the Victorian Cancer Trials Link (VCTL) database and sent to the 26 known cancer research locations across Victoria. Trial coordinators were asked to confirm the list of trials and complete four fields regarding the number of metropolitan and rural patients recruited and followed-up in each of these trials. Each returned spreadsheet was screened for completeness and consistency, and data verification was sought verbally, electronically or in person. Some sites required up to four versions of data clarification before analysis could begin. Data analysis comprised descriptive statistics, including proportions and rates.																
Results	<p>Twenty-five out of 26 sites submitted a grant application by the due date, an increase of 5 sites compared with 2008. Four of the new sites were private hospitals and 2 were in the Barwon South West Regional Integrated Cancer Service (ICS). Data were also submitted from a number of new departments within existing sites, including 3 haematology departments participating for the first time in 2009.</p> <table border="1"> <tbody> <tr> <td>Patient recruitment</td> <td> <ul style="list-style-type: none"> 1922 new patients were recruited, a 21.7% increase from 2008. This equates to a recruitment rate of 7.1%, based on 2007 cancer incidence in Victoria. The paediatric (0-14 years) recruitment rate was estimated as approximately 39%, based on 2007 cancer incidence in Victoria. 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Conclusion	Integration of CTMS and the VCTL in 2009 has led to a significant improvement in data quality; as a result this report contains the most comprehensive data to date. This is an important new benchmark for clinical trial activity in Victoria. The accurate benchmark is vitally important since the clinical trial participation rate in 2012 is a target indicator for the Victorian Cancer Action Plan. In 2009, the overall recruitment rate increased, and the paediatric recruitment rate was estimated for the first time. More clinical trial sites than ever submitted data, including increasing numbers of private and rural sites. The report makes ten recommendations, and most importantly highlights the need to undertake a major review of the present CTMS grant allocation process prior to the next funding round.																

Report on 2009 Clinical Trial Activity in Victoria

1. Background to the Cancer Trials Management Scheme (CTMS)/Victorian Cancer Trials Link (VCTL)

Now in its twenty-second year, the Cancer Trials Management Scheme (CTMS) was established by the Victorian Cooperative Oncology Group (VCOG) as a funding mechanism to increase participation in clinical trials, through the funding of on-site dedicated clinical trial coordinators.

Since 1988 the CTMS has grown substantially, in both the size of the annual grant available and the number of participating sites. In return for the grant monies, sites submit data regarding the trials they are conducting, including the type of trials and the number of patients recruited and followed-up.

A review of the CTMS funding mechanism in 2001 placed greater priority on supporting sites that conduct trials that are investigator or Cooperative Group initiated, and recruit rural participants. The specific funding algorithm has been described elsewhere.¹ Between 2006 and 2008 the algorithm was further adjusted to encourage recruitment of new patients rather than long-term follow-up, as this was considered best use of site resources. In 2008 a small incentive grant was offered to sites to encourage them to upload and update data on the Victorian Cancer Trials Link (VCTL), an online searchable database of all cancer clinical trials in Victoria.

In 2009 the CTMS and VCTL were fully integrated; as a result this report contains the most comprehensive data to date. This integration has provided a significant improvement in data quality, as well as a substantial reduction in the work required by sites and increased compliance with reporting requirements.

The CTMS remains the only source of comprehensive data on cancer clinical trial activity in Victoria.

2. Objective of this report

This report aims to summarise clinical trial activity in Victoria during 2009, as submitted by sites participating in the CTMS/VCTL for that year. Data collected through other components of the CTMS grant application (Table 1) will be reported elsewhere.

Table 1. Components of CTMS/VCTL 2009 grant application

Part 1a	VCTL site contact details – verification/correction only
Part 1b	Workforce summary data – completion of 5 fields
Part 2	Clinical trial activity spreadsheet, based on data exported from the VCTL – verification of VCTL data and completion of 4 fields
Part 3	Service Agreement – signed (sent after receipt of Parts 1 and 2, confirmation of data and calculation of grant)

3. Methods

On 4 February 2010 an invitation was sent to 26 known cancer clinical trial sites in Victoria to submit trial recruitment data for review, and to apply for data management grants. The grant application forms comprised four components (Table 1), including a spreadsheet listing their respective clinical trials, based on data exported from the Victorian Cancer Trials Link (VCTL) database the previous day.

On four occasions prior to this invitation, between December and February, sites were reminded to update their data on the VCTL since it would form the basis of the clinical trial activity spreadsheet used in their CTMS grant application. In previous years sites had been responsible for creating their own list of trials; it was hoped this new method would reduce site workload, increase data quality and overall efficiency of the CTMS.

Sites were required to confirm the list of trials included in Part 2, and to complete four fields regarding the number of metropolitan and rural patients recruited and followed-up in each of these trials.

New patients were defined as those recruited into the trial between 1 January and 31 December 2009. Follow-up patients were those recruited into trials prior to 1 January 2009 and still receiving trial treatment or participating in follow-up data monitoring activities in 2009. Some patients may have been counted more than once, since it was not possible to identify whether any individuals participated in multiple trials during 2009.

Rural patients were defined as those who reside in a postcode that is included in the CTMS “Victorian Rural Postcodes” list, or who reside in a regional ICS area.

The VCTL Program Manager checked all returned spreadsheets for completeness and consistency, and sought verification verbally, electronically or in person. Some sites required up to four versions of data clarification before analysis could begin.

¹ Clinical Trials Office. CTMS Overview, 2008. Cancer Council Victoria, 2009.

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Although trials may be cross-referenced to multiple tumour streams in VCTL, analysis only took place on the primary tumour stream for each trial. ‘Advanced cancer’ trials were defined as those early phase trials targeting patients who have cancer of any type which has progressed and where no further standard treatment is available.

Where possible, any trials not meeting the World Health Organization definition of a clinical trial² were removed from the data prior to analysis, including biology and tissue banking studies.

Unlike previous years, sites were not asked to priority rank trials – a process where each trial is allocated a rank based on the type of sponsor initiating and/or funding the trial. Rather, the VCTL Program Manager automatically calculated priority ranks in Excel based on the criteria in Table 2 (next page) using sponsor and collaborative group data listed in the spreadsheets. Again, this aimed to reduce site workload and improve consistency where the same trial was conducted across multiple sites.

