ANZCTR
Australian New Zealand Clinical Trials Registry

THE CLINICAL TRIALS LANDSCAPE IN AUSTRALIA 2006–2015

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ISBN: 978-0-6482309-0-8 (print edition)
ISBN: 978-0-6482309-1-5 (PDF edition)

Published by the Australian New Zealand Clinical Trials Registry (ANZCTR)
NHMRC Clinical Trials Centre
Level 6, 92-94 Parramatta Rd
Camperdown NSW 2050
www.anzctr.org.au

Suggested citation
Askie LM, Hunter KE, Berber S, Langford A, Tan-Koay AG, Vu T, Sausa R, Seidler AL, Ko H, Simes RJ. The clinical trials landscape in Australia 2006–2015. Sydney: Australian New Zealand Clinical Trials Registry 2017.

Edited by Cathy Gray
Designed by Alison White Designs
Printed by No Time To Lose Pty Ltd

Foreword

Clinical trials are an essential part of an effective and efficient health care sector. They ensure that the best treatments, to both prevent and treat illness, are assessed rigorously before being implemented into routine care. As such, it is vital to ensure that the clinical trials we are doing in Australia meet the needs of our citizens, and that the clinical trials sector remains robust and competitive by international standards.

This report represents one of the most comprehensive assessments of clinical trial activity in Australia ever undertaken. It also highlights the importance of the national clinical trials registry in ensuring Australia's leading role in promoting research transparency, both here and internationally.

Since 2005, the Australian Government has made a significant and ongoing investment in the Australian New Zealand Clinical Trials Registry (ANZCTR) via funding from the National Health and Medical Research Council and the federal departments of Health, Education and Training, and Industry, Innovation and Science. The recent Chief Scientist's report named the ANZCTR as one of the nation's critical pieces of research infrastructure. The information contained within this report will help consumers, clinicians, industry, universities and those in the health care sector to better prioritise, plan and perform clinical trials. This will lead to innovation and efficiency, and will help improve the health of all Australians.

I congratulate the ANZCTR on more than 10 years of high-quality data collection and recommend that those within the clinical trials and health care sectors use the information contained in this report to ensure the continued success of the Australian clinical trials landscape into the next decade and beyond.

Judith A Whitworth

Professor Judith Whitworth AC
Advisory Committee Chair
Australian New Zealand Clinical Trials Registry

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About the Australian New Zealand Clinical Trials Registry (ANZCTR)

The Australian New Zealand Clinical Trials Registry (ANZCTR) is an online (www.anzctr.org.au) registry of clinical trials and observational studies being undertaken in Australia, New Zealand and elsewhere. It includes trials from the full spectrum of therapeutic areas of pharmaceuticals, surgical procedures, preventive measures, lifestyle, devices, rehabilitation strategies and complementary therapies. Importantly, it enables researchers to fulfil their scientific, ethical and moral obligations to ensure that information about *all* clinical trials is made publicly available.

The ANZCTR was established in mid-2005 and is housed at the NHMRC Clinical Trials Centre, University of Sydney. It is publicly available to search or enter data, 24 hours a day, seven days per week. It was one of the first clinical trial registries to be endorsed by the International Committee of Medical Journal Editors (ICMJE) and then, in 2007, by the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) as a primary registry. The WHO recognises registries as primary registries if they fulfil certain criteria with respect to data content, quality and validity, accessibility, unique identification, technical capacity and administration.

Together with the 14 other primary registries and the US-based ClinicalTrials.gov, the ANZCTR has been at the forefront of the worldwide initiative to make public all clinical trials being conducted. This is essential in order to improve research transparency, facilitate trial participation, avoid duplication, promote research collaboration, improve trial quality and reduce research waste.

Since 2014 trial registration has been a mandatory condition of ethics approval for all Australian trials. However, without a national database of all trials that have received ethics approval, a complete denominator of all trials being conducted in Australian is not known.

Trials can be registered on ANZCTR at any time: before or after ethics approval or enrolment of the first participant. Updates to a trial registration record can also be made at any time, and the audit trail of those changes is publicly accessible. Researchers are encouraged to complete registration well before the first participant is enrolled and are reminded annually to keep their trial's registration record up-to-date.

As such, data from the ANZCTR represents the most complete picture of national clinical trials activity currently available in Australia.

About this report

In 2015, the ANZCTR celebrated 10 years since its formation. Now with over 6,500 Australian trials registered, the ANZCTR stands as an important national resource for clinical trial decision-making. When combined with almost 4,000 Australian trials registered on ClinicalTrials.gov, data from the 10,549 trials registered in the decade 2006–2015 that are contained within this report provide a unique overview of the current clinical trials landscape in Australia.

Acknowledgements

During the period covered by this report (2006–2015), the ANZCTR was funded by grants from the Australian National Health and Medical Research Council, the New Zealand Health Research Council and the Australian Government's National Collaborative Research Infrastructure Strategy program, which is administered via Therapeutic Innovation Australia.

In addition to its funders, the ANZCTR wishes to acknowledge the members of its external Advisory Committee and its founding co-director, Prof Davina Ghersi, for their ongoing strategic advice, summer students Elloise Smith and Lily Zhang, and Cathy Gray of Catherine Gray Editorial Services, for her dedication, care and expertise in the preparation of this report.

Overview and commentary

The Australian clinical trials landscape

During the decade 2006–2015, clinical trial activity in Australia has been substantial, with over 10,000 clinical trials conducted and more than 5 million participants enrolled – that is, more than 1,000 trials and 500,000 participants each year.

On a per capita basis this level of activity compares favourably with that of other countries, with Australia ranking in the top tier of national clinical trial activity. There is, however, still room for improvement. Countries such as Denmark, the Netherlands and Belgium, where clinical trials are considered a routine part of delivering quality health care, are leading the way with regard to this metric.

Australian clinical trials cover the full range of health care interventions and assess a wide range of health conditions, as well as studying healthy populations at risk for future disease. There has been proportionally more activity in the areas of greatest national disease burden, with the most common disease areas studied in Australian clinical trials being cancer, cardiovascular disease and mental health disorders. These represent 18 per cent, 10 per cent and 12 per cent of all trials, and 18 per cent, 19 per cent and 7 per cent of all trial participants respectively. However, some areas of high disease burden, such as dementia and obesity, remain under-represented. This partly relates to the sometimes limited availability of potentially effective interventions for evaluation within trials, but these conditions probably represent areas that warrant more attention in the future, especially as their burden of disease increases.

Clinical trials in Australia assess multiple types of interventions, including drug treatments (47 per cent), surgery (4 per cent), medical devices (10 per cent), behavioural therapies (10 per cent) and prevention strategies (11 per cent). The range of activity includes large, multicentre, phase 3 trials likely to have an impact on clinical practice directly, as well as early-phase trials testing novel therapies or interventions that may become the new best treatments of tomorrow.

Trends in clinical trial activity over the decade

The decade has seen several interesting trends in clinical trial activity. These include moderate growth in the total number of trials registered each year, mainly reflecting increases in non-industry-sponsored smaller-scale trials and non-drug interventions. The numbers of larger randomised trials, trials registered on ClinicalTrials.gov and industry-sponsored trials have remained reasonably steady.

Some of the growth may be due to an increase in the percentage of trials registered. This is now expected to be nearing 100 per cent based on the ethical requirement to register all clinical trials prospectively. However, it will be important to audit the rate of trial registration in the future, through tracking ethics committee cohorts for example, to validate this.

The increase in non-drug and non-industry-sponsored clinical trial activity is encouraging. Non-drug trials accounted for 58 per cent of trials registered in 2015, up from 43 per cent in 2006. It is often not appreciated that clinical trials can provide reliable evidence of the effectiveness of the full gamut of health care – not just drugs – and these trials have the potential to provide great health benefits.

Nevertheless, industry-funded trials (both trials conducted by industry and investigator-initiated trials funded by wholly or partly by industry) still represent a substantial source of support for Australian clinical trial activity. They also account for the largest investment in dollar terms – estimated at $930 million of the total $1.1 billion spent on clinical trials per annum in Australia. Currently government provides more than $164 million through the NHMRC and other sources for clinical trials[1] and a further important increase in government investment in clinical trials is anticipated over the coming years via the Medical Research Future Fund.

The reduction in trial size over the decade – from a median of 167 participants per trial down to 96 – is an important trend. It may reflect appropriate changes in design for more targeted therapies or, conversely, inappropriate reductions in sample size resulting in trials that are underpowered to detect significant, but moderate, treatment benefits. This is an area that warrants further in-depth assessment.

Value of clinical trials

More than $1 billion is invested in Australian clinical trials each year by both government and industry.[2,3] Clinical trials are expensive undertakings that often require millions of dollars to conduct in order to provide reliable evidence for the effectiveness of new or existing therapies.

Yet despite the large price tag, clinical trials represent great value for money. For example, a recent joint report by the Australian Clinical Trials Alliance and the Australian Commission on Safety and Quality in Health Care[4] showed that in investigator-initiated trials conducted within trial networks, for every $1 invested there was a greater than $5 return on investment. Several other studies, in Australia and elsewhere, have demonstrated significant return on investment[5] and improved health outcomes[6-9] in systems with high clinical trial research participation.

Value of clinical trial registries

Whilst the value of clinical trials has been highlighted in several recent reports as noted above, the value of clinical trial registries themselves is not always as well appreciated. Having a publicly accessible national database of all clinical trials conducted in Australia has several major benefits.

It has been argued that more than half of the research undertaken is wasted or under-utilised because many trials ask unnecessary questions or are not well designed, or their results are poorly reported or not published at all.[10] Clinical trial registries can help reduce such waste.

Registries can be used by funders as a requirement of the application process to check that applicants have ensured similar trials are not already underway or have recently been completed but not reported, thereby reducing unnecessary duplication or overlap, while still promoting prospectively planned research collaborations.[11]

Registries can also be used as repositories for documents such as protocols and operations manuals, which are not usually available as part of published research paper. The detailed information these documents provide can be invaluable for those wishing to either replicate a trial's findings or implement new, beneficial interventions directly into practice.

Further, clinical trial registries which offer a platform for posting results can ensure that even trials unwilling or unable to publish their findings in peer-reviewed journals, can make all their results publicly available thereby minimising publication bias[12, 13] and selective reporting of trial outcomes.[14]

Another important way in which clinical trial registries can maximise the benefits of research is by improving timely recruitment. Initiatives such as the Australian Clinical Trials portal (australianclinicaltrials.gov.au), Australian Cancer Trials website (australiancancertrials.gov.au) and ClinTrial Refer mobile phone app – all populated with data from the ANZCTR – provide user-friendly interfaces, 'plain language' summaries and Australian site-specific information for both clinicians and consumers, giving them easy access to currently recruiting trials in which they may be able to participate. Evaluations of these resources confirm that discussion about potential clinical trial participation increases when data from trial registries are easily accessible via such formats.[15]

Analysis of data from clinical trials registries can also add value by highlighting areas where there are research gaps.[16] This report, *The Clinical Trials Landscape in Australia*, is an example of such analysis, and updated editions are planned for every second year. This will make a major ongoing contribution to identifying the trends in Australian clinical trial activity over time, thereby enabling better targeting of research funding in the areas of greatest national need. Registry data can also provide a rich and reliable source of metrics for assessing the ongoing performance and efficiency of trials, including whether recruitment targets are being met and the timeliness of ethics approval processes. This will ensure Australia better prioritises, plans and performs globally relevant clinical trials.

Internationally, three major funders, ZonMw (the Netherlands), NIHR (United Kingdom) and PCORI (United States), have recognised these benefits and recently expressed their strong support for the role clinical trial registries play in ensuring that when research knowledge that leads to health benefits is generated, it is effectively and swiftly disseminated to end-users.[17]

In Australia, the Australian New Zealand Clinical Trials Registry (ANZCTR) and its associated publications are fundamental to this role, enabling Australian researchers to fulfil their ethical obligations[18] and publication requirements[19,20] through registration of their trials on their own national registry.

Future prioritisation

Future investment in clinical trials is likely to continue to produce large health benefits. Prioritisation of trials should be based on factors such as disease burden or gaps in health outcomes between different populations, and include those areas with the potential to have a greater impact and return on investment. For example, clinical trials targeting interventions in the perinatal or early childhood period could be important in terms of lifetime benefits. Ongoing investment in the national clinical trials registry itself needs to be secured to enable the ANZCTR to build on its role as key research infrastructure in line with the Chief Scientist's 2016 National Research Infrastructure Roadmap.[21]

Priority needs to be given to mechanisms for ensuring that all Australian clinical trials are prospectively registered and regularly updated and that their results are fully reported. This should include a requirement for prospective registration by all funders of clinical trials (both industry and non-industry) and all journal editors. All Australian ethics committees should ensure they comply with the Australian Health Ethics Committee requirement that prospective trial registration be a mandatory condition of ethics approval for all clinical trials. Funders and ethics committees could also require evidence of an up-to-date trial registration record as part of annual trial reporting processes.

Better ways of streamlining the flow of information currently collected about Australian clinical trials from various agencies, including ethics committees, government, funders and regulators, should continue to be actively pursued.

In summary

Clinical trials are a vital strategy in ensuring better health for all Australians. By conducting clinical trials in this country we enable Australians to access the best available health care options by capitalising on effective and efficient therapies, reducing research waste and maximising value for money from the health care dollars invested.

Clinical trial activity over the past decade has risen significantly and this growth is providing a greater range of health care benefits for both the prevention and treatment of disease. Some trends, such as trials of smaller size, need to be assessed further to ensure trials aimed at changing practice still provide reliable answers. The ANZCTR will remain a key component of the clinical trials landscape, enabling researchers to fulfil their scientific and ethical obligations, as well as capturing data on trial metrics and activity trends over time.

Given their demonstrable value, clinical trials in Australia appear to have a bright future, particularly if ongoing investment is made. The optimisation of such investment will require multiple strategies, including making full use of the data available through the ANZCTR, now and into the future.

Professor Lisa Askie
ANZCTR Manager

Professor John Simes
ANZCTR Director

Scope, terminology and methods

Clinical trials are research studies that recruit people to test new 'interventions'. These can be drugs, devices, vaccines, surgery, behavioural therapies, preventive care changes or other interventions, given to individuals or applied to systems, that are designed to help improve human health.

The World Health Organization (WHO) defines a clinical trial as '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'.

This report draws on 10,549 Australian clinical trials registered on either the Australian New Zealand Clinical Trials Registry (ANZCTR) or the ClinicalTrials.gov registry between January 2006 and December 2015.

'**Australian**' clinical trials are defined as those with Australia listed as a recruitment country. These trials may be recruiting within Australia at a single site, multiple sites, or be part of a multinational study with multiple recruitment countries in addition to Australia. Studies that did not involve an intervention, but were purely observational in nature, were not included.

The report reflects the majority of registered trial activity in Australia, with only 5 per cent of Australian trials registered on one of the other 14 World Health Organization primary registries (see Appendix 2). The ANZCTR accounts for approximately 60 per cent of registered Australian trials, and ClinicalTrials.gov for the remaining 35 per cent.

110 trials (1 per cent of the total) are known to be registered on both the ANZCTR and ClinicalTrials.gov, and therefore may be counted twice in some figures.

Unless otherwise noted, '**year**' refers to a trial's year of registration, i.e. the year the study was approved for listing on the ANZCTR or ClinicalTrials.gov. This does not necessarily reflect the year the trial started.

Where other terms have particular meanings in the context of this report, they are defined in the relevant section. (See also Appendix 4 for ANZCTR data field definitions.)

In the compilation of this report, all available data fields were extracted from both registries. A list of ANZCTR data fields and their definitions is available in Appendix 4. All data have been provided by the trial registrant, and the registrant is therefore responsible for their accuracy.