Data analysis, comprising descriptive statistics such as proportions and rates, was undertaken using Microsoft Excel pivot tables. Recruitment rates were calculated as a percentage of the number of patients recruited into a clinical trial during 2009 over the age-standardised cancer incidence in Victoria 2007 of 26,955 cases per 100,000 (standardised to World Standard Population).³ There is no standardised method of calculating recruitment rates, either nationally or internationally, however this method has been published previously.^{4,5} Except where specified, recruitment rates included: all age groups; both investigator- and sponsor-initiated trials; all phases; all tumour groups; and all cancer clinical trial types except palliative care, supportive care and prevention.

Table 2. Criteria for priority ranking of trials, CTMS/VCTL 2009

Priority Ranking	Criteria
0	Industry-initiated trials
1	Investigator-initiated, hypothesis driven, cancer clinical trials open at one or more Victorian sites, with a clearly defined intervention, endpoints and outcome measures and registered with an ICMJE ⁶ approved trial registry. Includes: <ol style="list-style-type: none"> Trials sponsored by local hospitals with state-wide sites, Unknown sponsor
2	Investigator-initiated, hypothesis driven, cancer clinical trials open at sites throughout Australia and/or internationally, with a clearly defined intervention, endpoints and outcome measures and registered with an ICMJE approved trial registry. Includes <ol style="list-style-type: none"> International Cooperative Group trials, National Cooperative Group Trials, State Cooperative Group trials with nation-wide sites, Local hospital sponsored trials with nation-wide sites

Grant funds totalling \$800,000 were available for allocation, comprising \$600,000 from the Cancer Council Victoria and the balance from Department of Health (Victorian Cancer Agency).

Grants were allocated using the CTMS funding algorithm, which placed greater priority on sites that:

- Conduct investigator or Cooperative Group initiated trials
- Recruit rural participants, and
- Recruit new patients rather than follow-up existing patients.

² “Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes” <http://www.who.int/ictrp/faq/en/index.html> (accessed 12/8/2010).

³ Canstats: Cancer in Victoria 2007, <http://www.cancervic.org.au/about-our-research/cancer-statistics> (accessed 10/7/2010).

⁴ Welberry H, Catazariti A, Edwards C, Bishop J. Cancer Clinical Trials in NSW, 2004-2006. Cancer Institute NSW, 2008.

⁵ Sateren WB, Trimble EL, Abrams J, et al. How sociodemographics, presence of oncology specialists, and hospital cancer programs affect accrual to cancer treatment trials. *J Clin Oncol* 2004; 20:2109-2117.

⁶ Which trials registries are acceptable to the ICMJE? http://www.icmje.org/faq_clinical.html (accessed 3/7/2010) .

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4. Results

4.1. Site Participation

Twenty-five out of 26 sites submitted Part 2 of the CTMS/VCTL grant application by the due date, March 30th (Appendix 1). This was an increase of 5 sites compared with 2008. Four of the new sites were private hospitals and 2 were in the Barwon South West Regional Integrated Cancer Service (ICS).

All metropolitan and regional ICS were represented in the data, with the exception of Gippsland. Presently there are no cancer clinical trials being conducted through the Latrobe Regional Hospital or other sites in that region.

Data were also submitted from a number of new departments within existing sites, including 3 haematology departments participating for the first time in 2009 (Appendix 1).

4.2. Patients by recruitment status

A total of 1922 new patients were recruited into 277 clinical trials in 2009, a 21.7% increase in recruitment from 2008 (Chart 1). This equates to a recruitment rate of 7.1%, based on 2007 cancer incidence in Victoria. Sites reported that 5077 patients were seen for follow up in 2009, a decrease of 1656 from 2008.

Approximately 3% (64/1922) of all newly recruited patients were seen by the Royal Children's Hospital, providing a suitable proxy for Statewide paediatric recruitment. Using the most current cancer incidence available,³ this estimates a paediatric (0-14 years) recruitment rate of approximately 39%.

Combined, the 8 regional sites recruited almost 13% (248/1922) of all new patients, and followed-up 17% (866/5077) of all existing patients.

Chart 1. Patient recruitment and follow up, CTMS 1988 to 2009

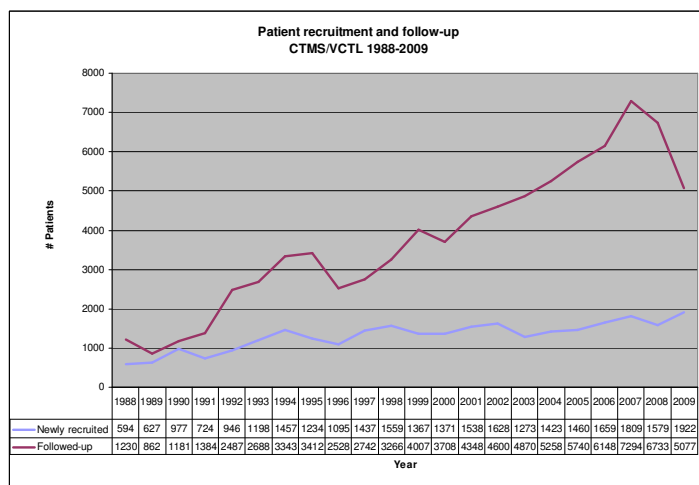
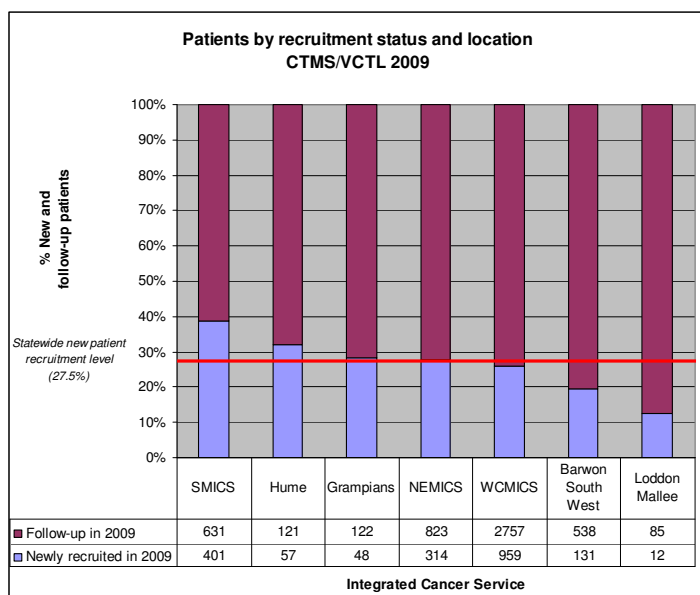


Chart 2. Patient recruitment types by ICS, CTMS/VCTL 2009



Almost half of all new patients starting on trials in Victoria were recruited in Western and Central Melbourne ICS (WCMICS) (49.9%, 959/1922). As a proportion of all trial participants by ICS, Southern Metropolitan ICS (SMICS) had the highest proportion of newly recruited patients (38.9%, 401/1032) (Chart 2).

More than half of all rural patients enrolled on trials in 2009 were recruited through metropolitan sites (56.0%, 316/564). Of those rural patients followed-up, slightly less than half were seen through metropolitan sites (49.2%, 838/1703) (Table 3).

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Table 3. Patient recruitment by type and location, CTMS/VCTL 2009

Location	Newly recruited in 2009		Followed-up in 2009		Total patients*
	Metro patients	Rural patients	Metro patients	Rural patients	
Metropolitan ICS	1339	316	3293	838	5786
Rural ICS	0	248	1	865	1114
Statewide*	1339	564	3294	1703	6900

* data could not be calculated for 99 patients

4.3. Trials by recruitment status

A total of 700 discrete trials were reported statewide, of which 41% were open to recruitment (n=287). This proportion did not differ significantly between metropolitan and regional sites (Table 4).

On a per trial basis, an average of 6.7 patients were recruited into open trials in Victoria during 2009 (median 4, range 1-70). The trial recruiting the highest number of patients was initiated by the Australasian Gastro-Intestinal Trials Group (AGITG) and was conducted by 12 sites across the state.⁷

Table 4. Trials by recruitment status and location, CTMS/VCTL 2009

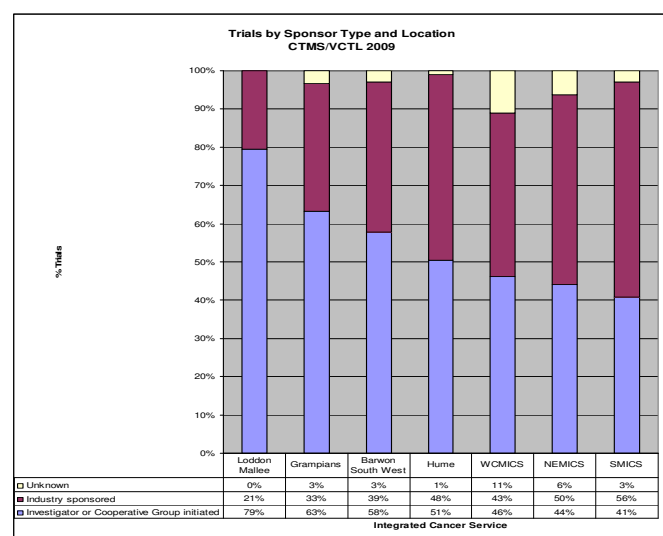
Location	N open trials			N closed trials		Total trials*
	Not yet recruiting	Recruiting	On hold	Closed (no longer recruiting)	Completed	
Metropolitan ICS	16	480	5	492	194	1187
Rural ICS	5	107	3	122	28	265
Statewide**	12	273	2	254	159	700

* trials may be conducted across several sites and therefore counted several times

** trials are only counted once in statewide totals

4.4. Trials by sponsor type

Chart 3. Sponsor types by ICS, CTMS/VCTL 2009



Approximately 37% of all trials (262/700) were initiated by local investigators or Cooperative Groups. This proportion was greater for trials that were undertaken in Regional ICS (58%, 155/265) and for those currently recruiting patients (45%, 128/287). Regional sites were more likely to have complete data for this field (2% vs 8% in metropolitan sites).

Of all open and closed trials, SMICS had the lowest proportion of investigator or Cooperative Group initiated trials, and Loddon Mallee the highest (41%, 115/281 vs 79%, 27/37) (Chart 3).

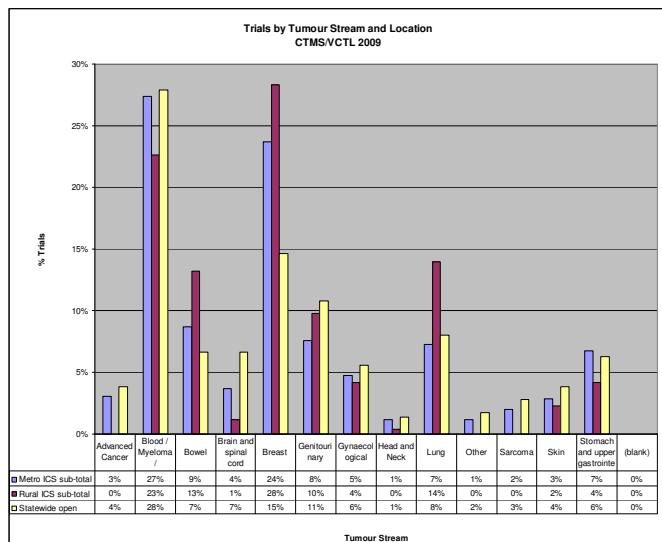
Of all the new patients recruited in 2009, half were enrolled into investigator or Cooperative Group initiated trials (50.6%, 973/1922), compared with 42% into industry sponsored trials (805/1922). One hundred and forty-six patients were recruited into trials with an unknown sponsor.

⁷ CO.20: A Phase III Randomized Study of Brivanib Alaninate (BMS-582664) in Combination with Cetuximab (Erbitux,™ C225) versus Placebo in Combination with Cetuximab (Erbitux,™ C225) in Patients Previously Treated with Combination Chemotherapy for Metastatic Colorectal Cancer (Registration numbers: ACTRN12607000589482, NCT00640471).