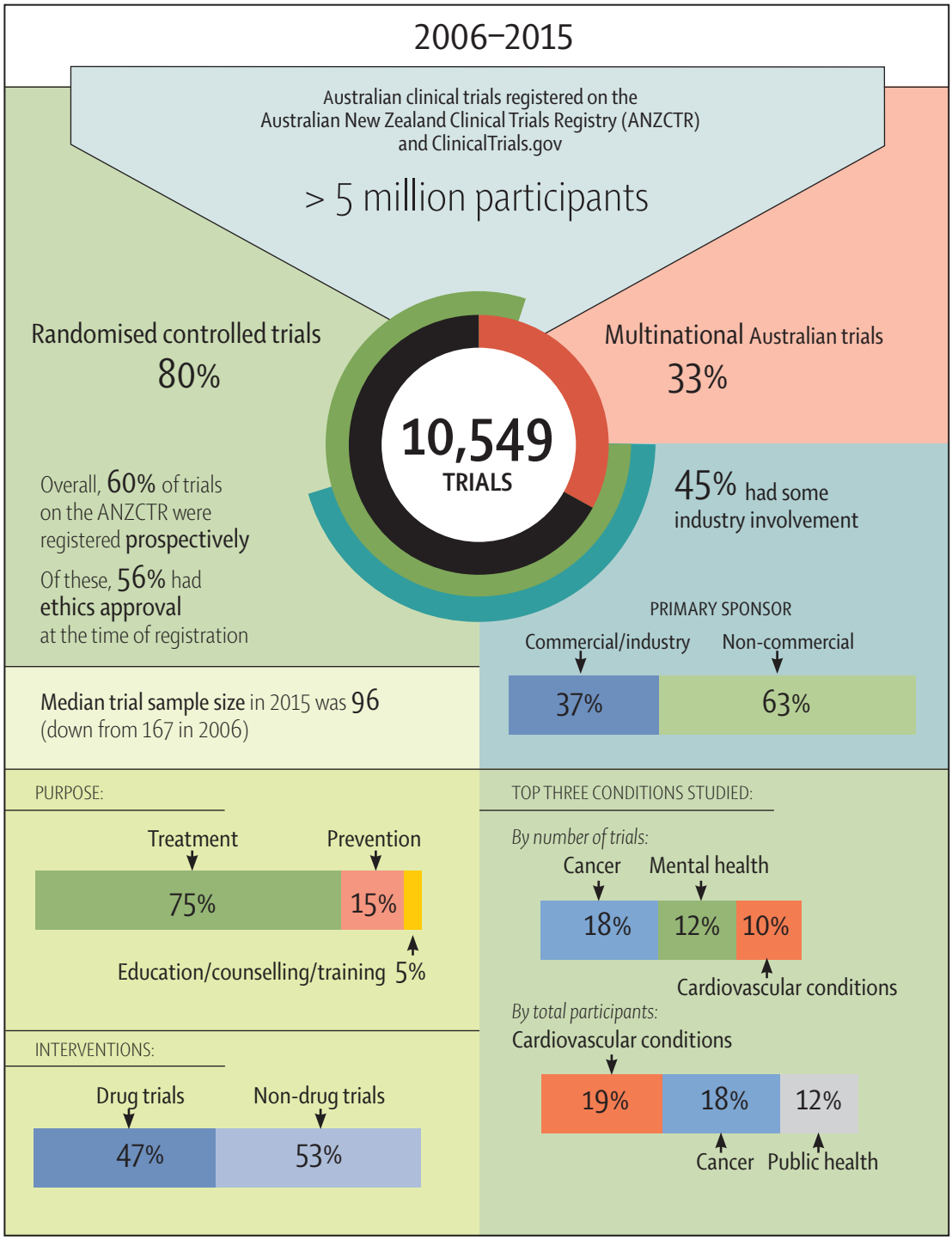
The data fields collected by ClinicalTrials.gov are slightly different from those collected by ANZCTR (see https://prsinfo.clinicaltrials.gov/definitions.html). Where possible, ClinicalTrials.gov fields were mapped to match ANZCTR fields, to enable synthesis of data. Details of data mapping can be found in Appendix 3.

Interventional trials were identified using the 'Study type' field on both registries. Those that selected 'Interventional' for this field were extracted from ANZCTR, and those that selected either 'Interventional' or 'Expanded Access' were extracted from ClinicalTrials.gov.

Analyses were conducted using a combination of Microsoft Excel, Stata IC Software, and the open-source software R.

It is important to note that the data cover registered trials only, and may not necessary reflect overall trends in clinical trial activity. For example, any growth may be an artefact of increased trial registration, rather than increased trial activity.

Fast facts


2006–2015
Australian clinical trials registered on the Australian New Zealand Clinical Trials Registry (ANZCTR) and ClinicalTrials.gov
> 5 million participants
Randomised controlled trials 80%
Multinational Australian trials 33%
10,549 TRIALS
Overall, 60% of trials on the ANZCTR were registered prospectively
Of these, 56% had ethics approval at the time of registration
45% had some industry involvement
PRIMARY SPONSOR
Commercial/industry
Non-commercial
37%
63%
Median trial sample size in 2015 was 96 (down from 167 in 2006)
PURPOSE:
Treatment
Prevention
75%
15%
Education/counselling/training 5%
INTERVENTIONS:
Drug trials
Non-drug trials
47%
53%
TOP THREE CONDITIONS STUDIED:
By number of trials:
Cancer
Mental health
18%
12%
10%
Cardiovascular conditions
By total participants:
Cardiovascular conditions
19%
18%
12%
Cancer
Public health

Part 1: Trial activity

An overview of clinical trial activity in Australia

Analysis of studies from the Australian New Zealand Clinical Trials Registry (ANZCTR) and ClinicalTrials.gov provides insights into the level of activity by registered trials undertaken in Australia over the 10 years to 2015, including the incidence of multinational trials, types of primary sponsor and comparisons to levels of activity in other countries.

This section uses combined ANZCTR and ClinicalTrials.gov data unless otherwise noted.

Data are displayed as per ANZCTR registration form categories and data from ClinicalTrials.gov have been mapped to the closest relevant ANZCTR category. Details of this mapping can be found in Appendix 3.

Only registered Australian clinical trials are included (i.e. interventional studies with at least one recruitment site in Australia).

Unless otherwise noted, 'year' refers to year of trial registration.

1.1 Key findings

- Registered clinical trial activity in Australia has been **increasing**, with the number of new studies registered each year rising from 725 in 2006 to 1,303 in 2015. In total, 10,549 Australian trials have been added to the ANZCTR and ClinicalTrials.gov databases over the decade.
- A total of **5.2 million people** have participated in Australian clinical trials registered over the 10 years 2006–2015.
- Australia ranks towards the **middle of comparable nations** in terms of clinical trial activity on a per capita basis, above Canada and Ireland, for example, and below Sweden and New Zealand.
- **Multinational trials** – those recruiting in other countries in addition to Australia – accounted for 33 per cent of trials registered between 2006 and 2015, a total of 3,483 trials. Multinational activity has remained relatively steady over the decade, with around 350 new trials registered annually as recruiting both in Australia and elsewhere. A quarter of Australian multinational trials report recruitment in more than 15 countries as well as Australia.
- **Industry or commercial bodies** have been responsible for around 300–400 new trials annually – around a third of registrations overall. However, **non-commercial sponsors** have been playing an increasing role. Specifically, strong growth has occurred in non-commercial sponsors other than government, such as hospitals and universities, with annual registrations in this category rising from 336 (46 per cent) in 2006 to 851 (65 per cent) in 2015.
- Just under half (45 per cent) of the Australian clinical trials registered over the decade have some kind of **industry involvement**, either as a funding source, primary sponsor, secondary sponsor or other collaborator.

1.2 Number of trials

The number of Australian clinical trials registered on ANZCTR and ClinicalTrials.gov has increased markedly over the decade, from 1,061 at the beginning of 2006 to a cumulative total of 11,610 at the end of 2015.

Registrations on ClinicalTrials.gov have grown relatively steadily, with around 350–450 new trials added each year. The ANZCTR has seen more rapid growth since 2008, with 443 new trials registered that year rising sharply to 734 in 2009 and 887 in 2015. As a result, by the end of 2015, the ANZCTR accounted for significantly more registered Australian trials (a total of 7,212 or 62 per cent) than ClinicalTrials.gov (4,398 or 38 per cent).

Figure 1. Growth in registered Australian clinical trial activity, 2006–2015

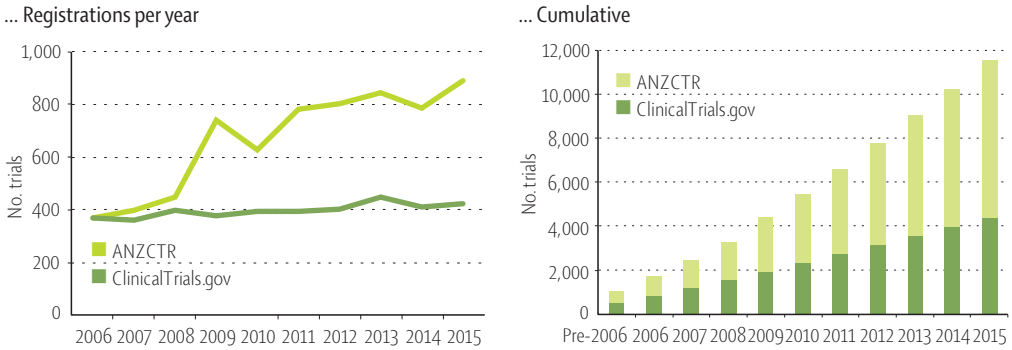


Table 1. Number of Australian clinical trials registered on the ANZCTR and ClinicalTrials.gov, per year and cumulatively, to December 2015

	NUMBER REGISTERED PER YEAR			CUMULATIVE REGISTRATIONS		
	ANZCTR	CLINICALTRIALS.GOV	TOTAL	ANZCTR	CLINICALTRIALS.GOV	TOTAL
Pre-2006	575	486	1,061	575	486	1,061
2006	363	362	725	938	848	1,786
2007	392	355	747	1,330	1,203	2,533
2008	443	393	836	1,773	1,596	3,369
2009	734	371	1,105	2,507	1,967	4,474
2010	623	388	1,011	3,130	2,355	5,485
2011	776	386	1,162	3,906	2,741	6,647
2012	799	396	1,195	4,705	3,137	7,842
2013	838	443	1,281	5,543	3,580	9,123
2014	782	402	1,184	6,325	3,982	10,307
2015	887	416	1,303	7,212	4,398	11,610
TOTALS	TOTAL NEW REGISTRATIONS 2006–2015			PROPORTION OF ALL TRIALS REGISTERED		
	6,637	3,912	10,549	62%	38%	

Most of the Australian trials registered on ClinicalTrials.gov are multinational (see page 13). They are more likely to be industry-sponsored (page 15), focus on drug interventions (page 30), and to have relatively large sample sizes (page 38). Trials registered on the ANZCTR tend to be recruiting only in Australia and are more diverse in terms of the interventions studied, types of sponsor and design characteristics like sample size.

1.3 Number of participants

A total of 5.2 million people have participated in Australian clinical trials over the 10 years 2006–2015.

Each year participant numbers vary according to the number of trials registered and their sample sizes. However, a general upward trend is evident, mainly reflecting the growing number of trials registered on the ANZCTR each year (Figure 1, page 8). Sample sizes per trial have not increased (see section 3.2, page 38).

Figure 2. Trends in the number of participants in Australian clinical trials registered 2006–2015

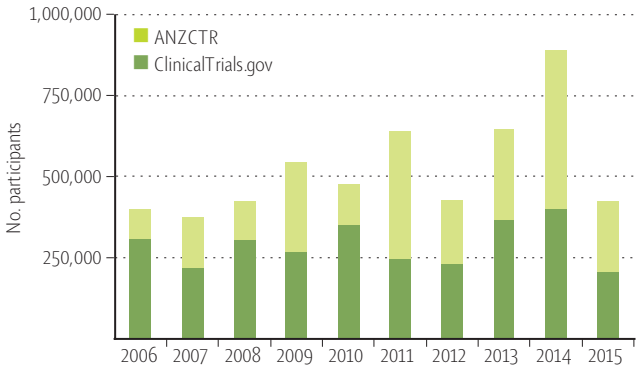


Table 2. Number of participants in Australian clinical trials registered each year on the ANZCTR and ClinicalTrials.gov, 2006–2015

	ANZCTR TRIALS	CLINICALTTRIALS.GOV TRIALS	ALL REGISTERED TRIALS
2006	90,394	307,896	398,290
2007	153,439	219,943	373,382
2008	119,618	303,109	422,727
2009	273,687	269,883	543,570
2010	126,134	349,991	476,125
2011	391,885	247,601	639,486
2012	195,581	231,400	426,981
2013	277,004	368,828	645,832
2014	488,234	400,247	888,481
2015	217,274	205,807	423,081
TOTAL	**2,333,250**	**2,904,705**	**5,237,955**

DATA NOTES

Sample size is a mandatory field on both the ANZCTR and ClinicalTrials.gov registration forms. Data are missing for 29 trials registered on ClinicalTrials.gov.

The ANZCTR collects either target or actual sample size or both, depending on the recruitment status at the time of registration and any subsequent updates. Values obtained are the 'actual' sample size where provided, or the 'target' if no 'actual' value is available, e.g. for trials with ongoing recruitment. ClinicalTrials.gov collects a single value for sample size along with an 'anticipated' or 'actual' label.

1.4 Activity in Australia compared to other countries

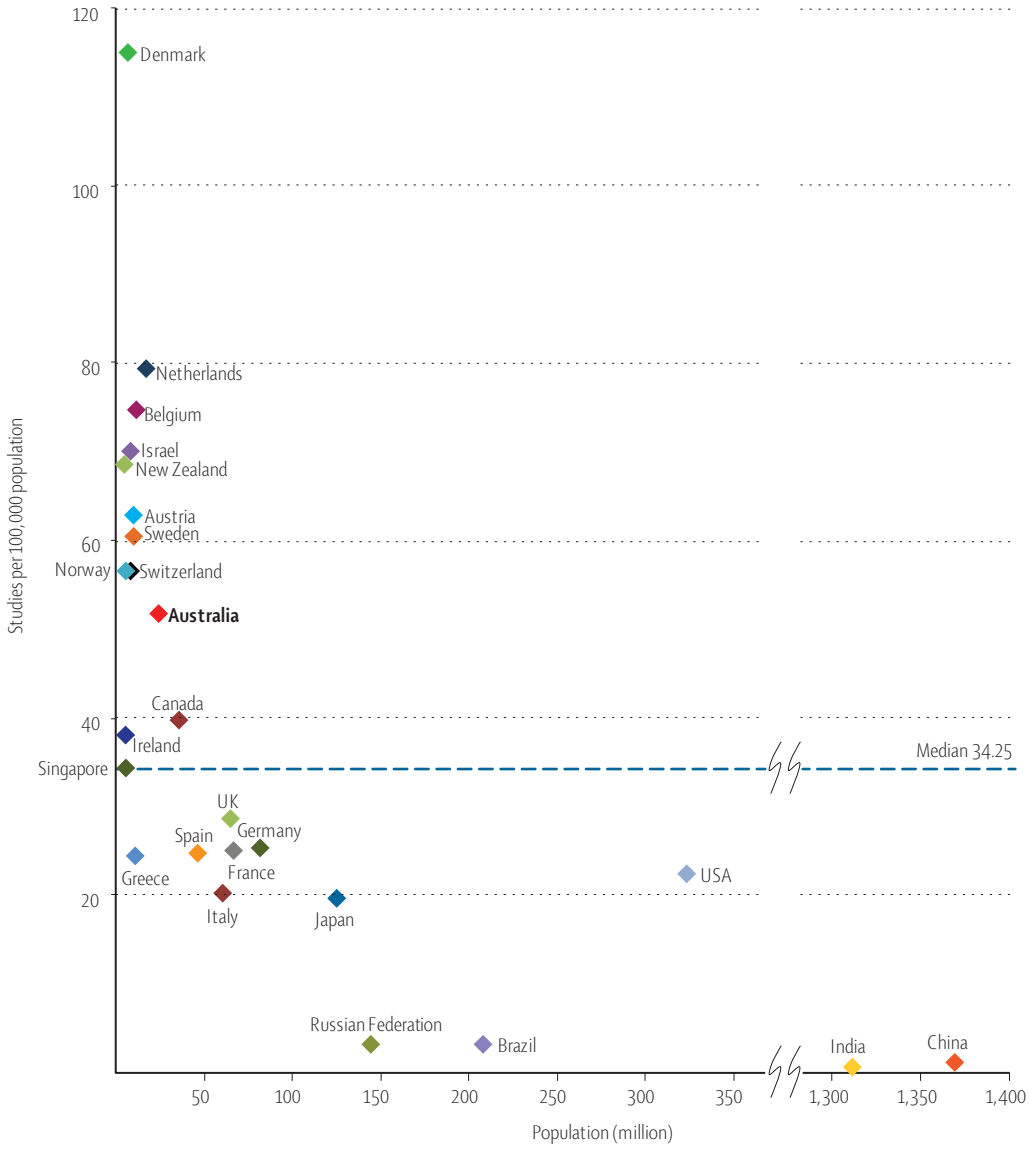
Given the size of its population, Australia has a comparable level of activity to that of countries such as Switzerland, Norway, Austria, Sweden and Canada. On a per capita basis, the number of studies conducted in Australia over the decade to 2015 sits well below Denmark, which ranks at number 1, but above Germany, France, the UK and USA. This analysis includes observational studies as well as interventional clinical trials, with the former comprising an estimated 10 per cent of the total.

Table 3. Population, number of registered studies (interventional and observational) and studies per capita, for Australia and selected countries

COUNTRY	POPULATION 2015	NO. STUDIES 2006–2015	STUDY ACTIVITY PER 100,000 PEOPLE
Denmark	5,683,000	6,517	114.68
Netherlands	16,940,000	13,461	79.46
Belgium	11,249,000	8,478	75.37
Israel	8,380,000	5,882	70.19
New Zealand	4,596,000	3,146	68.45
Austria	8,638,000	5,436	62.93
Sweden	9,799,000	5,935	60.57
Switzerland	8,281,000	4,680	56.51
Norway	5,190,000	2,930	56.45
Australia	**23,790,000**	**12,329**	**51.82**
Canada	35,849,000	14,263	39.79
Ireland	4,644,000	1,765	38.01
Singapore	5,535,000	1,896	34.25
UK	65,129,000	18,733	28.76
Germany	81,680,000	20,763	25.42
France	66,538,000	16,545	24.87
Spain	46,444,000	11,520	24.80
Greece	10,821,000	2,634	24.34
USA	321,419,000	73,548	22.88
Italy	60,731,000	12,256	20.18
Japan	126,958,000	25,253	19.89
Brazil	207,848,000	6,984	3.36
Russian Federation	144,097,000	4,396	3.05
China	1,371,220,000	15,940	1.16
India	1,311,051,000	9,509	0.73

DATA NOTES
Sources: WHO Global Observatory on Health R&D; The World Bank.
For this data set, 'year' is when recruitment started.
Includes both interventional and observational studies uploaded to the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP).

Figure 3. Registered study activity 2006–2015 (interventional and observational), plotted against population for selected countries, 2015



1.5 Multinational clinical trials in Australia

Clinical trials recruiting in multiple countries account for 33 per cent of Australian trials registered between 2006 and 2015, or a total of 3,483 studies. This includes 548 trials recruiting in only one country in addition to Australia (see Table 5).