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4.5. Trials by tumour stream

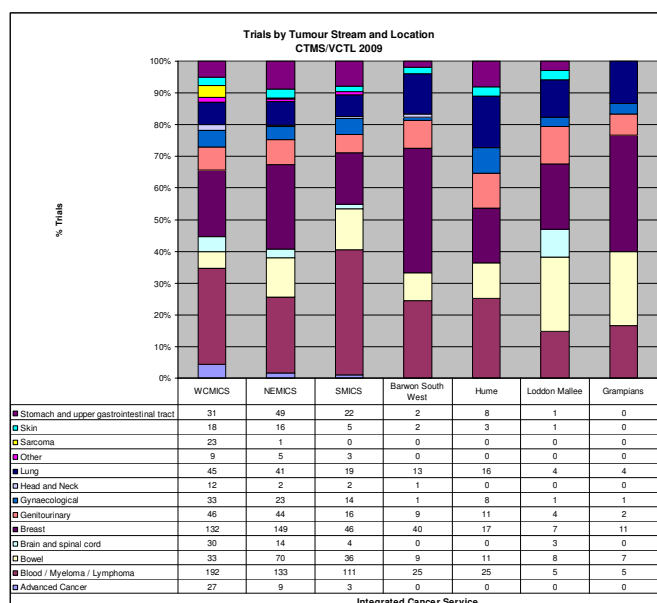
Chart 4. Trials by tumour stream and location, CTMS/VCTL 2009



Statewide, the largest proportion of open trials were in the 'Blood/Myeloma/Lymphoma' tumour stream (28%, 80/287), followed by Breast (15%, 43/287) and Genitourinary (11%, 31/287) trials (Chart 4).

This was not reflected in regional sites, however, where the largest proportion of open trials were Breast trials (28%, 75/265 vs Blood trials 23%, 60/265).

Chart 5. Trials by ICS and tumour stream, CTMS/VCTL 2009



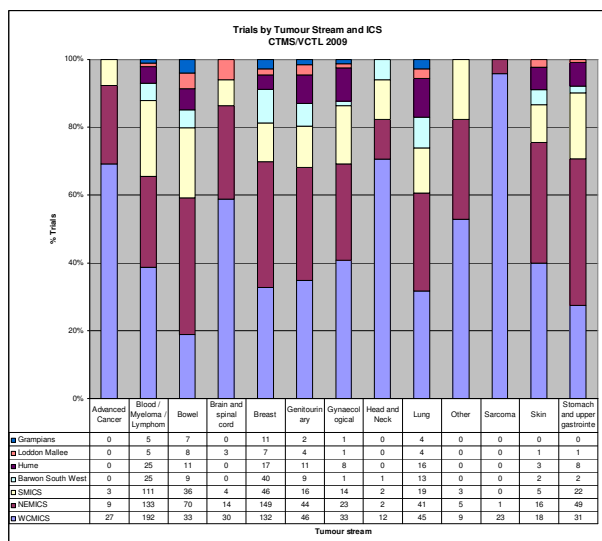
Regional sites conducted a higher proportion of Bowel, Breast, Genitourinary and Lung trials compared with metropolitan sites.

When analysed by ICS, Blood trials comprised the the highest proportion of all trials undertaken in SMICS (40%, 111/281), WCMICS (30%, 192/631) and Hume (25%, 25/99) (Chart 5).

Breast trials were the highest proportion of all trials undertaken in Grampians Regional ICS (37%, 11/30), North Eastern Metropolitan ICS (NEMICS) (27%, 149/55) and Barwon South West (39%, 40/102).

The highest proportion of all trials undertaken in Loddon Mallee were Bowel (24%, 8/34).

Chart 6. Trials by tumour stream and ICS, CTMS/VCTL 2009



Regional ICS conducted only 26% (37/142) of all Lung trials and 13.6% (11/81) of Gynaecological trials, and no Advanced cancer trials (Chart 6). Loddon Mallee was the only regional ICS location conducting Brain and Spinal Cord trials.

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Patient recruitment was highest amongst breast cancer trials (11.1 patients recruited per open trial) and lowest for Brain and Spinal Cord trials (2.1 patients/trial) (Table 5).

Blood trials ranked 5th despite having the largest number of patients recruited (n=535), and the highest number of trials open (n=80).

Table 5. Recruitment rate per open trial, by tumour stream, 2009 CTMS/VCTL

Tumour stream	N patients recruited	N trials open	N patients per trial
Breast	465	42	11.1
Bowel	188	19	9.9
Genitourinary	297	31	9.6
Other	43	5	8.6
Blood / Myeloma / Lymphoma	535	80	6.7
Gynaecological	86	16	5.4
Head and Neck	19	4	4.8
Advanced cancer	52	11	4.7
Stomach and upper gastrointestinal tract	63	18	3.5
Skin	38	11	3.5
Lung	77	23	3.3
Sarcoma	19	8	2.4
Brain and spinal cord	40	19	2.1
Total	1922	287	6.7

Table 6. Common Scientific Outline (CSO) categories⁸

Common Scientific Outline (CSO) categories	Open trials N	%
Aetiology	1	0.3
Biology	1	0.3
Cancer Control Survivorship and Outcomes Research	11	3.8
Cancer Drug Discovery and Development	1	0.3
Early Detection Diagnosis and Prognosis	5	1.7
Prevention	9	3.1
Supportive care	1	0.3
Treatment	247	85.7
Blank	12	4.2
Total	287	100

4.6. Trials by Common Scientific Outline (CSO)

At least one trial was allocated to each of the 8 CSO categories (Table 6), with open trials most frequently falling into the CSO 'Treatment' category (86%, 246/287). Data incompleteness for this field was 4.2% (12/287).

4.7. Trials by phase

The majority of open trials were Phase III (46%, 131/287) (Table 7 and Chart 7) with regional sites more likely to conduct Phase III or IV trials than metropolitan sites (66%, 175/265 vs 56%, 663/1187) (Table 8).

Approximately 11% of all trials (80/700) did not have this field completed.

On a per trial basis, Phase IV trials recruited the highest number of patients per trial (14.3 patients recruited per trial).

Table 7. Recruitment rate per open trial, by Phase, 2009 CTMS/VCTL

Phase	N patients recruited	N trials open	N patients per trial
Phase 0	1	1	1.0
Phase I	143	26	5.5
Phase I/II	114	20	5.7
Phase II	374	63	5.9
Phase II/III	8	4	2.0
Phase III	827	131	6.3
Phase III/IV	4	1	4.0
Phase IV	43	3	14.3
Not applicable	178	19	9.4
Blank	232	19	12.2
Total	1922	287	6.7

⁸ International Cancer Research Portfolio, <http://www.cancerportfolio.org/cso.jsp> (accessed 12/7/2010).