Multinational activity in Australia has remained relatively steady over the decade, with around 350 new multinational trials registered annually, mostly on ClinicalTrials.gov. The increasing number of Australia-only trials registered each year closely follows the growth in ANZCTR registrations. Overall, 88 per cent of multinational trials recruiting in Australia have been registered on ClinicalTrials.gov.

Figure 4. Proportion of Australian clinical trials registered 2006-2015 with multinational recruitment

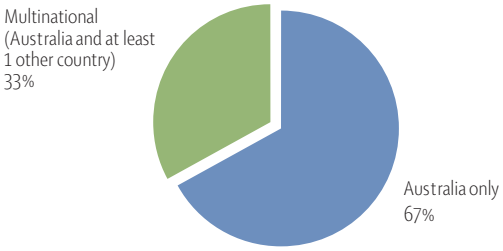


Figure 5. Trends in the number of registered Australian clinical trials with multinational recruitment compared to Australia-only trials, 2006–2015

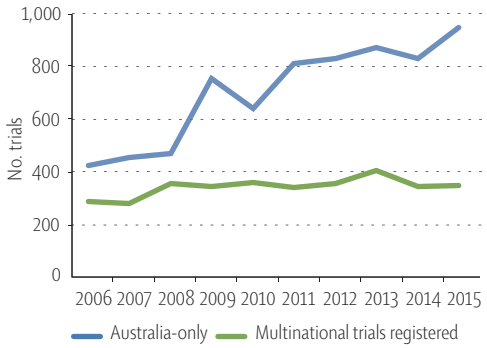


Table 4. Number of clinical trials registered in Australia each year, 2006–2015, by recruitment location – Australia-only and multinational

	AUSTRALIA-ONLY RECRUITMENT		MULTINATIONAL RECRUITMENT INCLUDING AUSTRALIA	
	NO.	PROPORTION	NO.	PROPORTION
2006	430	59%	295	41%
2007	461	62%	286	38%
2008	476	57%	360	43%
2009	756	68%	349	32%
2010	645	64%	366	36%
2011	814	70%	348	30%
2012	832	70%	363	30%
2013	872	68%	409	32%
2014	832	70%	352	30%
2015	948	73%	355	27%
TOTAL	7,066	67%	3,483	33%

DATA NOTES

Listing at least one country of recruitment is mandatory for registration on ANZCTR or ClinicalTrials.gov.

For the purposes of this report, 'multinational' trials refers to trials recruiting in at least two countries including Australia.

1.5.1 Multinational clinical trials by country of recruitment

Most multinational clinical trials (84 per cent) in Australia have recruited in more than one other country, with 61 per cent recruiting in more than five other countries, and 26 per cent in more than 15. The registered trial with the largest number of recruitment countries lists 59 countries, not counting Australia.

Where a trial reports recruiting in only one other country, this is usually New Zealand (244 trials) followed by the USA (161 trials).

Overall, the USA is the most commonly cited country of recruitment for multinational clinical trials in Australia, with 2,413 studies, followed by Canada (1,853) and Germany (1,818).

Figure 6. Number of recruitment countries per trial in addition to Australia, for multinational clinical trials registered 2006–2015

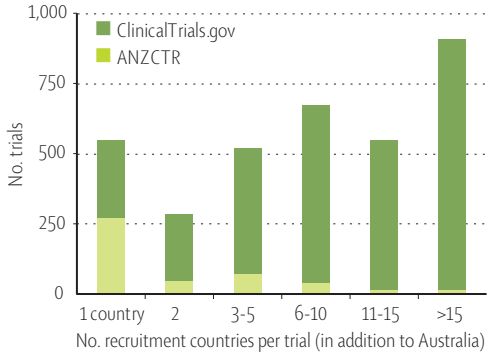


Table 5. Total number of multinational clinical trials in Australia registered 2006–2015, by number of recruitment countries per trial

	RECRUITMENT COUNTRIES PER TRIAL (IN ADDITION TO AUSTRALIA)					
	1 COUNTRY	2 COUNTRIES	3–5	6–10	11–15	>15
ANZCTR	271	47	73	41	19	19
CLINICALTRIALS.GOV	277	236	447	633	530	890
TOTAL	548 (16%)	283 (8%)	520 (15%)	674 (19%)	549 (16%)	909 (26%)

Table 6. For multinational clinical trials recruiting in Australia registered 2006–2015, top 10 other recruitment countries by number of trials

RANK	COUNTRY	ANZCTR	CLINICALTRIALS.GOV	TOTAL
1	USA	110	2,303	2,413
2	Canada	79	1,774	1,853
3	Germany	73	1,745	1,818
4	UK	120	1,547	1,667
5	Spain	51	1,574	1,625
6	France	69	1,555	1,624
7	Italy	53	1,422	1,475
8	Belgium	45	1,217	1,262
9	Poland	36	1,196	1,232
10	New Zealand	259	806	1,065

1.6 Primary sponsor

'Primary sponsor' is defined by the National Health and Medical Research Council (NHMRC) and Therapeutic Goods Administration (TGA) as the 'individual, company, institution or organisation that takes responsibility for the initiation, management and/or financing of a clinical trial'. This includes ensuring that the design and conduct of the study, as well as arrangements for reporting, meet appropriate standards.

Sponsorship by the commercial/industry sector has remained consistent over the decade, accounting for around 300–400 trials registered each year. However, non-commercial sponsors have been playing an increasing role, accounting for 63 per cent of trial registrations overall between 2006 and 2015. Specifically, strong growth has occurred in non-commercial sponsors other than government, with annual registrations in this category rising from 336 (46 per cent) in 2006 to 851 (65 per cent) in 2015. (See section 1.6.1 for more details.)

Figure 7. Trends in commercial and non-commercial primary sponsor type for registered Australian clinical trials, 2006–2015

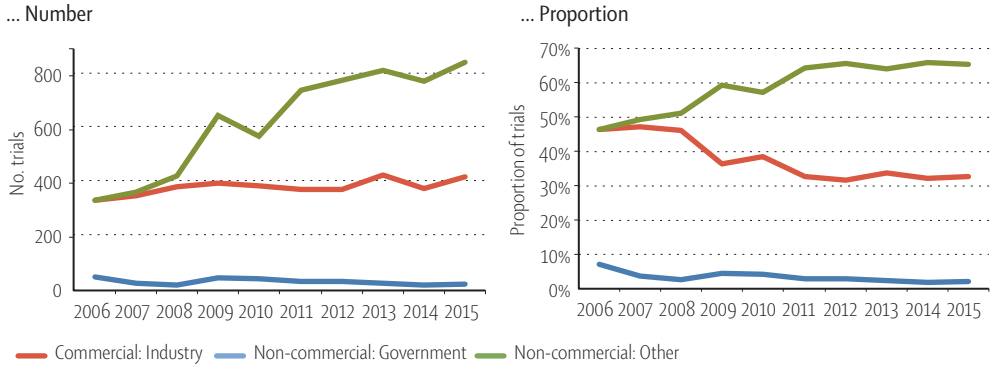


Table 7. Number and proportion of Australian clinical trials registered each year, 2006–2015, by commercial and non-commercial primary sponsor

	COMMERCIAL: INDUSTRY		NON-COMMERCIAL: GOVERNMENT		NON-COMMERCIAL: OTHER	
	NO.	PROPORTION	NO.	PROPORTION	NO.	PROPORTION
2006	336	46%	52	7%	336	46%
2007	353	47%	27	4%	367	49%
2008	386	46%	23	3%	427	51%
2009	402	36%	49	4%	654	59%
2010	390	39%	44	4%	577	57%
2011	379	33%	35	3%	747	64%
2012	377	32%	34	3%	784	66%
2013	431	34%	29	2%	821	64%
2014	382	32%	21	2%	781	66%
2015	426	33%	26	2%	851	65%
TOTAL	3,862	37%	340	3%	6,345	60%

DATA NOTES

Type of primary sponsor is mandatory for registration on ANZCTR.

ClinicalTrials.gov uses fewer categories for sponsor type than ANZCTR, and these have been mapped to ANZCTR options where possible (see Appendix 3 for more details).

'Non-commercial: Other' includes universities, charities and foundations, hospitals, collaborative groups and individuals. N=10,547.

There were 2 trials with no data on primary sponsor: 1 on ANZCTR and 1 on ClinicalTrials.gov

1.6.1 Non-commercial primary sponsors

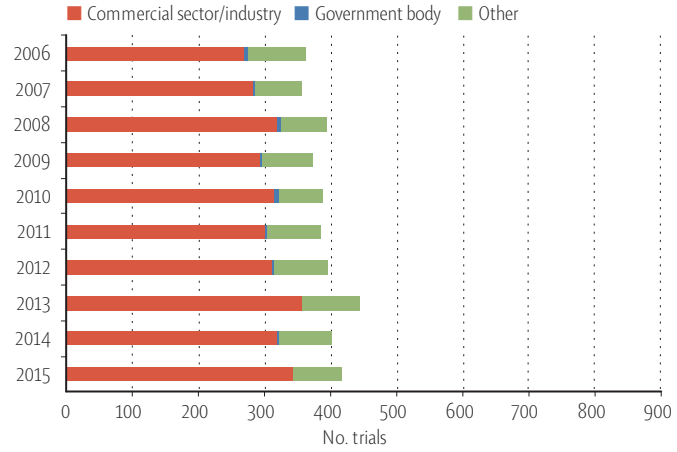
Non-commercial sponsors are more typical for the diverse trials registered on the ANZCTR than for ClinicalTrials.gov, where no breakdown is available beyond 'government body' and 'other'.

Hospitals and universities are making an increasing contribution. After the commercial sector/industry, with a total of 3,862 trials sponsored across both registries, universities represent the second most common sponsoring organisation, with 2,004 trials registered on the ANZCTR alone, followed by hospitals with 1,288.

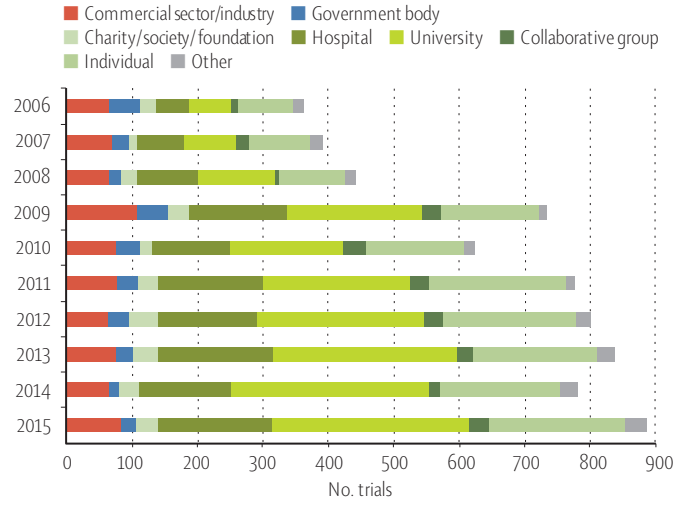
Individuals also play a significant part – an academic lead, for example, perhaps acting as sponsor for a trial with multiple stakeholders and/or funding sources. Individuals are listed as the primary sponsor for 1,571 trials registered on the ANZCTR over the decade.

Figure 8. Trends in primary sponsor type for Australian clinical trials, 2006–2015, registered on

... ClinicalTrials.gov



... ANZCTR



1.6.1 continued ...

Table 8. Number of Australian clinical trials registered each year, 2006–2015, by primary sponsor type, on ClinicalTrials.gov and on the ANZCTR

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	TOTAL
CLINICALTRIALS.GOV											
Industry	270	282	320	293	315	300	311	356	318	342	3,107
US government body	4	2	4	3	6	4	3	1	4	2	33
Other	88	71	69	75	67	81	82	86	80	72	771
ANZCTR											
Commercial sector/industry	66	71	66	109	75	79	66	75	64	84	775
Government body	48	25	19	46	38	31	31	28	17	24	307
University	65	82	116	206	173	224	254	280	301	303	2,004
Hospital	51	70	94	150	118	161	153	176	143	172	1,288
Charity/society/foundation	22	13	23	33	19	30	43	38	29	33	283
Collaborative group	11	18	7	29	35	30	28	25	17	29	229
Individual	82	93	102	150	149	208	204	190	184	209	1,571
Other	17	20	16	11	16	13	20	26	27	33	199

1.7 Industry involvement

Just under half (45 per cent) of the Australian clinical trials registered 2006–2015 have some kind of industry involvement, either as a funding source, primary sponsor, secondary sponsor or other collaborator.

Trials registered on ClinicalTrials.gov are much more likely to have industry involvement (83 per cent) than those registered on the ANZCTR (23 per cent).

Figure 9. Proportion of Australian clinical trials registered 2006–2015 with any industry involvement

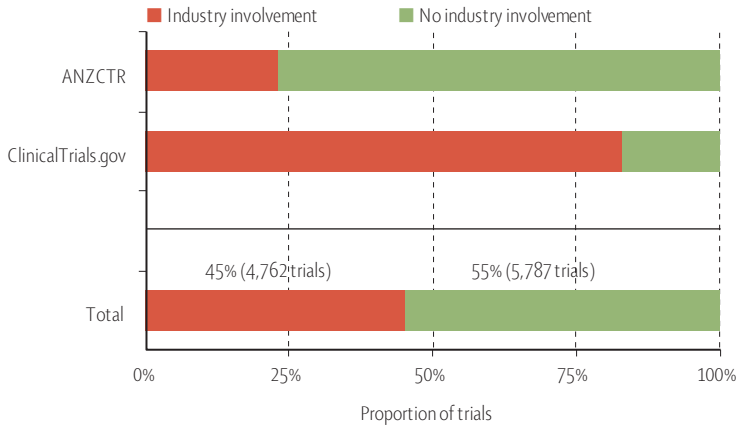


Table 9. Number and proportion of Australian clinical trials registered 2006–2015, with and without industry involvement

	INDUSTRY INVOLVEMENT		NO INDUSTRY INVOLVEMENT	
	NO.	PROPORTION	NO.	PROPORTION
ANZCTR	1,526	23%	5,111	77%
CLINICALTRIALS.GOV	3,236	83%	676	17%
TOTAL	**4,762**	**45%**	**5,787**	**55%**

DATA NOTES

Trials can choose more than one funding source, secondary sponsor or collaborator.

'Any industry involvement' derived as follows:

- ANZCTR: selection of 'Commercial sector/Industry' for funding source or primary sponsor or secondary sponsor or other collaborator
- ClinicalTrials.gov: selection of 'Commercial sector/Industry' for any sponsor/collaborators.

Part 2: Trial focus

Health conditions and interventions studied in Australian clinical trials

This section uses combined ANZCTR and ClinicalTrials.gov data unless otherwise noted.

Data are displayed as per ANZCTR registration form categories and data from ClinicalTrials.gov have been mapped to the closest relevant ANZCTR category. Details of this mapping can be found in Appendix 3.

Only registered Australian clinical trials are included (i.e. interventional studies with at least one recruitment site in Australia).

Unless otherwise noted, 'year' refers to year of trial registration.

2.1 Key findings

- **Cancer** has been the most frequently studied health issue in Australian clinical trials registered between 2006 and 2015, with 1,870 trials (18 per cent of the total) selecting this category, followed by **mental health** with 1,229 (12 per cent) and **cardiovascular conditions** with 1,034 (10 per cent).
- Trial activity in **mental health has grown steadily** since 2006, and trials registered each year in this area have outnumbered trials for all other health conditions, except cancer, since 2010.
- In terms of numbers of **trial participants**, the most studied condition is **cardiovascular disease**, involving a total of 0.96 million people over the decade. **Cancer** trials are next, with 0.92 million participants.
- Measured against the **relative 'burden of disease'** represented by the top National Health Priority Area conditions, cardiovascular disease has seen fewer trials than would be expected but significantly more participants. For mental health, the number of trials is close to what would be expected, but the total number of trial participants is lower.
- The majority (75 per cent) of clinical trials conducted in Australia aim to assess the effects of **treatments**, with investigation of **preventive strategies** the next most common purpose (15 per cent). Trials focusing on '**education/ counselling/ training**' have increased their share over the decade, from 27 studies (4 per cent) in 2006 to 87 (7 per cent) in 2015.
- **Drugs** are the single most researched intervention in Australian clinical trials, accounting for 47 per cent of trials registered between 2006 and 2015. However, the share of trial activity they represent has fallen over the decade, from 57 per cent in 2006 to 42 per cent in 2015.
- Most drug trials (56 per cent) have focused on a combination of the **safety and efficacy** of the intervention, with an additional 27 per cent looking at efficacy alone and 10 per cent assessing safety alone.
- Among the **non-drug trials**, those focusing on treatments other than devices or surgery have shown particular growth, from just 72 in 2006 (10 per cent of all trials) to 298 in 2015 (23 per cent). This category includes interventions such as exercise, physiotherapy, cognitive therapy, special diets, herbal medicines, web-based treatments, motivational classes, music therapy and stem cell interventions.
- **Efficacy** has been the most common focus specified for non-drug trials, accounting for 66 per cent, with an additional 28 per cent assessing a combination of efficacy and safety.

2.2 Conditions studied

2.2.1 Most studied conditions by number of trials

Cancer has been the most commonly studied health issue in Australian clinical trials registered between 2006 and 2015, with 1,870 trials in total selecting this category, followed by mental health with 1,229 and cardiovascular conditions with 1,034 (Figure 10).

As a proportion of Australian clinical trials registered each year, those investigating cancer and cardiovascular disease have remained relatively consistent since 2008, cancer at around 16–18 per cent each year and cardiovascular disease at around 8–12 per cent (Figure 11).

However, trial activity in mental health has seen a significant increase over the decade, from 45 trials in 2006 (approximately 6 per cent of trials registered that year) to 185 trials (14 per cent) in 2015. Mental health trials have outnumbered trials for all other health conditions, except cancer, each year since 2010.

Trial activity investigating general public health issues has also grown significantly, with only 8 trials registered in 2006 (1 per cent of registrations that year), increasing to 112 in 2014 (9 per cent) and 99 (8 per cent) in 2015.

Figure 10. Top 15 conditions by number of trials, for Australian clinical trials registered 2006–2015

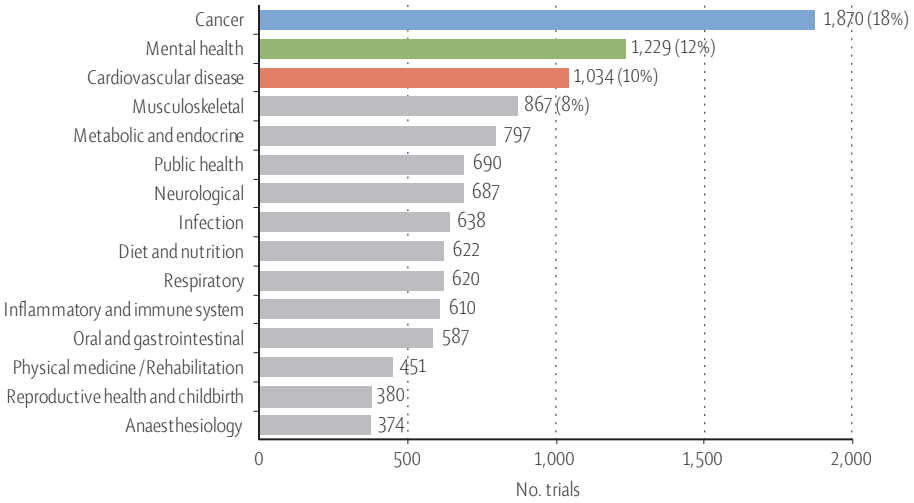
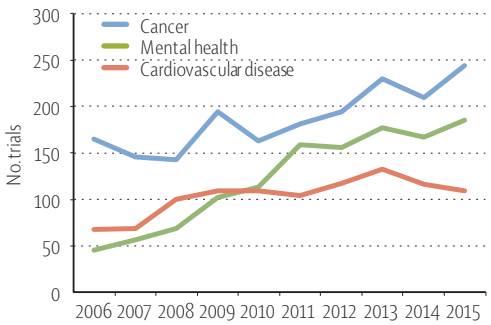


Figure 11. Trends in the top three types of condition studied by Australian clinical trials registered 2006–2015

... Number



... Proportion

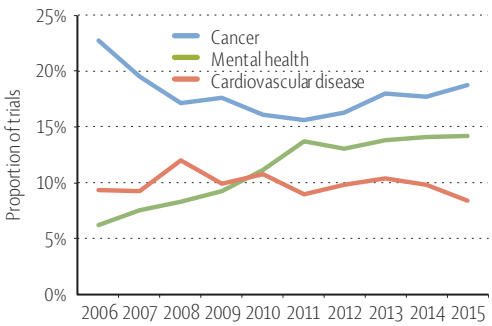


Table 10. Number of Australian clinical trials registered each year, 2006–2015, by condition

CONDITION	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	TOTAL
Cancer	165	146	143	194	163	181	194	230	210	244	1,870
Mental health	45	56	69	102	113	159	156	177	167	185	1,229
Cardiovascular disease	68	69	100	109	109	104	117	133	116	109	1,034
Musculoskeletal	58	65	56	96	87	76	94	103	99	133	867
Metabolic and endocrine	53	50	58	71	81	80	103	99	105	97	797
Public health	8	18	26	56	60	92	112	107	112	99	690
Neurological	44	46	60	51	54	64	90	95	79	104	687
Infection	32	45	56	58	59	72	71	87	63	95	638
Diet and nutrition	25	29	29	58	64	80	84	86	81	86	622
Respiratory	47	51	50	67	55	76	76	73	69	56	620
Inflammatory and immune system	50	32	43	55	70	70	71	77	67	75	610
Oral and gastrointestinal	38	42	31	44	69	82	89	57	51	84	587
Physical medicine / Rehabilitation	10	12	20	37	24	46	50	71	85	94	451
Reproductive health and childbirth	23	22	18	34	33	44	52	52	53	49	380
Anaesthesiology	8	7	25	41	40	41	46	47	56	63	374
Injuries and accidents	27	25	23	30	38	35	35	41	45	61	360
Surgery	7	7	17	34	21	30	38	45	38	66	303
Renal and urogenital	17	18	26	28	31	45	27	30	36	19	277
Skin	12	21	11	24	37	29	34	36	31	35	270
Blood	27	25	20	23	19	26	34	34	35	23	266
Alternative and complementary medicine	1	5	17	29	32	30	38	25	15	25	217
Eye	10	10	18	22	20	29	33	21	21	22	206
Human genetics and inherited disorders	9	11	13	19	22	27	29	23	21	25	199
Stroke	9	7	9	14	11	17	13	29	20	23	152
Ear	1	1	3	3	4	3	4	7	5	6	37
Other	25	17	23	32	24	24	24	20	25	21	235

DATA NOTES

Condition category is a mandatory field on both the ANZCTR and ClinicalTrials.gov registration forms.

At time of analysis, the ANZCTR form allowed for entry of up to three condition codes from a pre-specified list (see Appendix 4).

ClinicalTrials.gov registration form allows for entry of multiple condition descriptors, which are based on MeSH codes. Only the first health condition (primary condition) in a trial's record has been mapped to the relevant ANZCTR conditions codes. Therefore, the true number of conditions studied by trials registered on ClinicalTrials.gov is likely to be understated.

As multiple condition codes can be selected for each trial, the total count of trials selecting each condition is more than the total number of trials registered.

Proportions are of number of registered trials each year and in total (N=10,549).

2.2.2 Most studied conditions by number of trial participants

Trials focusing on cardiovascular conditions have involved the most participants, with a total of 962,981 people participating over the decade, followed by cancer (916,685). Trials with a public health focus come next, with 611,766 participants, while mental health trials move down to fifth place, as they tend to have smaller sample sizes per trial.

On an annual basis, the total number of participants has tended to fluctuate, although an upward trend is evident for public health trials (Figure 13).

Figure 12. Top 15 conditions by total number of trial participants, for Australian clinical trials registered 2006–2015

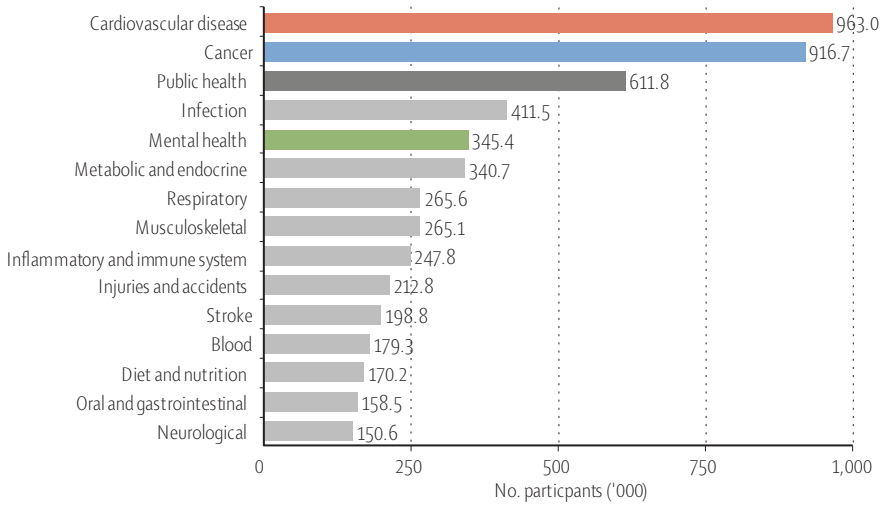
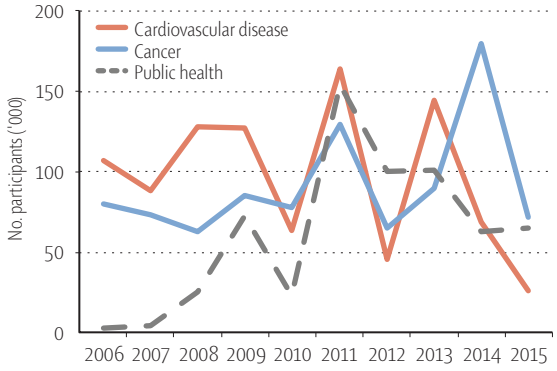


Figure 13. Trends in the top three conditions by total number of trial participants, for registered Australian clinical trials 2006–2015



DATA NOTES

Sample size is a mandatory field on both the ANZCTR and ClinicalTrials.gov registration forms. Data are missing for 29 trials registered on ClinicalTrials.gov.

The ANZCTR collects either target or actual sample size or both, depending on the recruitment status at the time of registration and any subsequent updates. Values obtained are the 'actual' sample size where provided, or the 'target' if no 'actual' value is available, e.g. for trials with ongoing recruitment. ClinicalTrials.gov collects a single value for sample size along with an 'anticipated' or 'actual' label.

Table 11. Total trial participants ('000s) for Australian clinical trials registered each year, 2006–2015, by condition

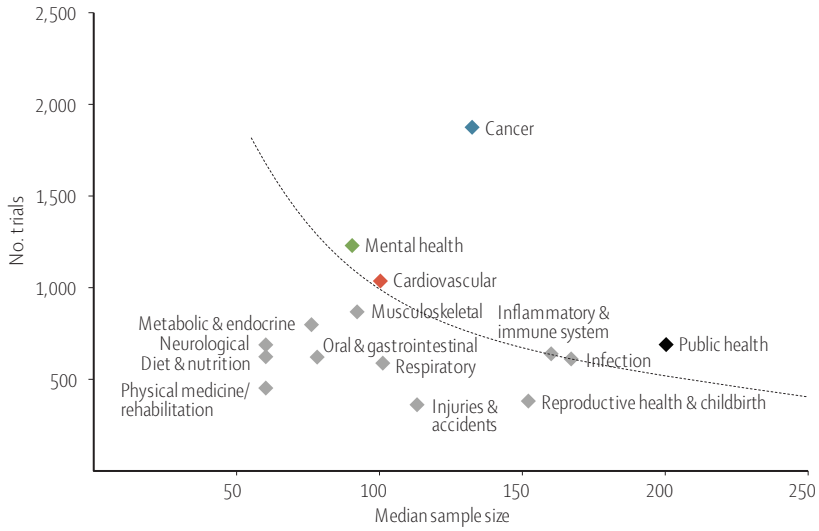
CONDITION	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	TOTAL
Cardiovascular disease	106.7	88.0	127.7	127.4	63.3	164.3	45.8	144.7	68.9	26.1	**963.0**
Cancer	79.9	73.6	63.1	85.7	77.6	129.6	65.2	90.0	180.1	72.0	**916.7**
Public health	3.0	4.4	25.3	72.4	23.1	154.0	100.1	101.3	62.8	65.3	**611.8**
Infection	23.9	24.4	31.8	48.0	51.3	37.3	19.5	59.8	32.1	83.2	**411.5**
Mental health	10.0	13.8	23.2	13.9	22.6	71.3	30.2	88.5	35.9	36.0	**345.4**
Metabolic and endocrine	18.0	11.6	13.0	25.7	76.9	33.7	49.9	57.6	30.0	24.2	**340.7**
Respiratory	15.7	11.3	14.6	23.8	29.7	51.2	15.8	20.9	43.8	38.8	**265.6**
Musculoskeletal	50.1	23.3	24.3	22.7	23.9	10.5	40.8	24.6	20.4	24.6	**265.1**
Inflammatory and immune system	46.4	16.1	16.7	14.0	29.2	23.5	21.4	21.6	30.4	28.5	**247.8**
Injuries and accidents	6.4	4.6	8.1	24.8	9.2	45.6	40.0	11.5	17.0	45.7	**212.8**
Stroke	17.8	17.8	5.1	2.7	23.3	49.9	2.3	19.4	52.2	8.3	**198.8**
Blood	24.2	34.9	28.9	18.4	1.8	2.2	16.5	35.9	12.5	4.0	**179.3**
Diet and nutrition	2.8	48.4	5.1	13.1	10.1	15.2	9.7	38.6	13.5	13.7	**170.2**
Oral and gastrointestinal	16.6	15.0	15.7	8.9	15.0	23.6	11.9	12.5	13.9	25.4	**158.5**
Neurological	12.3	12.8	17.6	13.9	8.7	9.0	15.1	19.0	13.4	28.8	**150.6**
Reproductive health and childbirth*	3.7	11.3	7.0	10.4	17.4	22.2	14.7	19.6	17.0	20.0	**143.2**
Renal and urogenital	4.4	4.3	8.5	5.1	6.4	46.4	2.8	22.4	12.8	2.0	**115.2**
Skin	1.5	2.3	14.2	8.9	11.0	8.2	18.8	7.2	8.3	10.4	**90.9**
Physical medicine / Rehabilitation	2.5	2.7	3.6	5.2	3.1	4.5	4.6	7.1	15.5	13.8	**62.6**
Anaesthesiology	1.8	1.2	2.1	4.2	3.9	3.7	9.9	6.8	17.4	7.5	**58.6**
Surgery	1.2	1.1	1.8	4.9	1.8	7.9	5.4	6.1	7.7	12.4	**50.3**
Alternative and complementary medicine	0.2	0.5	2.0	4.1	3.1	4.0	3.5	23.3	1.8	3.3	**45.8**
Eye	1.9	1.1	4.9	1.9	1.7	2.8	3.0	9.4	4.3	4.2	**35.1**
Human genetics and inherited disorders	0.4	1.8	2.1	1.4	3.6	3.5	6.6	4.8	1.8	2.6	**28.7**
Ear	0.2	0.1	0.9	0.4	0.9	0.3	0.2	1.0	2.6	0.7	**7.5**
Other	22.7	2.3	28.4	80.0	13.9	66.5	22.4	4.4	8.9	11.8	**261.1**

* An outlier has been removed from the analysis for the 'reproductive health and childbirth' condition category. This was a cluster randomised controlled trial with 300,000 participants.

2.2.3 Trial activity – number and scale of trials – by condition

Multiplying the number of trials by the median sample size for a particular condition can provide another useful indicator of trial activity – a combination of how common and how large the trials for that condition have tended to be. By this measure, cancer has been the number one focus for registered Australian clinical trials over the decade. However, the next most prevalent condition category is public health, due to the larger sample sizes that characterise trials in this category (see section 3.2.2, page 41).

Figure 14. Top 15 conditions by number of trials and median sample size for Australian clinical trials registered 2006–2015



The dotted line in the figure represents a trial activity indicator value of 100,000, where trial activity = number of trials selecting a condition category x median sample size for that category.

DATA NOTES

Condition category is a mandatory field on both the ANZCTR and ClinicalTrials.gov registration forms.
At time of analysis, the ANZCTR form allowed for entry of up to three condition codes from a pre-specified list (see Appendix 4).
ClinicalTrials.gov registration form allows for entry of multiple condition descriptors, which are based on MeSH codes.
Only the first health condition (primary condition) in a trial's record has been mapped to the relevant ANZCTR conditions codes.
Therefore, the true number of conditions studied by trials registered on ClinicalTrials.gov is likely to be understated.
As multiple condition codes can be selected for each trial, the total count of trials selecting each condition is more than the total number of trials registered.
Sample size is a mandatory field on both the ANZCTR and ClinicalTrials.gov registration forms. Data are missing for 29 trials registered on ClinicalTrials.gov.
The ANZCTR collects either target or actual sample size or both, depending on the recruitment status at the time of registration and any subsequent updates. Values obtained are the 'actual' sample size where provided, or the 'target' if no 'actual' value is available, e.g. for trials with ongoing recruitment. ClinicalTrials.gov collects a single value for sample size along with an 'anticipated' or 'actual' label.

Table 12. Summary of key statistics for conditions studied by Australian clinical trials registered 2006–2015, ranked by trial activity indicator

CONDITION	NO. TRIALS	SAMPLE SIZE		TOTAL NO. PARTICIPANTS	TRIAL ACTIVITY INDICATOR*
		Median	IQR		
Cancer	1,870	132	45–435	916,685	246,840
Public health	690	200	90–510	611,766	138,000
Mental health	1,229	90	42–200	345,373	110,610
Cardiovascular	1,034	100	40–420	962,981	103,400
Infection	638	160	44–495	411,450	102,080
Inflammatory and immune system	610	167	48–472	247,767	101,870
Musculoskeletal	867	92	42–220	265,059	79,764
Metabolic and endocrine	797	76	30–250	340,688	60,572
Oral and gastrointestinal	587	101	40–337	158,494	59,287
Reproductive health and childbirth**	379	152	61–381	143,227	57,760
Respiratory	620	78	30–280	265,558	48,360
Neurological	687	60	30–200	150,634	41,220
Injuries and accidents	360	113	48–300	212,833	40,680
Diet and nutrition	622	60	32–148	170,241	37,320
Physical medicine/rehabilitation	451	60	30–124	62,585	27,060
Blood	266	100	38–300	179,296	26,600
Surgery	303	86	40–162	50,264	26,058
Anaesthesiology	374	60	40–120	58,636	22,440
Renal and urogenital	277	80	41–220	115,196	22,160
Skin	270	80	32–302	90,857	21,600
Alternative and complementary medicine	217	62	36–140	45,817	13,454
Eye	206	60	35–151	35,125	12,360
Stroke	152	70	35–300	198,753	10,640
Human genetics and inherited disorders	199	48	21–132	28,676	9,552
Ear	37	100	30–250	7,458	3,700
Other	235	70	30–223	261,129	16,450

* Trial activity indicator = number of trials selecting a condition category x median sample size for that category.
** An outlier has been removed from the analysis for the 'reproductive health and childbirth' condition category. This was a cluster randomised controlled trial with a target of 300,000 participants.