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Chart 7. Trials by Phase and location, CTMS/VCTL 2009

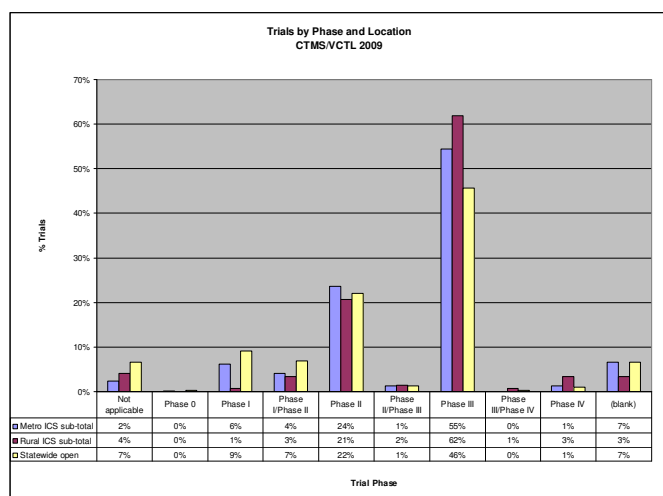


Table 8. Trials by phase and location (open and closed trials), 2009 CTMS/VCTL

Location	Phase 0, I or II		Phase III or IV		Other		Total trials*
Metropolitan ICS	419	35%	663	56%	105	9%	1187
Rural ICS	70	26%	175	66%	20	8%	265
Statewide open**	114	40%	135	47%	38	13%	287

* trials may be conducted across several sites and therefore counted several times

** trials are only counted once in statewide totals; these data refer only to those trials open and recruiting patients

4.8. Trials by registration type

More than 85% (246/287) of all open trials were registered with at least one of the following clinical trial registers, approved data providers to the World Health Organization's International Clinical Trials Search Platform:⁹

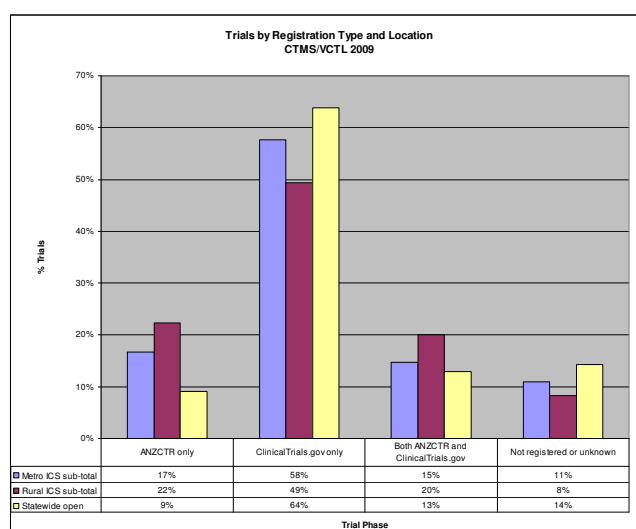
- ClinicalTrials.gov
- Australian and New Zealand Clinical Trials Register (ANZCTR) (Chart 8).

Compared to metropolitan sites, regional sites were more likely to conduct trials that were registered in both locations (20%, 53/265 vs 15% 175/1187). Overall the US service, ClinicalTrials.gov, was the register of choice.

4.9. Trials by number of sites

The majority of Victorian cancer trials were conducted through a single research site (56%, 394/700). Of multi-site trials, 35% were conducted at 2-4 sites (n=245), 3% at 5 sites (n=22) and 6% at 6 or more sites (n=39).

Chart 8. Trials by registration type and location, CTMS/VCTL 2009

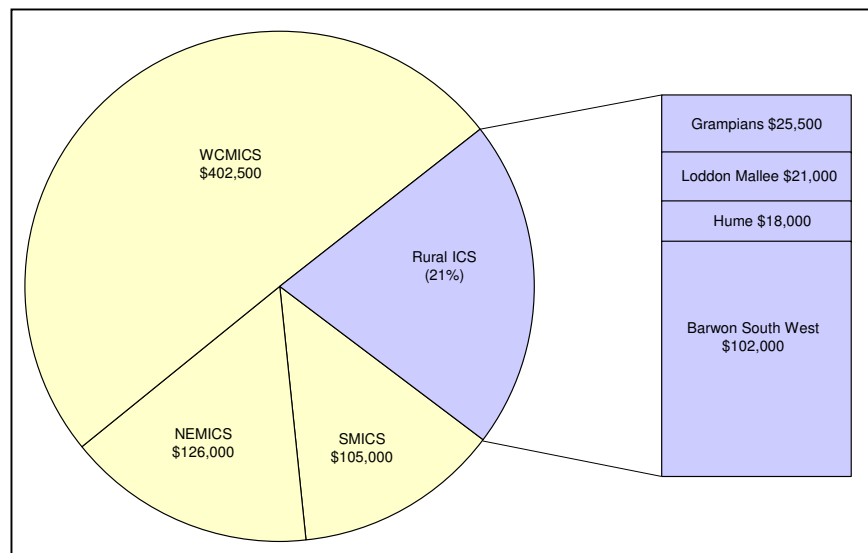


⁹ International Clinical Trials Search Platform, <http://www.who.int/ictrp/en/> (accessed 12/7/2010).