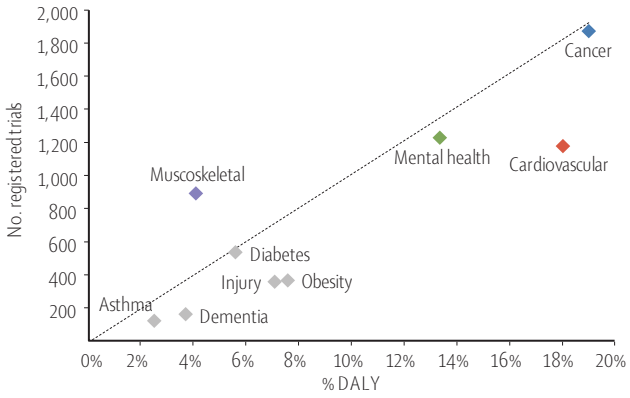
2.2.4 Number of trials per condition compared to burden of disease

In an update to the approach taken by Lam 2015,[16] Australian estimates of disability-adjusted life-years (DALYs) have been used to quantify the burden of disease for condition categories identified as National Health Priority Areas.[22] These %DALYs have then been compared to the levels of Australian clinical trial activity in these areas.

In the case of cancer, mental health and diabetes, the number of registered trials is close to what would be expected given the relative disease burden each represents. For cardiovascular conditions, as well as obesity, injury, dementia and asthma, the actual number of trials registered is lower than would be expected, while higher than expected levels of trial activity are shown for musculoskeletal conditions.

The pattern is different for some conditions when considering the scale of trial activity in terms of the total number of participants recruited (see section 2.2.5).

Figure 15. Relationship between number of trials and %DALY (as an indicator of relative burden of disease) for National Health Priority Area conditions studied by Australian clinical trials registered 2006–2015



Diagonal line represents the line of equality, where %DALY is equal to trial number as a percentage of total registered trials. Markers below the line show conditions where the variable falls below the %DALY.

Table 13. Number of registered Australian clinical trials focusing on National Health Priority Area (NHPA) conditions as a percentage of total trial activity, and comparison to the expected number based on %DALY, for trials registered 2006–2015

	BURDEN OF DISEASE		NUMBER OF TRIALS				
			Observed				
NHPA CONDITION	Rank	%DALY	Rank	no.	%	Expected no. (based on %DALY)	Observed/ expected %
Cancer	1	19%	1	1,870	18.5%	1,923	97%
Cardiovascular (incl. stroke)	2	18%	3	1,176	11.6%	1,828	65%
Mental health	3	13%	2	1,229	12.1%	1,346	91%
Obesity	4	8%	6	368	3.6%	759	48%
Injury	5	7%	7	360	3.6%	708	51%
Diabetes mellitus	6	6%	5	538	5.3%	557	97%
Arthritis & musculoskeletal conditions	7	4%	4	892	8.8%	405	220%
Dementia	8	4%	8	164	1.6%	364	45%
Asthma	9	2%	9	124	1.2%	243	51%

DATA NOTES

%DALY is derived from Begg, 2007[23]

Trial data for this section have been extracted from the ANZCTR and ClinicalTrials.gov according to the National Health Priority Areas and may not match data for the condition categories elsewhere in the report.

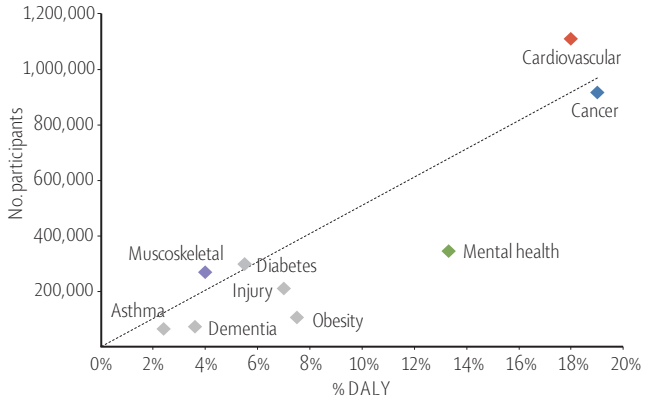
2.2.5 Number of trial participants per condition compared to burden of disease

The burden of disease associated with National Health Priority Area conditions can also be compared with the scale of trial activity in terms of numbers of participants.

Participant numbers for cancer and diabetes trials are close to what would be expected given their relative burden of disease, while cardiovascular trials show a slightly higher than expected number of participants, possibly reflecting the larger sample sizes characterising these trials early in the decade (see section 3.2.2, page 41).

However, trials focusing on mental health show significantly fewer participants than would be expected, as do obesity, injury, dementia and asthma trials.

Figure 16. Relationship between total number of trial participants and %DALY (as an indicator of relative burden of disease) for National Health Priority Area conditions studied by Australian clinical trials registered 2006–2015



Diagonal line represents the line of equality, where %DALY is equal to trial participants for a condition as a percentage of total participants in all registered trials. Markers below the line show conditions where the variable falls below the %DALY.

Table 14. Number of participants in registered Australian clinical trials focusing on National Health Priority Area (NHPA) conditions as a percentage of total number of participants, and comparison to the expected number based on %DALY, for trials registered 2006–2015

	BURDEN OF DISEASE		NUMBER OF TRIAL PARTICIPANTS				
				Observed			
NHPA CONDITION	Rank	%DALY	Rank	no.	%	Expected no. (based on %DALY)	Observed/ expected %
Cancer	1	19%	2	916,685	18.0%	968,883	95%
Cardiovascular (incl. stroke)	2	18%	1	1,109,610	21.8%	917,889	121%
Mental health	3	13%	3	345,373	6.8%	678,218	51%
Obesity	4	8%	7	108,596	2.1%	382,454	28%
Injury	5	7%	6	212,833	4.2%	356,957	60%
Diabetes mellitus	6	6%	4	300,672	5.9%	280,466	107%
Arthritis & musculoskeletal conditions	7	4%	5	269,493	5.3%	203,975	132%
Dementia	8	4%	8	75,313	1.5%	183,578	41%
Asthma	9	2%	9	67,351	1.3%	122,385	55%

DATA NOTES
%DALY is derived from Begg, 2007[23]
Trial data for this section have been extracted from the ANZCTR and ClinicalTrials.gov according to the National Health Priority Areas and may not match data for the condition categories elsewhere in the report.
(See also data notes on sample size, page 22.)

2.3 Purpose of study – treatment, prevention, diagnosis, education

'Purpose of study' has been analysed according to the four categories available on the ANZCTR registration form.

Overall, of the 10,430 Australian clinical trials registered 2006–2015 that specify a purpose, three-quarters cite 'treatment', 15 per cent 'prevention', 5 per cent 'education/counselling/training' and 3 per cent 'diagnosis' (Figure 17).

Trials aiming to investigate treatment interventions have fallen slightly as a proportion of registrations each year, accounting for 79 per cent of trials in 2006 and 73 per cent in 2015 (Figure 18). 'Prevention' and 'diagnosis' trials have remained relatively stable, but activity with a purpose of 'education/ counselling/ training' has grown over the decade, from 27 studies (4 per cent) in 2006 to 87 (7 per cent) in 2015.

Table 15. Number of Australian clinical trials registered each year, 2006–2015, by purpose of study

	TREATMENT	PREVENTION	EDUCATION/ COUNSELLING/ TRAINING	DIAGNOSIS	OTHER	TOTAL WITH PURPOSE LISTED
2006	570	111	27	15	0	723
2007	570	104	30	31	7	742
2008	636	120	39	23	10	828
2009	831	166	55	27	16	1095
2010	772	154	32	27	6	991
2011	858	162	68	43	21	1152
2012	872	195	68	31	9	1175
2013	963	182	79	32	12	1268
2014	850	186	73	41	18	1168
2015	944	199	87	45	13	1288
TOTAL	7,866 (75%)	1,579 (15%)	558 (5%)	315 (3%)	112 (1%)	10,430

Figure 17. Purpose of study for Australian clinical trials registered 2006–2015

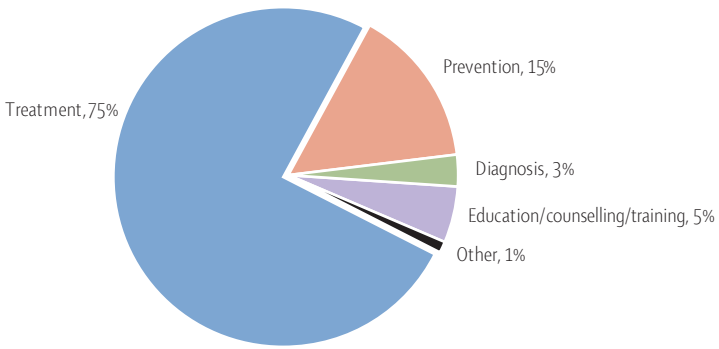
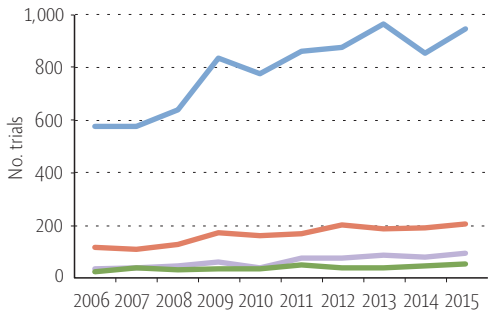
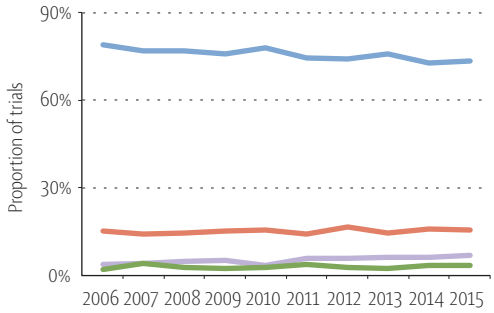


Figure 18. Trends in purpose of study for registered Australian clinical trials, 2006–2015

... Number



... Proportion



Treatment
Prevention
Education/counselling/training
Diagnosis

DATA NOTES

This is a mandatory field with only one selection allowed on both the ANZCTR and ClinicalTrials.gov registration forms.

Options available differ slightly between the ANZCTR and ClinicalTrials.gov forms. (See Appendix 3 for mapping details.)

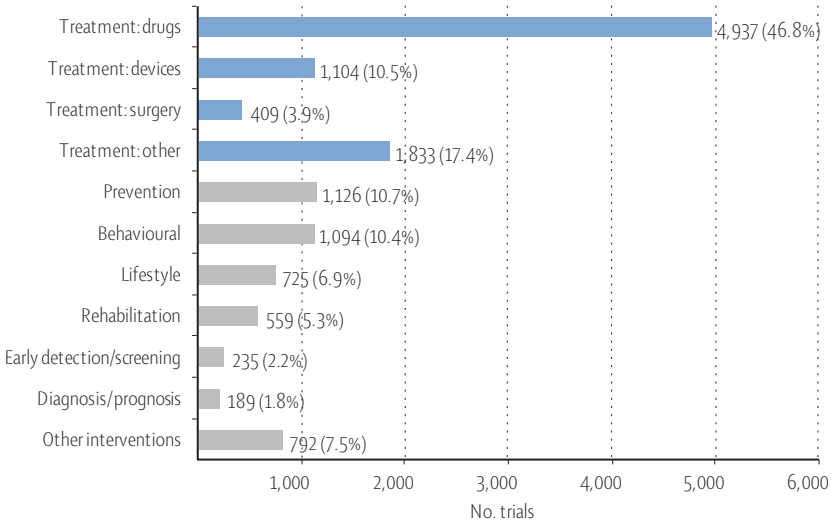
Proportions are of total trials where purpose is listed (N=10,430, including 112 registered on ClinicalTrials.gov with 'other' purposes – supportive care, screening, basic science, health service research). 119 trials registered on ClinicalTrials.gov have no purpose listed and are not included in this analysis.

2.4 Intervention type – drugs, devices, behavioural interventions, screening programs

Drugs are the most commonly researched intervention in Australian clinical trials, studied by 47 per cent of trials registered 2006–2015. However, although around 500 new drug trials have been registered each year since 2009, they have fallen as a proportion of overall registered trial activity, from 57 per cent in 2006 to 42 per cent in 2015.

At the same time, the number of trials of preventive interventions, of devices, and of treatments other than drugs, devices or surgery, has been growing. In particular, trial activity focusing on the 'other treatment' category has increased, from just 72 in 2006 (10 per cent of trials) to 298 in 2015 (23 per cent). This category includes interventions such as exercise, physiotherapy, cognitive therapy, special diets, herbal medicines, web-based treatments, motivational classes, music therapy and stem cell interventions.

Figure 19. Types of intervention studied by Australian clinical trials registered 2006–2015



DATA NOTES

Intervention type is a mandatory field on both the ANZCTR and ClinicalTrials.gov registration forms.
The ANZCTR form allows for entry of up to three intervention codes chosen from a specified list (see Appendix 4).
ClinicalTrials.gov allows entry of any number of intervention codes from a specified list, with the same code able to be entered more than once (where, for example, more than one drug type comprises an intervention).
Proportions are of total number of trials registered: N=10,549.

Figure 20. Trends in treatment interventions studied by registered Australian clinical trials, 2006–2015

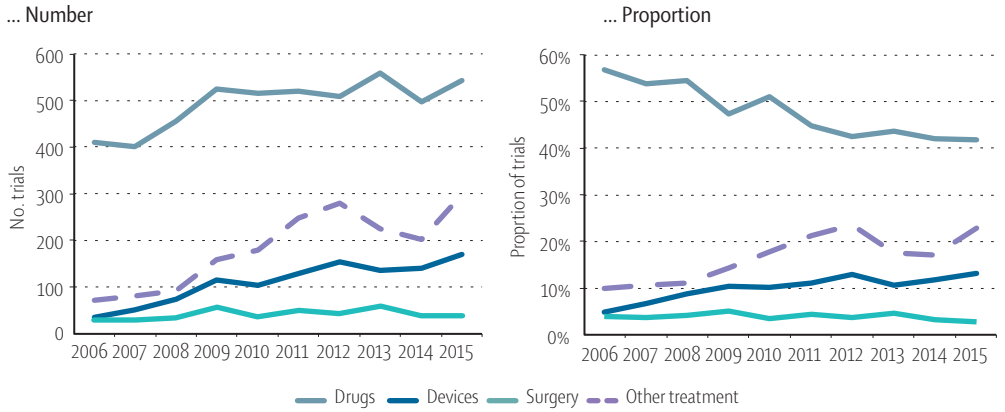


Table 16. Number of Australian clinical trials registered each year, 2006–2015, by intervention type

INTERVENTION TYPE	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Treatment: drugs	411	402	455	524	516	521	508	558	498	544
Treatment: devices	35	50	73	115	103	129	154	135	140	170
Treatment: surgery	29	28	34	56	35	50	43	58	39	37
Treatment: other	72	80	92	159	179	247	280	225	201	298
Prevention	43	57	68	95	125	137	176	130	129	166
Behaviour	17	34	46	71	83	156	158	174	182	173
Lifestyle	25	17	38	68	67	97	113	87	100	113
Rehabilitation	24	28	39	57	41	55	64	80	88	83
Early detection/ screening	3	5	14	16	20	39	38	36	32	32
Diagnosis/ prognosis	7	14	8	17	21	28	17	23	24	30
Other interventions	53	57	73	94	99	69	78	93	91	85
None/not applicable	42	6	2	2	1	0	0	0	0	0
TOTAL TRIALS REGISTERED*	725	747	836	1,105	1,011	1,162	1,195	1,281	1,184	1,303

* As multiple Intervention codes can be selected for each trial, the total count of trials selecting each intervention code is more than the total number of trials registered.

2.5 Intervention endpoint – safety, efficacy, other outcomes

The 'endpoint' is what a trial aims to establish about an intervention. This may be, according to ANZCTR field definitions:

- Efficacy – to measure an intervention's influence on a health condition
- Safety – whether the intervention is safe under the conditions of the proposed protocol/use
- Pharmacokinetics – what happens to a drug in the body over time, including the process of absorption, distribution and localisation in tissue, biotransformation and excretion (i.e. what the body does to the drug)
- Pharmacodynamics – the action of a drug in living systems (i.e. what the drug does to the body)
- Bio-equivalence – a scientific basis for comparing generic and brand name drugs
- Bio-availability – the rate and extent to which a drug is absorbed or otherwise available to the treatment site in the body.

For drug trials, the most common focus has been a combination of the safety and efficacy of the intervention, accounting for 56 per cent of drug trials specifying an endpoint. An additional 27 per cent specified efficacy alone and 10 per cent safety alone. 303 trials (7 per cent) cited assessment of the other endpoint categories, looking at specific aspects of drug actions and effects. All categories have remained relatively stable as a proportion of trials registered each year, although there has been a slight shift over the decade away from safety/efficacy towards efficacy alone.

Predictably, efficacy has been the most frequently specified focus for non-drug trials, accounting for 66 per cent of trials, with an additional 28 per cent citing a combination of efficacy and safety. Only 5 per cent of non-drug trials looked at safety alone. Again, these proportions have remained relatively stable over the decade to 2015.

Figure 21. Types of intervention endpoint for Australian clinical trials registered 2006-2015

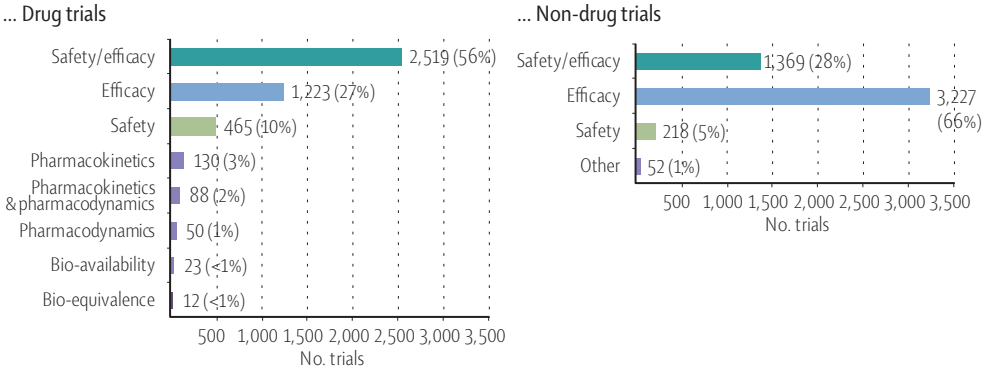


Figure 22. Trends in type of intervention endpoint for registered Australian clinical trials, 2006–2015

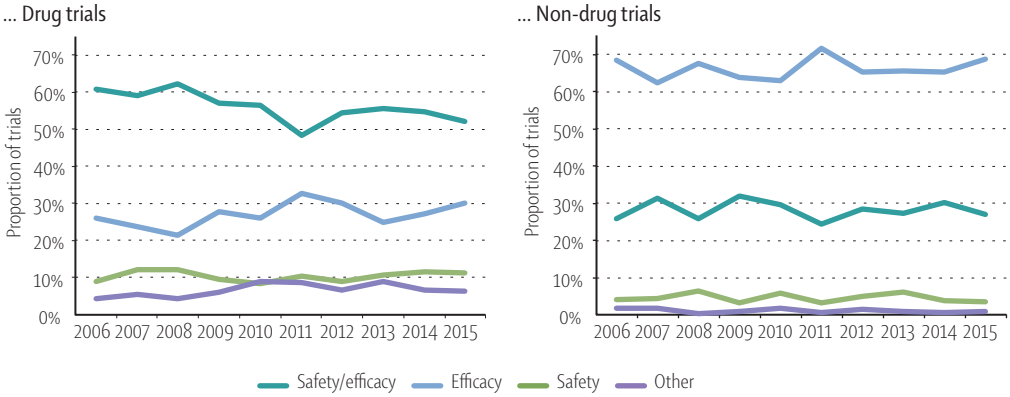


Table 17. Number of Australian clinical trials registered each year, 2006–2015, by type of endpoint

a. Drug trials

	SAFETY/ EFFICACY	EFFICACY	SAFETY	PHARMACOKINETICS	PHARMACOKINETICS/ PHARMACODYNAMICS	PHARMACODYNAMICS	BIO-AVAILABILITY	BIO-EQUIVALENCE	NOT SPECIFIED
2006	239	103	35	6	7	3	-	1	17
2007	230	92	47	7	6	7	-	1	12
2008	266	92	52	4	7	5	1	1	27
2009	256	124	42	10	12	3	2	-	75
2010	257	119	38	21	9	7	2	2	61
2011	227	153	48	18	11	5	6	1	52
2012	251	139	41	12	10	5	3	1	46
2013	284	127	54	21	12	6	4	2	48
2014	248	123	52	14	7	5	3	1	45
2015	261	151	56	17	7	4	2	2	44
TOTAL	2,519 (55.9%)	1,223 (27.1%)	465 (10.3%)	130 (2.9%)	88 (2.0%)	50 (1.1%)	23 (0.5%)	12 (0.3%)	427

b. Non-drug trials

	SAFETY/ EFFICACY	EFFICACY	SAFETY	OTHER	NOT SPECIFIED
2006	80	212	13	5	4
2007	99	198	14	6	28
2008	90	235	22	1	33
2009	158	317	16	5	85
2010	121	258	24	7	85
2011	137	400	18	4	82
2012	174	401	31	9	72
2013	165	396	36	6	120
2014	175	378	22	4	107
2015	170	432	22	5	130
TOTAL	1,369 (28.1%)	3,227 (66.3%)	218 (4.5%)	52 (1.1%)	746

DATA NOTES

Drug trials have been defined as any trial selecting intervention code 'Treatment: drugs'. 'Endpoint' is not a mandatory field on the ANZCTR or ClinicalTrials.gov. A total of 427 drug trials and 746 non-drug trials did not specify an endpoint. All proportions are of trials where endpoint has been specified (a total of 4,510 drug trials and 4,866 non-drug trials).

2.6 Phase of investigation for drug trials

Phase of investigation refers to the research steps used to investigate new interventions, most commonly new drugs, with each phase designed to address a specific question. The findings below are for drug trials where phase has been specified (4,563 out of a total of 4,937 registered Australian drug trials), and the phase descriptions reflect ANZCTR field definitions.

- **Phase 0** trials are exploratory, first-in-human trials, also known as human micro-dosing studies, which carry no therapeutic intent. There have only been 16 registered phase 0 drug trials over the decade to 2015, and of these all but one have been registered since 2011.
- **Phase 1** trials evaluate the metabolism and pharmacological action of drugs, and monitor side effects. They may also aim to gain early evidence of effectiveness. Overall, 790 phase 1 drug trials have been registered between 2006 and 2015 (including 162 combined phase 1/2 trials), accounting for 17 per cent of drug trials specifying a phase. On an annual basis, phase 1 trials have grown as a proportion of trials registered, from 9 per cent in 2006 to 22 per cent in 2015.
- **Phase 2** trials are controlled studies designed to evaluate the effectiveness of new drugs in patients with the disease or condition being studied and to determine common short-term side effects and risks. This is the second-most-common stage of research for Australian drug trials, with 1,285 phase 2 trials registered, accounting for 28 per cent of drug trials overall. This level of activity, which includes 139 combined phase 2/3 trials, has remained relatively stable over the decade.
- **Phase 3** trials are undertaken after preliminary evidence suggesting effectiveness of the drug has been obtained, in order to gather additional information on benefits and risk, including possible adverse reactions. A total of 1,833 phase 3 studies have been registered (including 73 combined phase 3/4 trials), accounting for 40 per cent of registered drug trials overall. This makes phase 3 the most common stage of research among Australian drug trials, although its share has been trending downward, falling from 50 per cent in 2006 to 35 per cent in 2015.
- **Phase 4** trials are undertaken to gain additional information after a drug has been marketed, monitoring aspects such as toxicity, risks, utility, benefits and optimal use. A total of 639 phase 4 studies have been registered between 2006 and 2015, accounting for 14 per cent of drug trials overall and a relatively consistent 12–16 per cent each year.

DATA NOTES

Drug trials have been defined as any trial selecting intervention code 'Treatment: drugs'.
Trial phase is a mandatory field on ClinicalTrials.gov registration form but not on the ANZCTR form. There are 169 drug trials on the ANZCTR with no value in the study phase field.
Only one selection is possible on both the ANZCTR and ClinicalTrials.gov forms.
Selection of 'Not applicable' is possible on both the ANZCTR and ClinicalTrials.gov registration forms. The ANZCTR recommends that a study phase is selected for drug trials, but permits 'Not applicable' if the registrant believes that study phase is not relevant for their trial, for example, where drugs may be administered as part of the intervention but this is not the main focus of the trial. A total of 205 drug trials selected 'Not applicable'.
All proportions are of drug trials where phase has been specified (a total of 4,563 trials).

Figure 23. Trends in phase of study for registered Australian drug trials, 2006–2015

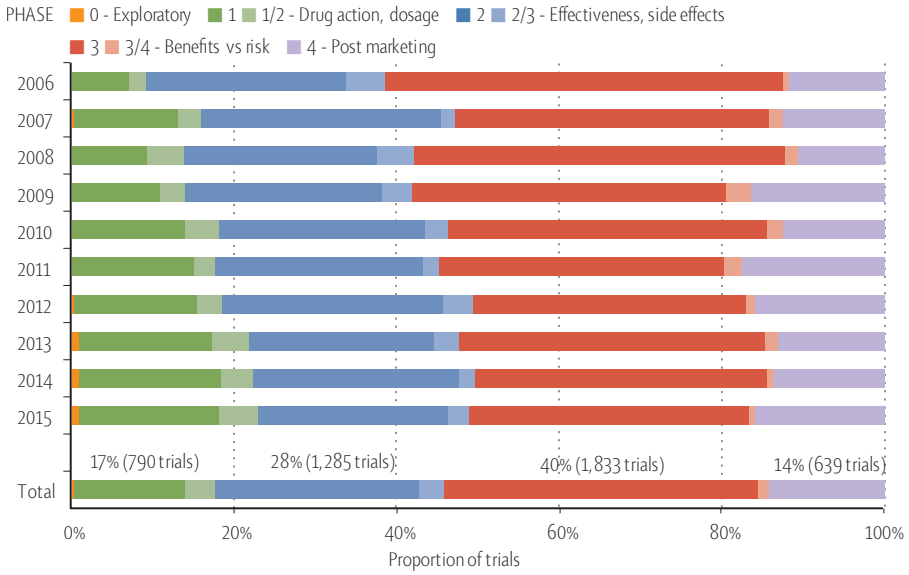


Table 18. Number of registered Australian clinical drug trials registered each year, 2006–2015, by phase of study

	PHASE 0	PHASE 1	PHASE 1/2	PHASE 2	PHASE 2/3	PHASE 3	PHASE 3/4	PHASE 4
2006	0	27	8	97	18	191	4	45
2007	1	48	10	109	6	144	6	46
2008	0	39	19	101	19	193	7	44
2009	0	53	14	116	18	186	15	78
2010	0	66	20	121	13	188	9	59
2011	1	71	12	122	10	167	10	84
2012	1	71	15	127	17	159	5	74
2013	5	85	22	119	16	194	9	67
2014	4	80	18	115	10	163	4	62
2015	4	88	24	119	12	175	4	80
TOTAL	16 (0.4%)	628 (13.8%)	162 (3.6%)	1146 (25.1%)	139 (3.0%)	1760 (38.6%)	73 (1.6%)	639 (14.0%)

Part 3: Trial design

Design aspects of Australian clinical trials

This section uses combined ANZCTR and ClinicalTrials.gov data unless otherwise noted.

Data are displayed as per ANZCTR registration form categories and data from ClinicalTrials.gov have been mapped to the closest relevant ANZCTR category. Details of this mapping can be found in Appendix 3.

Only registered Australian clinical trials are included (i.e. interventional studies with at least one recruitment site in Australia).

Unless otherwise noted, 'year' refers to year of trial registration.

3.1 Key findings

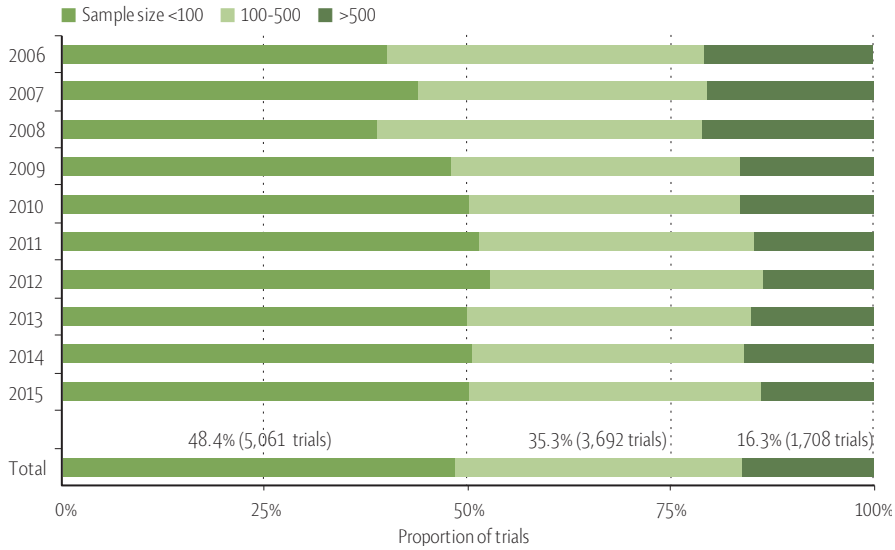
- The median **sample size** for all Australian clinical trials has remained at around 100 participants since 2009, down from a high of 167 in 2006.
- **Drug trials** have tended to involve more participants than non-drug trials. However, drug trials have also seen a sharper contraction in sample sizes over time, with the median falling by 40 per cent between 2006 and 2015, from 200 to 121, compared to a 20 per cent fall for non-drug trials, from 100 to 80.
- Trials with a **public health focus** have tended to use larger sample sizes than other trials as they often involve prevention or screening for disease in otherwise well populations. The overall median for public health trials was 200 participants compared to 132 for **cancer trials** and 100 for **cardiovascular trials**. Earlier in the decade cardiovascular trials were characterised by much larger sample sizes, with medians of 260–300 from 2006 to 2008.
- The majority (87 per cent) of registered Australian clinical trials have recruited **both male and female** participants. Trials recruiting only women have fallen slightly as a proportion of trials registered each year, from around 10 per cent in 2006–2008 to 6 per cent in 2014 and 2015.
- Approximately 80 per cent of Australian clinical trials registered each year have been **randomised controlled trials** and this proportion has remained consistent throughout the 10-year period from 2006 to 2015. There is no difference in the proportion of drug and non-drug trials using random allocation.
- Parallel assignment, where different groups of participants receive different interventions during the same time period, has been the most common **method for assigning interventions** to trial participants, used by 67 per cent of trials specifying a method.

3.2 Sample sizes

The median sample size for all registered Australian clinical trials has remained at around 100 participants since 2009. Before that, trials registered from 2006 to 2008 were characterised by higher medians of 120–160 (Table 19), with a larger proportion recruiting more than 500 participants (Figure 24). This period saw several significant cardiovascular trials characterised by large sample sizes (see section 3.2.2, page 41).

Generally, as Figure 25 shows, trials registered on ClinicalTrials.gov tend to have larger sample sizes than those registered on the ANZCTR, reflecting the higher proportion of multinational drug trials registered on ClinicalTrials.gov (see section 1.5, page 12).

Figure 24. Trends in sample size for registered Australian clinical trials, 2006–2015



DATA NOTES

Sample size is a mandatory field on both ANZCTR and ClinicalTrials.gov registration forms. Data are missing for 29 trials registered on ClinicalTrials.gov.

The ANZCTR collects either target or actual sample size or both, depending on the recruitment status at the time of registration and any subsequent updates. Values obtained are the 'actual' sample size where provided, or the 'target' if no 'actual' value is available, e.g. for trials with ongoing recruitment.

ClinicalTrials.gov collects a single value for sample size along with an 'anticipated' or 'actual' label.

Figure 25. Trends in median sample size and interquartile range (IQR) for registered Australian clinical trials, 2006–2015

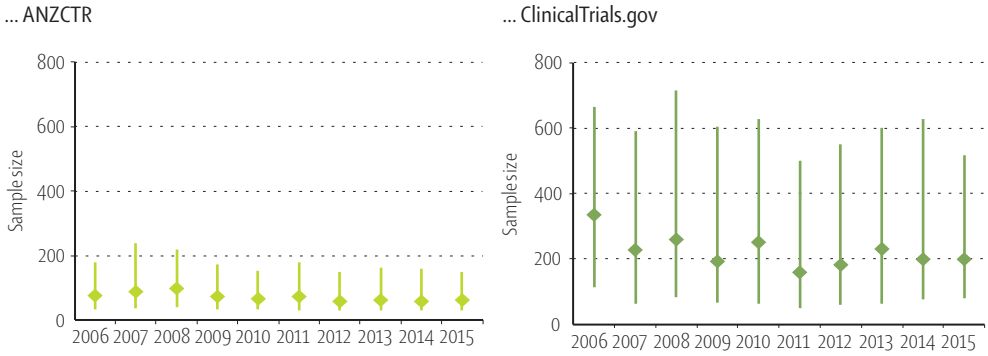


Table 19. Median sample size and interquartile range (IQR) for Australian clinical trials registered on the ANZCTR and on ClinicalTrials.gov, 2006–2015

	ANZCTR			CLINICALTRIALS.GOV			COMBINED		
	NO. TRIALS	MEDIAN SAMPLE SIZE	IQR	NO. TRIALS	MEDIAN SAMPLE SIZE	IQR	NO. TRIALS	MEDIAN SAMPLE SIZE	IQR
2006	363	78	36–181	315	336	115–665	678	167	50–423
2007	392	90	36–241	332	229	64–593	724	123	45–389
2008	443	100	40–220	390	261	84–717	833	140	50–402
2009	734	75	35–175	370	194	65–605	1,104	100	40–296
2010	623	68	35–154	383	252	64–627	1,006	97	40–312
2011	776	75	32–180	384	160	48–501	1,160	90	40–250
2012	799	60	30–150	394	183	59–551	1,193	84	35–232
2013	838	64	35–164	438	232	61–600	1,276	100	36–288
2014	782	60	30–160	402	200	75–628	1,184	96	40–280
2015	887	64	30–150	416	200	80–516	1,303	96	40–240
TOTAL	**6,637**	**70**	**32–168**	**3,912**	**220**	**61–600**	**10,549**	**100**	**40–300**

3.2.1 Drug trials versus non-drug trials

Drug trials registered each year have tended to involve more participants than non-drug trials, with a median sample size of 200 participants in 2006 compared to 100 for non-drug trials.