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4.10. Grant allocations

Chart 9. Grant allocation by Integrated Cancer Service, CTMS/VCTL 2009



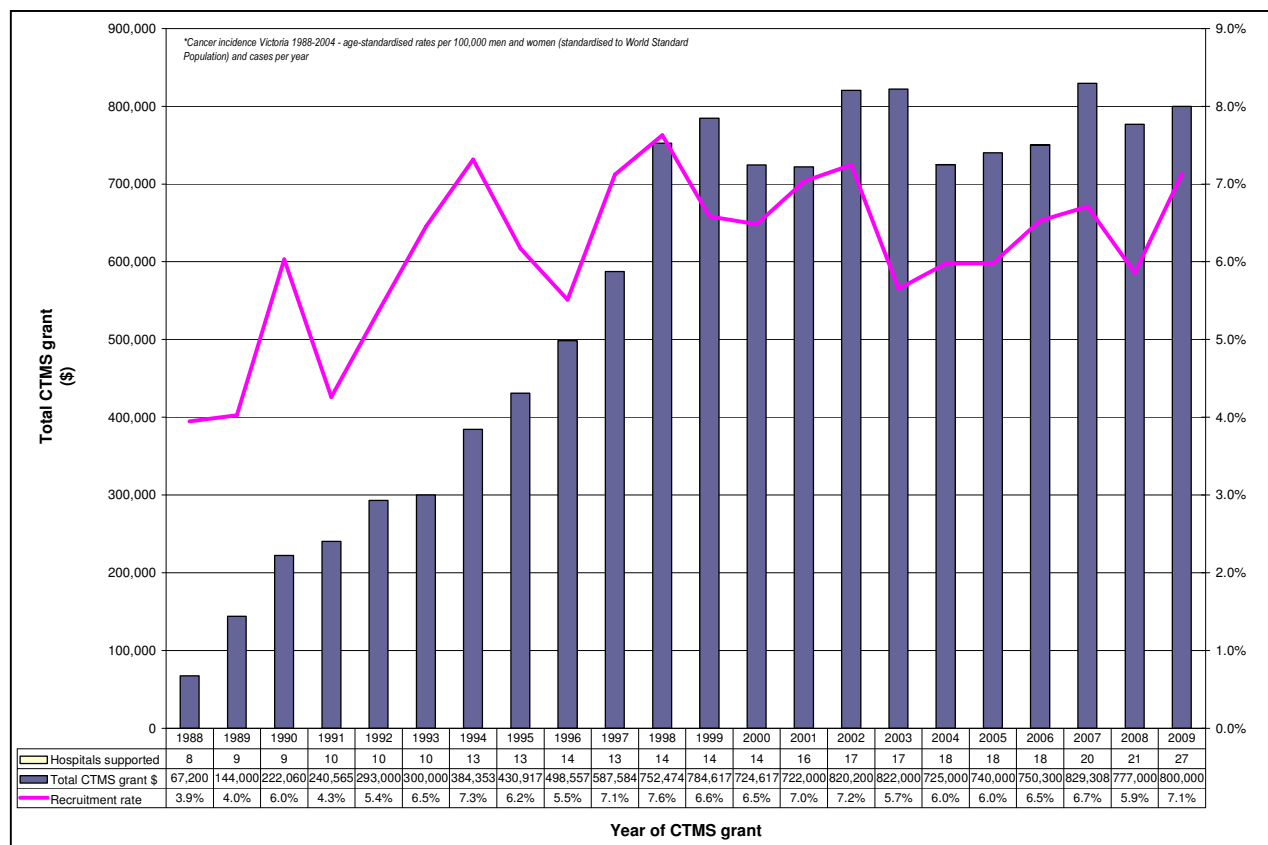
Almost 80% (\$633,500/\$800,000) of funds were allocated to metropolitan sites (Chart 9), of which half (\$402,500) was disbursed amongst the 9 research centres in WCMICS.

The average payment per site ranged from \$10,500 in Loddon Mallee to \$44,722 in WCMICS, with metropolitan sites receiving on average about \$16,300 more per site than regional sites (\$37,300 vs \$21,000).

The average grant payment per patient recruited was higher in Regional than Metro ICS (\$671.37 vs \$377.98).

Since commencement of the Cancer Trials Management Scheme (CTMS) in 1988, a total of 28,877 new patients have been recruited into cancer clinical trials in Victoria, and 82,906 patients followed up. Grants totalling more than 12 million dollars have been disbursed to participating sites, which have grown from 8 to 27 during this time (Chart 10).

Chart 10. CTMS funding and recruitment rate by year – 1988 to 2009



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5. Discussion and recommendations

There are several limitations to the data reported here:

- Whilst data exported from the VCTL was verified by sites, it is possible that some trials are missing, and that cancer clinical trials are being conducted at sites or departments not included in the CTMS.
- Palliative care, supportive care and prevention trials have not yet been included on the VCTL and hence were not included in the analysis, thereby underestimating the true recruitment and follow-up figures.
- Whilst attempts were made to remove from the analysis any trials not meeting the World Health Organization definition of a clinical trial, it is possible that some non-clinical trials remained in the dataset.
- Due to a lack of standardised methods to calculate recruitment rates, both nationally and internationally, it is difficult to compare our results with those published elsewhere.
- Since individual patient details are not reported it was not possible to calculate adolescent and young adult (AYA) recruitment rates.
- Paediatric recruitment rates have been estimated based on recruitment figures from the Royal Children's Hospital, which may not represent all trial activity in this age group.
- Due to database complexities it was not always possible to report ICS-specific data by open trials, rather both open and closed trials were combined.

Additional limitations with this report are included in the discussion below. Recommendations are highlighted in yellow.

5.1 Methods

- Anecdotally it appears the new method of exporting trial information from the VCTL to form the basis of reports has **reduced workload** for sites and **streamlined** the reporting process significantly.
- It also provided a good opportunity for **data verification** and therefore increased the quality of VCTL data.
- Sites submitted data in a **timely manner**, possibly due to the ease of completion, and the **consistent format** made it much easier for data cleaning and verification.
- Formal feedback from sites regarding satisfaction with the new methodology **should be requested**.
- Using VCTL data increased the quality of CTMS data by ensuring trials could be matched across multiple sites and **identified easily** due to correct acronyms and titles.
- The automatic assignment of Priority Ranks by the VCTL Program Manager **avoided previously identified issues** of inconsistency and incorrect attribution by sites, and should be continued.
- Approximately 75 non-clinical trials, such as biology and tissue banking studies, were **removed from the data** prior to analysis.

5.2 Site Participation

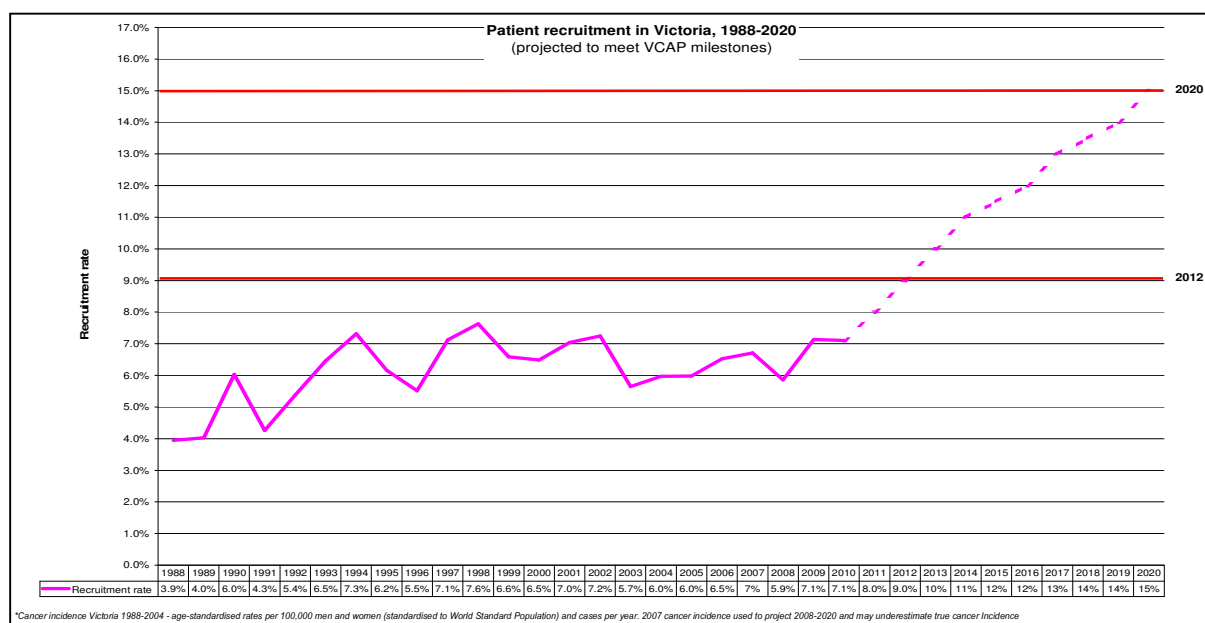
- The increase in participating sites and departments is welcome. It is particularly pleasing to see the **addition of both private and regional sites** in 2009.
- The persistent lack of a clinical trial **presence in the Gippland Regional ICS** is noted.