The difference became less pronounced in 2009, when the median sample size for drug trials fell by 40 per cent to 121 participants. It has remained around that level since then. Over the same period the median sample size for non-drug trials has fallen by 20 per cent to 80 participants in 2015.

Figure 26. Trends in median sample size and interquartile range (IQR) for registered Australian clinical trials, 2006–2015

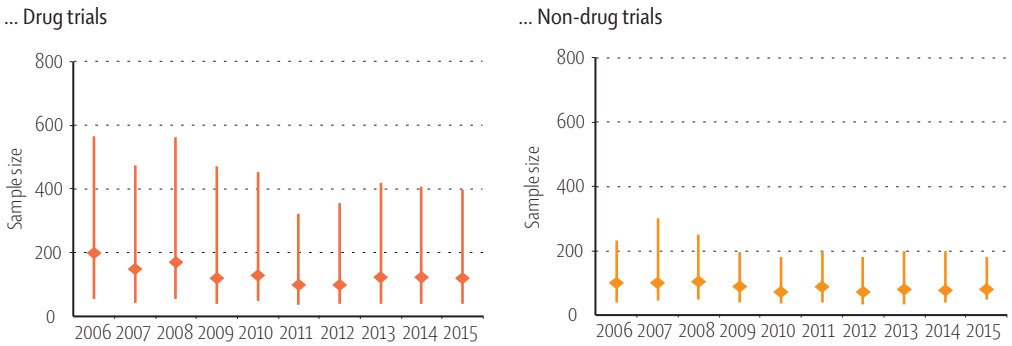


Table 20. Median sample size and interquartile range (IQR) for registered Australian drug and non-drug clinical trials, 2006–2015

	DRUG TRIALS			NON-DRUG TRIALS		
	NO. TRIALS	MEDIAN SAMPLE SIZE	IQR	NO. TRIALS	MEDIAN SAMPLE SIZE	IQR
2006	411	200	56–564	267	100	40–232
2007	402	150	44–473	322	100	45–300
2008	455	171	55–562	378	104	48–250
2009	524	121	40–471	580	89	40–197
2010	516	130	48–452	490	72	36–181
2011	521	100	37–322	639	88	40–200
2012	508	100	40–357	685	72	34–180
2013	558	124	40–419	718	80	34–200
2014	498	124	40–408	686	77	39–200
2015	544	121	40–399	759	80	48–180
TOTAL	4,937	127	40–445	5,612	80	40–200

DATA NOTES

Trials have been defined as 'Drug trials' or 'Non-drug trials' based on whether or not 'Treatment: drugs' was selected as an intervention code.

Sample size uses the 'Actual' sample size value if available or the 'Target' sample size value if no 'Actual' value has been provided on the ANZCTR.

3.2.2 Sample size by condition

Trials with a public health focus have tended to be larger than other trials as they often involve prevention or screening for disease in otherwise well populations. As Table 22 shows, the overall median for public health trials is 200 participants, followed by trials involving inflammatory and immune system conditions (167 participants), infection (160 participants), and reproductive health and childbirth (152 participants).

Of the four most frequently studied conditions (Table 21), cancer trials have an overall median sample size of 132 participants and cardiovascular trials 100 participants, while mental health and musculoskeletal trials are characterised by smaller sample sizes, with medians of 90 and 92 participants respectively.

Earlier in the decade cardiovascular trials were characterised by much larger sample sizes, with medians of 262 participants in 2006, 300 in 2007 and 292 in 2008. The median sample size then dropped back to around 100 participants from 2010 to 2015, below that for cancer trials, but similar to trials involving mental health and musculoskeletal conditions (Figure 27).

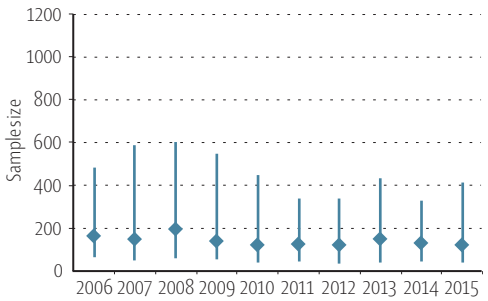
Table 21. Median sample size and interquartile range (IQR) of Australian clinical trials registered each year, 2006–2015, for the four types of condition most frequently studied

	CANCER		CARDIOVASCULAR CONDITIONS		MENTAL HEALTH CONDITIONS		MUSCULOSKELETAL CONDITIONS	
	MEDIAN SAMPLE SIZE	IQR	MEDIAN SAMPLE SIZE	IQR	MEDIAN SAMPLE SIZE	IQR	MEDIAN SAMPLE SIZE	IQR
2006	162	64–482	262	52–825	120	52–200	137	80–461
2007	147	48–587	300	80–1,197	115	65–245	124	47–349
2008	194	60–600	292	76–1,075	160	80–300	102	54–207
2009	138	54–550	120	60–522	69	40–140	93	30–211
2010	120	41–447	114	40–356	90	50–176	100	50–332
2011	124	43–339	76	30–350	90	40–160	62	40–132
2012	120	36–340	69	35–190	82	40–160	88	48–184
2013	148	41–431	80	39–300	90	40–200	85	40–276
2014	129	44–330	110	49–425	90	40–260	80	40–196
2015	120	40–414	80	32–170	90	40–180	80	40–160
TOTAL	132	45–435	100	40–420	90	42–200	92	42–220

3.2.2 continued ...

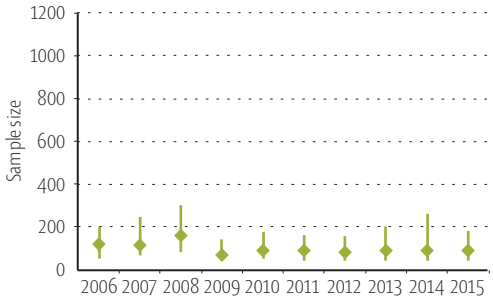
Figure 27. Trends in median sample size and interquartile range (IQR) of registered Australian clinical trials, 2006–2015, for the four types of condition most frequently studied

... Cancer



... Cardiovascular conditions

... Mental health



... Musculoskeletal conditions

DATA NOTES

Sample size is a mandatory field on both the ANZCTR and ClinicalTrials.gov registration forms. Data are missing for 29 trials registered on ClinicalTrials.gov.

The ANZCTR collects either target or actual sample size or both, depending on the recruitment status at the time of registration and any subsequent updates. Values obtained are the 'actual' sample size where provided, or the 'target' if no 'actual' value is available, e.g. for trials with ongoing recruitment.

ClinicalTrials.gov collects a single value for sample size along with an 'anticipated' or 'actual' label.

Table 22. Median sample size for Australian clinical trials registered each year, 2006–2015, by condition

CONDITION	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	TOTAL
Public health	215	153	277	198	174	234	200	200	204	186	200
Inflammatory and immune system	303	335	158	124	195	109	143	124	200	202	167
Infection	425	178	129	201	200	183	99	156	150	130	160
Reproductive health and childbirth	90	300	320	120	100	218	134	154	120	180	152
Cancer	162	147	194	138	120	124	120	148	129	120	132
Injuries and accidents	139	120	140	65	118	90	125	100	120	100	113
Oral and gastrointestinal	105	150	400	100	72	196	72	126	120	100	101
Cardiovascular	262	300	292	120	114	76	69	80	110	80	100
Blood	231	186	586	171	72	67	81	101	125	64	100
Ear	210	126	300	48	248	80	55	60	200	110	100
Musculoskeletal	137	124	102	93	100	62	88	85	80	80	92
Mental health	120	115	160	69	90	90	82	90	90	90	90
Surgery	80	60	60	90	60	98	80	90	114	90	86
Renal and urogenital	150	200	105	92	120	60	50	95	80	72	80
Skin	65	36	265	235	60	46	130	58	75	130	80
Respiratory	60	108	48	60	85	90	88	70	72	81	78
Metabolic and endocrine	87	120	142	78	80	78	72	88	51	40	76
Stroke	331	156	150	43	200	160	50	60	60	64	70
Alternative and complementary medicine	174	40	120	60	58	63	60	60	60	72	62
Neurological	160	120	125	114	60	40	60	60	50	49	60
Diet and nutrition	60	110	80	60	50	62	53	78	76	60	60
Physical medicine / Rehabilitation	45	40	130	70	96	56	61	48	50	57	60
Anaesthesiology	100	70	60	50	70	60	60	63	55	60	60
Eye	198	55	90	45	40	47	40	120	60	80	60
Human genetics and inherited disorders	21	66	45	50	60	43	30	90	54	78	48
Other	95	65	100	119	60	71	46	59	76	60	70

3.3 Participant recruitment by sex

The majority (87 per cent) of registered Australian clinical trials have recruited both male and female participants. Trials recruiting only women have fallen slightly as a proportion of trials registered each year, from around 10 per cent in 2006–2008 to 6 per cent in 2014 and 2015. At the same time, there has been a slight increase in the proportion of trials recruiting only men (from 3 per cent in 2006 to 5 per cent in 2015) and both genders (from 86 per cent to 89 per cent).

It should be noted that these data only describe participant eligibility and are not representative of the actual participation rate for each gender.

Figure 28. Trends in the eligibility of male and female participants for registered Australian clinical trials, 2006–2015

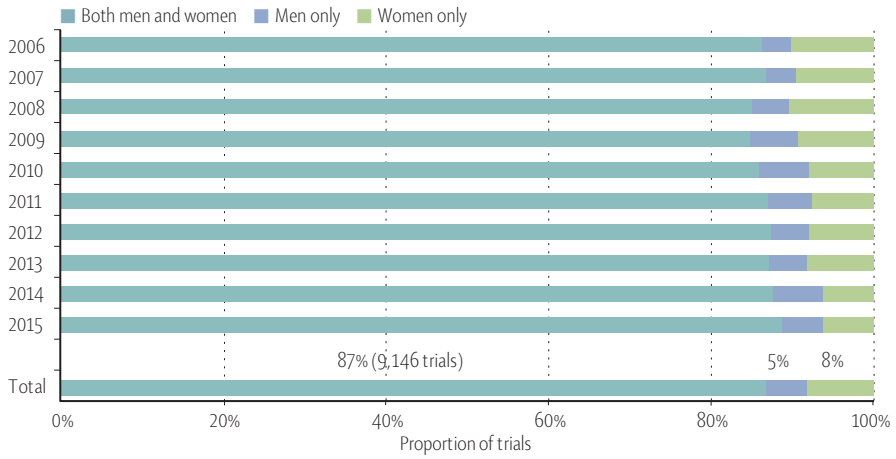


Table 23. Number and proportion of Australian clinical trials registered each year, 2006–2015, by eligible sex

	BOTH MEN AND WOMEN		MEN ONLY		WOMEN ONLY	
	NO.	PROPORTION	NO.	PROPORTION	NO.	PROPORTION
2006	625	86.2%	25	3.4%	75	10.3%
2007	647	86.7%	28	3.8%	71	9.5%
2008	710	84.9%	38	4.5%	88	10.5%
2009	937	84.8%	63	5.7%	105	9.5%
2010	867	85.8%	64	6.3%	80	7.9%
2011	1,012	87.1%	61	5.2%	89	7.7%
2012	1,042	87.2%	59	4.9%	94	7.9%
2013	1,113	86.9%	64	5.0%	104	8.1%
2014	1,037	87.6%	73	6.2%	74	6.3%
2015	1,156	88.7%	65	5.0%	82	6.3%
TOTAL	**9,146**	**87%**	**540**	**5%**	**862**	**8%**

DATA NOTES

Selecting sex of participants eligible for a trial is mandatory for both the ANZCTR and ClinicalTrials.gov.
However, there is one trial record registered on the ANZCTR with missing values for eligible sex. N=10,548.

3.4 Participant allocation method – randomised or not

In a randomised controlled trial subjects are allocated randomly to either the intervention or the control group. A non-randomised trial is one in which subjects are allocated deliberately or not at random; this term may also apply to a single-arm trial with no comparator/control arm.

Approximately 80 per cent of Australian clinical trials registered each year are randomised controlled trials and this proportion has remained consistent throughout the 10-year period from 2006 to 2015. There appears to be no difference in the proportion of drug and non-drug trials using randomised allocation.

Figure 29. Trends in randomised controlled trials as a proportion of total trials (where allocation method has been specified), for drug and non-drug trials, 2006–2015

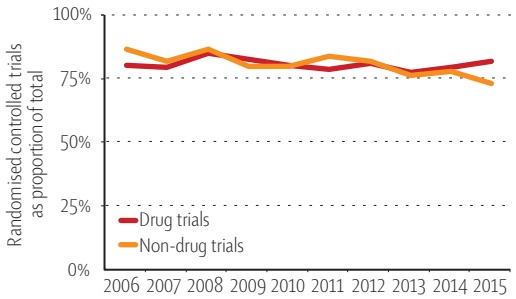


Table 24. Number of Australian drug trials and non-drug trials registered each year, 2006–2015, by participant allocation method

	DRUG TRIALS			NON-DRUG TRIALS		
	RANDOMISED	NON-RANDOMISED	NOT SPECIFIED	RANDOMISED	NON-RANDOMISED	NOT SPECIFIED
2006	314	79	18	270	44	0
2007	296	79	27	274	63	8
2008	346	64	45	322	53	6
2009	407	89	28	451	117	13
2010	374	95	47	377	98	20
2011	385	108	28	519	103	19
2012	377	91	40	526	120	41
2013	404	121	33	529	169	25
2014	354	94	50	512	148	26
2015	405	92	47	528	198	33
TOTAL	3,662 (80%)	912 (20%)	363	4,308 (79%)	1,113 (21%)	191

DATA NOTES
The allocation method field is mandatory on the ANZCTR but optional for ClinicalTrials.gov; a total of 363 drug trials and 191 non-drug trials registered on ClinicalTrials.gov provided no information on participant allocation (listed as 'Not specified' above).
Proportions are of trials where allocation method has been specified (a total of 4,574 drug trials and 5,421 non-drug trials)

3.5 Intervention assignment method

This indicator reflects the way interventions are assigned to trial participants.

The main methods are:

- **Parallel** assignment, where different groups of participants receive different interventions during the same time period. This is the most common assignment method for registered Australian clinical trials, used by 67 per cent of those specifying a method.
- **Single group** assignment, where all participants receive the same intervention. This is the second most common method, accounting for 19 per cent of trials.

Less common assignment methods, which together account for 14 per cent of trials specifying a method, are:

- **Crossover** assignment, where participants receive all interventions, one at a time and in either a random or non-random sequence.
- **Factorial** assignment, where participants are randomly allocated to receive two or more interventions, either in combination, each intervention alone or no intervention.
- **Other methods**, for example sequential cohort dose escalation trials and stepped wedge cluster trials.

The proportion of interventional trials by assignment type has been fairly consistent over the 10-year period from 2006 to 2015.

DATA NOTES

Specifying which assignment method is used is optional for both the ANZCTR and ClinicalTrials.gov.
A total of 663 trials did not provide information on assignment; these are listed as 'Not specified'.
Proportions are of trials specifying an assignment method (a total of 9,886 trials).

Figure 30. Trends in methods of assigning interventions to participants for registered Australian clinical trials, 2006–2015

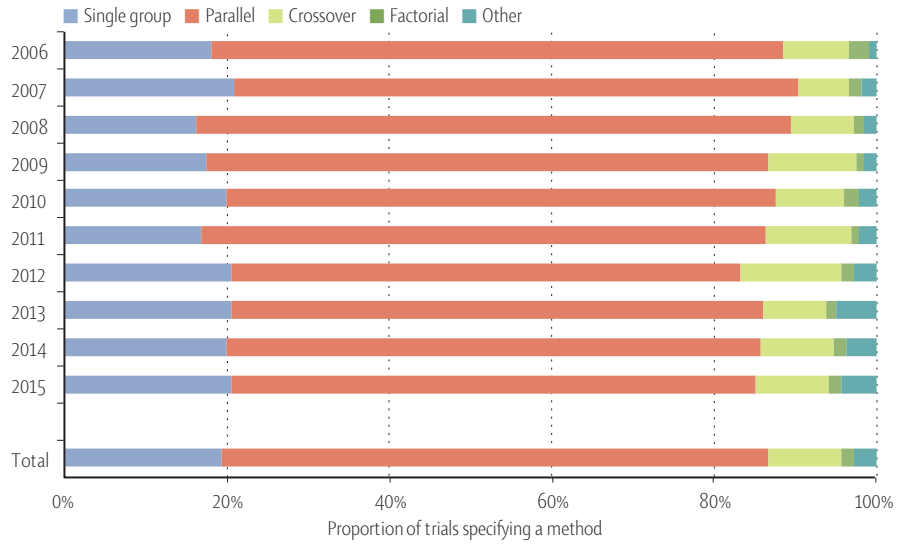


Table 25. Number of Australian clinical trials registered each year, 2006–2015, by assignment method

	SINGLE GROUP	PARALLEL	CROSSOVER	FACTORIAL	OTHER	NOT SPECIFIED
2006	131	509	59	17	6	3
2007	154	511	46	12	12	12
2008	131	592	64	10	11	28
2009	175	692	109	10	14	105
2010	187	630	79	18	19	78
2011	184	769	115	12	22	60
2012	234	715	139	20	29	58
2013	242	767	92	14	57	109
2014	215	711	98	15	39	106
2015	245	775	109	18	52	104
TOTAL	1,898 (19%)	6,671 (67%)	910 (9%)	146 (1%)	261 (2%)	663

Part 4: Trial registration

Timing of registration and ethics approval status

Registration of clinical trials on a publicly accessible database such as the ANZCTR is important to improve research transparency, identify research gaps, avoid duplication of research effort and promote collaboration, as well as to facilitate trial participation.