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5.3 Patient recruitment

- Clinical trial recruitment rates over the past 10 years have fluctuated between about 6 and 7% of all incident cancer cases in Victoria; the slight rate increase in 2009 is reassuring although **consistent with previous data**.
- Approximately **2426 people will need to be recruited** into clinical trials each year in order to reach the 2012 Victorian Cancer Action Plan (VCAP) target of 9%, and 4043 recruited annually to reach the 2020 VCAP target of 15%. These figures have been estimated using 2007 Victorian cancer incidence, and are an underestimate if cancer incidence grows beyond 27,000 cases per year (Chart 11).¹⁰

Chart 11. Patient recruitment rate by year in Victoria, projected to meet VCAP milestones – 1988 to 2015



- Patient recruitment through regional sites increased slightly from 2008 (n=203 ,11%) to 2009 (n=248, 13%).
- The number of patients recruited into trials by ICS does not necessarily relate to **the corresponding cancer burden in each Region**, since some trials are only open at a select number of sites and patients travel outside their locality.
- Metropolitan sites recruited 56.0% of all rural patients, further illustrating the challenge of interpreting ICS-specific data and clarifying the **absence of ICS-specific recruitment rates** in this report.
- In this report, all patients recruited through sites in the Barwon South West RICS were classified as rural. However a new rurality index (ASGC-RA¹¹) introduced by the Federal Government in July 2010¹² will result in those living in Geelong and surrounds being reclassified as living in an RA1 area the same as 'major cities' like Melbourne¹³. Consideration should be given to this in future CTMS reports, recognising the **possible impact on data used to measure the VCAP target** of doubling regional patient participation by 2012.¹⁴
- The **decrease in follow-up patients** is thought to be due to a number of large ongoing trials ending during the year of data collection, and is not of concern.

¹⁰ "By 2012 we will increase patient participation in cancer clinical trials from 6 percent to 9 percent and to 15 percent in 2020." State of Victoria. Victoria's Cancer Action Plan 2008-2011. Victorian Government Department of Human Services, 2008.

¹¹ What is this new ASGC-RA? <http://www.rripa.com.au/Resources/tabid/366/language/en-AU/Default.aspx> (accessed 16/9/2010).

¹² Federal Budget 2009-10 - Frequently Asked Questions, <http://www.rripa.com.au/LinkClick.aspx?fileticket=tgFf3dHJonE%3D&tabid=56&mid=736&language=en-AU> (accessed 16/9/2010).

¹³ RRMA/ASGC-RA Town/Postcode Search, http://www.healthworkforce.com.au/main_rma.asp?NodeID=27679 (accessed 16/9/2010).

¹⁴ "We will work towards doubling the level of patient participation from Victorian regional areas in cancer trials by 2012". State of Victoria. Victoria's Cancer Action Plan 2008-2011. Victorian Government Department of Human Services, 2008.

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- We **estimate paediatric recruitment rates** for the first time, reporting approximately 39% of all newly diagnosed paediatric cancer patients (0-14 years) are recruited into clinical trials. This is consistent with data published in 2004 which reported 34% of children aged 10-19 years were treated within clinical trials.¹⁵ No VCAP target has been set for paediatric recruitment into clinical trials, however **this rate should be calculated in future CTMS reports.**

5.4 Trial recruitment status

- Only 41% of trials were open to recruitment, a slightly higher proportion than in previous years (36% in 2007).
- In future CTMS reports, trials which are completed and have had no patients followed up **should not be included** in the VCTL export sent to sites for verification.

5.5 Trial sponsors

- The proportion of investigator or Cooperative Group-initiated trials was **slightly lower** than in previous years (45% of currently recruiting trials vs 52% in 2007).
- 7% missing data in the trial sponsor field is **not satisfactory**, since this field is utilised by the funding algorithm to calculate grant monies.

5.6 Tumour streams

- There is **considerable variation** in the tumour streams represented across metropolitan and regional ICS.
- This means opportunities for patients to participate in clinical trials are inconsistent. Promotion and **utilisation of the VCTL** to identify suitable trials, particularly for niche or rare tumours is one strategy to overcome this issue.
- **Recruitment rates vary by tumour stream**, with Head and Neck trials recruiting more patients per trial than Brain and Spinal Cord trials, for example. The reasons for this might include recruitment criteria, trial location, competition between trials, clinician reluctance to refer or differing levels of patient health literacy.
- In future CTMS reports, **tumour stream specific recruitment rates** should be calculated, acknowledging that for rare tumours there may always be insufficient numbers to justify disease-specific clinical trials.

5.7 Common Scientific Outline (CSO)

- The majority of trials reported are treatment oriented, which may reflect a bias in the data collected through VCTL. In future, a format is needed to ensure clinical trials from other CSO categories, such as preventive trials, can be **displayed on the VCTL** where appropriate.

5.8 Phase

- Almost 50% of all open trials in Victoria are Phase III, which will maximise the likelihood of patient outcomes through **translation to standard treatment.**
- All early phase trials are being conducted at larger clinical trial sites in the metropolitan area.
- The level of missing data (11%) in the phase field is **not satisfactory**, however data cleaning should concentrate on trials which are currently open to recruitment.

¹⁵ Mitchell AE, Scarcella DL, Rigutto GL, et al. Cancer in adolescents and young adults: treatment and outcome in Victoria. MJA 2004; 180: 59–62.

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5.9 Trial registration

- Trial registration (prior to randomisation of the first patient) is strongly recommended by a number of key clinical trial guidelines used in Australia^{16, 17}, and is a condition of publication in member journals of the International Committee of Medical Journal Editors (ICMJE).¹⁸
- Given this, there is scope for **improved registration of trials**, with 14% of open trials reported as not registered.
- A VCTL policy preventing unregistered trials from being added to the database was suspended on 1/1/2010. The policy was directed at improving the quality of trials listed on the database, however if implemented, would have had a significant negative impact on the completeness of the data. Once registration of trials becomes more universal, the **policy will be reconsidered**.

5.10 Single-site trials

- The majority of trials were conducted at only one site (56%). This differs considerably from data published by NSW where only 35% were single-site trials.¹⁹
- Such single-site trials **will not benefit from multi-site ethics review**, or similar efficiencies associated with multiple site research.
- The introduction of research collaborations such as Cancer Trials Australia may see this figure decrease in future.

5.11 Grant allocations

- The increase in sites submitting data in 2009 has not be accompanied by an increase in funds. This means that some sites witnessed a decrease in grant funding **despite submitting favourable data**.
- Funding and data calculations have **increased in complexity** with: 1) some sites submitting data for multiple departments, and 2) some sites having multiple “campuses” across the state. Individual departments or campuses are now wanting to ensure funds are **allocated to their cost centre**, rather than being deposited into general hospital revenue.
- Although the Statewise patient recruitment rate has not grown commensurate with funding, rapidly growing clinical trial complexity and increased regulatory and governance requirements have greatly increased site workload.
- Due to the growth in site numbers, the integration of VCTL into the CTMS and the change in reporting methods, the current grant allocation process requires a **major review by the Reference Group** prior to the next funding round. Specifically:

Reviewing the objectives of Cancer Trials Management Scheme and clinical trial funding priorities, including the funding algorithm; providing more clarity regarding the type of clinical trial activity to be supported, and quantification of RCTs vs non-randomised CTs, screening, prevention and diagnostic trials; identifying CCV, state and site data needs; and improving transparency.

¹⁶ World Medical Association Declaration of Helsinki, 7th revision, <http://www.wma.net/en/30publications/10policies/b3/index.html> (accessed 16/9/2010).

¹⁷ NHMRC Australian Code for the Responsible Conduct of Research, http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/r39.pdf (accessed 16/9/2010).

¹⁸ International Committee of Medical Journal Editors, http://www.icmje.org/publishing_10register.html (accessed 16/9/2010).

¹⁹ Welberry H, Catazariti A, Edwards C, Bishop J. Cancer Clinical Trials in NSW, 2004-2006. Cancer Institute NSW, 2008.

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6. Summary

Since commencement of the Cancer Trials Management Scheme (CTMS) in 1988, a total of 28,877 new patients have been recruited into cancer clinical trials in Victoria, and 82,906 patients followed up. Grants totalling more than 12 million dollars have been disbursed to participating sites, which have grown from 8 to 27 during this time.

Integration of CTMS and the VCTL in 2009 has resulted in a significant improvement in data quality; as a result this report contains the most comprehensive data to date.

This is an important new benchmark for clinical trial activity in Victoria. The accurate benchmark is vitally important since the clinical trial participation rate in 2012 is a target indicator for Victorian Cancer Action Plan. In 2009, the overall recruitment rate increased, and the paediatric recruitment rate was estimated for the first time. More clinical trial sites than ever submitted data, including increasing numbers of private and rural sites.

The report makes ten recommendations, and most importantly highlights the need to undertake a major review of the present CTMS grant allocation process prior to the next funding round.

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APPENDIX 1.

Appendix 1. Sites invited to participate, CTMS/VCTL 2009

Integrated Cancer Service (ICS)	Site name	Specific departments included	Private / Public	Data submitted
Southern Melbourne	Bayside Health, Alfred Hospital	Haematology, Medical Oncology, Radiation Oncology	Public	Yes
	Cabrini Hospital*		Private	Yes
	Peninsula Health, Frankston		Public	Yes
	Peninsula Oncology Centre		Private	No
	Southern Health, Monash Medical Centre	Medical and Radiation Oncology, Haematology*	Public	Yes
	Peter MacCallum Cancer Centre	Moorabbin Radiation Oncology*	Public	Yes
North Eastern Metropolitan	Austin Health		Public	Yes
	Eastern Health, Box Hill	Breast Centre, Haematology*, Medical and Radiation Oncology	Public	Yes
	Eastern Health, Maroondah	Maroondah Breast Clinic	Public	Yes
	Peter MacCallum Cancer Centre	Box Hill Radiation Oncology	Public	Yes
	Mercy Hospital for Women		Public	Yes
	Northern Hospital		Public	Yes
Western and Central Melbourne	Epworth Freemasons*		Private	Yes
	Epworth Richmond*		Private	Yes
	John Fawkner Hospital		Private	Yes
	Mercy Private Breast Clinic		Private	Yes
	Peter MacCallum Cancer Centre	East Melbourne Medical Oncology, East Melbourne Radiation Oncology	Public	Yes
	Royal Children's Hospital		Public	Yes
	Royal Melbourne Hospital	Colorectal, Medical and Radiation Oncology	Public	Yes
	Royal Women's Hospital		Public	Yes
	St Vincent's Hospital	Haematology*, Medical and Radiation Oncology	Public	Yes
Western Hospital		Public	Yes	
Grampians	Ballarat Health		Public	Yes
	Ballarat Oncology & Haematology		Private	Yes
Gippsland	Latrobe Regional Hospital		Public	No**
Loddon-Mallee	Bendigo Health		Public	Yes
	Peter MacCallum Cancer Centre	Bendigo Radiation Oncology	Public	Yes
Hume	Murray Valley Private Hospital	Border Medical Oncology	Private	Yes
Barwon South West	Barwon Health, Geelong		Public	Yes
	St John of God Healthcare, Geelong*		Private	Yes
	South West Healthcare, Warrnambool Hospital*		Public	Yes

* first time submitting data in 2009

** not invited to participate as no cancer clinical trials being conducted presently