Ideally, registration should be completed prospectively – before enrolment of the first participant.

This section uses data on Australian clinical trials registered on the ANZCTR only.

Equivalent analysis is not possible for ClinicalTrials.gov, as it only collects data on the month, not the specific date, that recruitment starts.

'Year' refers to year of trial registration.

4.1 Key findings

- The proportion of Australian studies **registered prospectively** on the ANZCTR each year increased from 48 per cent in 2006 to 67 per cent in 2012, and has since plateaued at around 65–70 per cent.
- For prospectively registered studies, the median number of **days between trial registration and start of enrolment** has hovered consistently around 40–50 days since 2007. For trials registering retrospectively, the median time between start of enrolment and registration has ranged from 103 days for trials registered in 2015 up to 321 days for trials registered in 2011.
- Among the trials registered prospectively between 2006 and 2015, 56 per cent had **ethics approval** at time of registration. This proportion has remained relatively consistent since 2007.

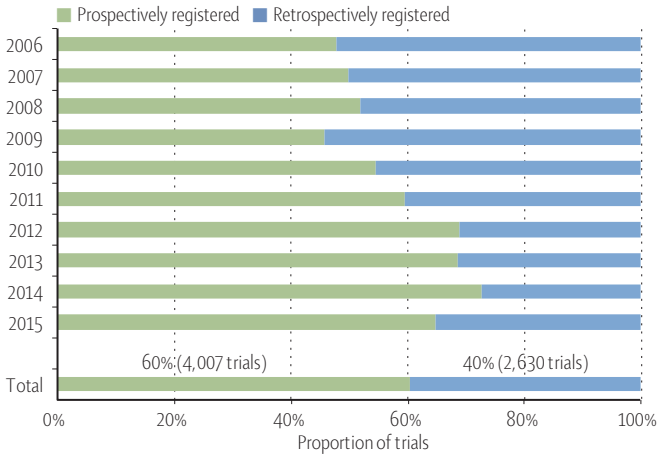
4.2 Prospective versus retrospective registration on the ANZCTR

Studies can be registered on the ANZCTR regardless of whether recruitment has not yet begun, is ongoing, or has already been completed.

Prospective registration means the process is complete and a registration number has been allocated *before* the first participant is enrolled. Prospective registration is supported and encouraged by numerous organisations nationally and internationally. For example, the International Committee of Medical Journals Editors (ICMJE) declared that from 1 July 2005, they would not consider a trial for publication without evidence that it had been registered in a publicly accessible trials registry prior to enrolment of the first participant.[19] The Declaration of Helsinki now also explicitly states that 'every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.'[18]

The proportion of Australian studies registered prospectively on the ANZCTR each year increased from 48 per cent in 2006 to 69 per cent in 2012, and has since plateaued at around 65–70 per cent.

Figure 31. Trends in prospective versus retrospective registration of Australian clinical trials on the ANZCTR, 2006–2015



DATA NOTES

A prospective/retrospective label is automatically generated by the ANZCTR system based on the registration date and the actual date of first participant enrolment provided by the registrant, or the anticipated date of first participant enrolment if the actual date is not provided. If the registration date occurs after the listed start date the record is labelled as retrospectively registered. If registration occurs prior to the start date the trial is labelled as prospectively registered.

Table 26. Number and proportion of Australian clinical trials registered on the ANZCTR, 2006–2015, by prospective versus retrospective registration

	PROSPECTIVELY REGISTERED		RETROSPECTIVELY REGISTERED		
	NO.	PROPORTION	NO.	PROPORTION	TOTAL
2006	174	48%	189	52%	363
2007	196	50%	196	50%	392
2008	230	52%	213	48%	443
2009	336	46%	398	54%	734
2010	339	54%	284	46%	623
2011	462	60%	314	40%	776
2012	551	69%	248	31%	799
2013	574	68%	264	32%	838
2014	569	73%	213	27%	782
2015	576	65%	311	35%	887
TOTAL	4,007	60%	2,630	40%	6,637

4.3 Time between registration and participant enrolment

For prospectively registered trials, the median number of days between trial registration and start of participant enrolment has remained around 40–50 days since 2007. For trials registering retrospectively, the median time between start of enrolment and registration has ranged from 103 days for trials registered in 2015 up to 321 days for trials registered in 2011.

Figure 32. Trends in the median number of days between trial registration and enrolment of the first participant, for Australian trials registered on the ANZCTR 2006–2015

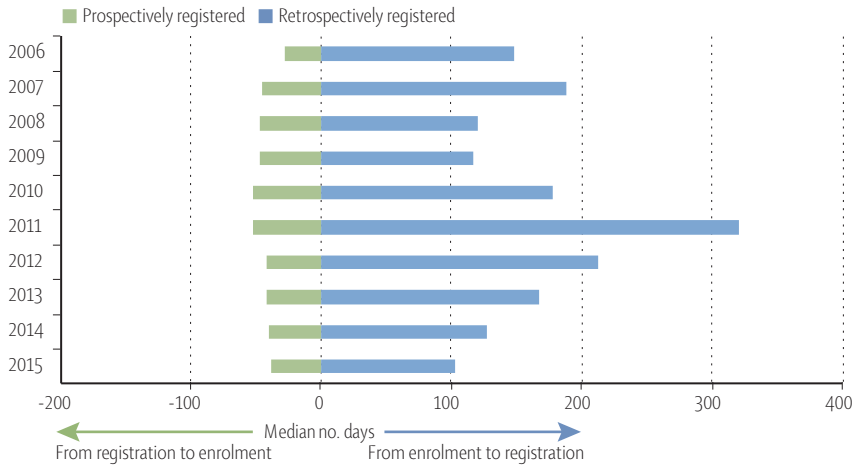


Table 27. Time between registration on the ANZCTR and enrolment of the first participant, for prospectively and retrospectively registered Australian clinical trials, 2006–2015

	MEDIAN NUMBER OF DAYS	
	PROSPECTIVELY REGISTERED TRIALS	RETROSPECTIVELY REGISTERED TRIALS
2006	29	148
2007	46	188
2008	46	121
2009	46	117
2010	52	178
2011	52	321
2012	41	213
2013	42	167
2014	40	128
2015	38	103

4.4 Ethics approval status

Ethics approval is not specifically required at the time of registration unless recruitment has already commenced.

Among the 4,007 trials registered prospectively on the ANZCTR between 2006 and 2015, 56 per cent had ethics approval in place at time of registration. This proportion has remained relatively consistent since 2007, after a high of 73 per cent in 2006.

As of the end of 2015, there were only 31 trials on the ANZCTR where recruitment had begun but there was no ethics approval recorded. All of these had been registered before 2015, when logic rules were implemented to prevent registrants from indicating that a trial had commenced without ethics approval.

Figure 33. Trends in the proportion of Australian clinical trials registered prospectively with ethics approval in place, 2006–2015

DATA NOTES

Ethics application status is provided by the registrant for each study record at the time of registration and can then be updated at any point, for example if the ethics application is approved after allocation of the ANZCTR registration number. No application status has been registered for 2 trials.

Table 28. Number and proportion of Australian clinical trials registered prospectively on the ANZCTR with ethics approved at registration, 2006–2015

	NO. TRIALS PROSPECTIVELY REGISTERED	TRIALS WITH ETHICS APPROVED	
		NO.	PROPORTION
2006	174	127	73%
2007	196	94	48%
2008	230	123	53%
2009	336	169	50%
2010	339	196	58%
2011	462	240	52%
2012	551	309	56%
2013	574	333	58%
2014	569	349	61%
2015	576	297	52%
TOTAL	4,007	2,237	56%

Table 29. Ethics approval and recruitment status of Australian clinical trials registered on the ANZCTR 2006–2015

ETHICS STATUS	RECRUITMENT STATUS	
	NOT YET COMMENCED: 1,794	COMMENCED: 4,841
Not yet approved: 766 trials	Still planning (or not updated): 735	Recruiting but no ethics approval: 31 (all registered before 2015)
Approved: 5,869 trials	Ethics approved and ready to start recruiting: 1,059	Recruiting with ethics approval: 4,810

Appendices

Appendix 1: Trial registration in Australia

In Australia the registration of clinical trials on a publicly accessible trial registry is a mandatory condition of ethics approval. Investigators wishing to undertake a clinical trial need to:

- enter data regarding key aspects of their trial on a trial registry (either the ANZCTR or another registry recognised by the World Health Organization [WHO] (see Appendix 2);
- submit an ethics application form (either electronically or in hard copy) to one or more Human Research Ethics Committees (HRECs); and
- (where applicable) submit a Clinical Trial Notification or Exemption (CTN/CTX) form to the Therapeutic Goods Administration (TGA).

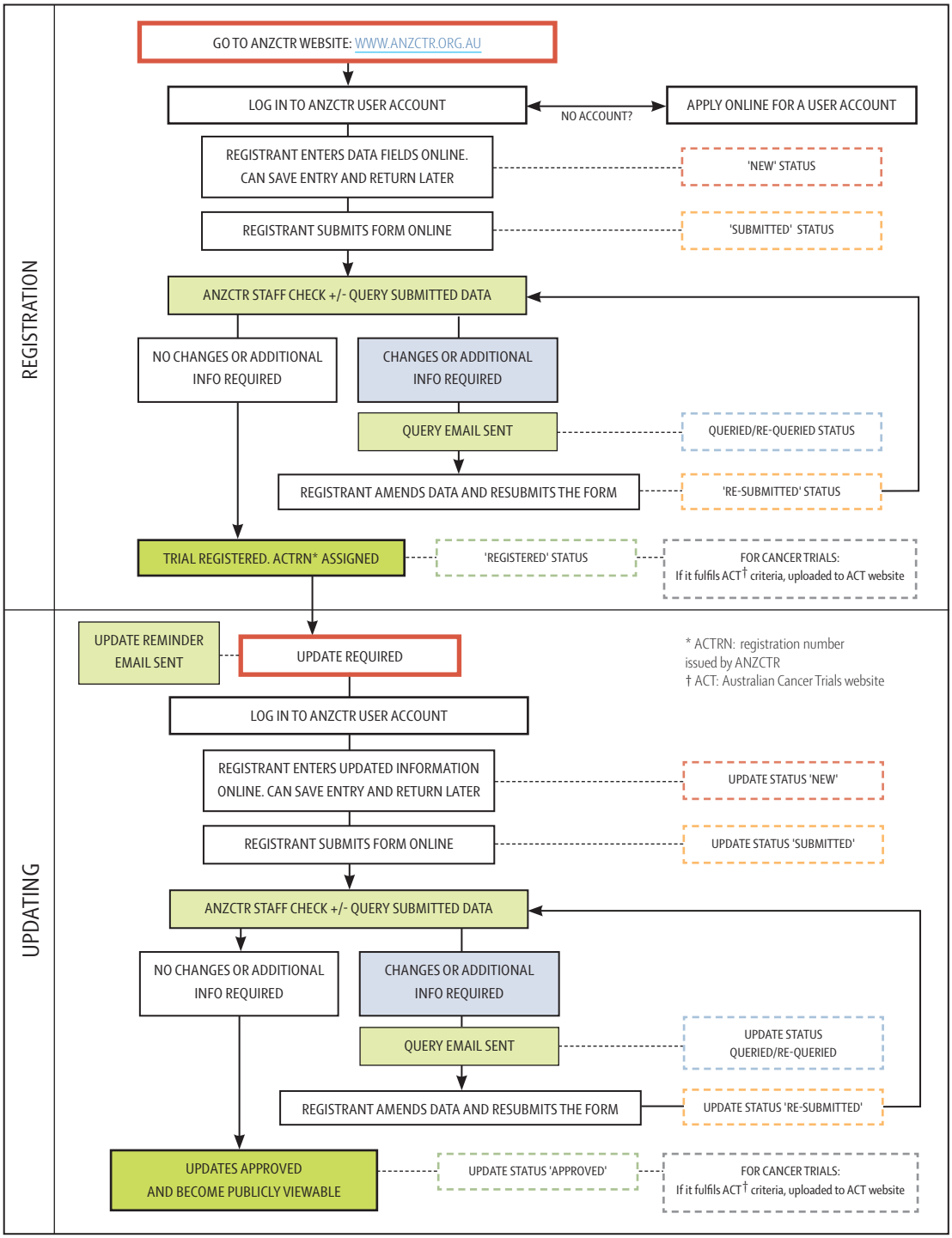
Data entry for these three agencies is currently not fully harmonised nor is data exchanged. Data lodged with the TGA and HRECs are not publicly available.

Figure 34 provides an overview of the process of registering and updating a study on the ANZCTR.

Key characteristics of the registration process include:

- Only the study's primary sponsor or their authorised representative should register the study.
- The study should be registered with the ANZCTR only once and preferably with only one WHO primary registry (see Appendix 2).
- For registrants from a country with a WHO primary registry, the ANZCTR recommends registration with the registry from that country.
- A study can be submitted for registration with the ANZCTR before or after ethics approval has been obtained. If a study is registered before receiving ethics approval, a 'Provisional' watermark label appears on the record.
- All submitted data are checked by ANZCTR staff to ensure all WHO dataset requirements are met before allocation of a registration number. Data are also checked for clarity and consistency, validity, logic and formatting.
- The registrant is responsible for all information provided in the ANZCTR record. Registration on the ANZCTR does not reflect endorsement by the ANZCTR.
- Registration records can be updated at any point, with all changes viewable via a publicly accessible audit trail.

Figure 34. ANZCTR trial registration and updating processes



ANZCTR online

The ANZCTR website, at www.anzctr.org.au, offers:

- the ability to search both the ANZCTR and ClinicalTrials.gov registries for Australian studies
- the ability to register a study on the ANZCTR
- a range of summary statistics for the ANZCTR, updated monthly
- links to other registries and data sources.

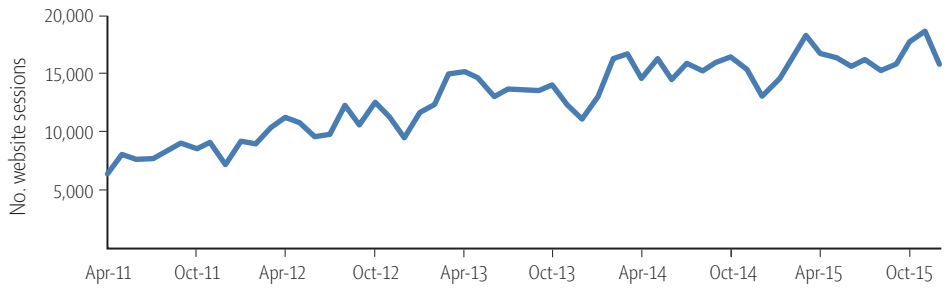
Website usage has been measured using a Google Analytics account since April 2011.

A total of 408,245 unique visitors used the site to 31 December 2015, with an average of 236 visitors per day (for 1,733 days inclusive). There were 4,210,727 page views during this period (approximately 73,872 page views per month), suggesting that approximately 10 pages were viewed per user.

A total of 738,180 sessions (total visits) were recorded during this period, with an average duration of approximately 6 minutes and 6 pages viewed per session. A 53.40 per cent 'bounce rate' for these visits indicates the proportion of people who visited a single page before leaving.

Figure 35 shows monthly visits to the ANZCTR website from April 2011 to December 2015 (inclusive). The overall number of monthly visits has progressively increased since monitoring with Google Analytics started, with dips occurring during December/January periods.

Figure 35. Trends in monthly visits to the ANZCTR website



Appendix 2: Other trial registries

WHO-recognised clinical trial registries

The World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) recognises registries as **primary registries** if they fulfil certain criteria with respect to data content, quality and validity, accessibility, unique identification, technical capacity and administration.

Partner registries meet the same criteria as primary registries in the WHO Registry Network (i.e. for content, quality and validity, etc) except they do not need to:

- have a national or regional remit or the support of government
- be managed by a not-for-profit agency
- be open to all prospective registrants.

For example, they may be limited to trials in a particular condition or intervention.

All partner registries must also be affiliated with either a primary registry in the WHO Registry Network or a registry approved by the International Committee of Medical Journal Editors (ICMJE).

Data providers are responsible for a database that is used by one or more registries, and provide data to WHO for inclusion in the ICTRP search portal. The ICTRP will accept trial records from data providers if it is satisfied that those trial records have been created and managed in a manner that is consistent with the WHO Registry Criteria.[24]

Table 30. Clinical trial registries in the WHO Registry Network

NAME	STATUS
Australian New Zealand Clinical Trials Registry (ANZCTR)	Primary registry, Data provider
Brazilian Clinical Trials Registry (ReBec)	Primary registry, Data provider
Chinese Clinical Trial Registry (ChiCTR)	Primary registry, Data provider
Clinical Research Information Service (CRiS), Republic of Korea	Primary registry, Data provider
Clinical Trials Registry – India (CTRI)	Primary registry, Data provider
Cuban Public Registry of Clinical Trials (RPCEC)	Primary registry, Data provider
EU Clinical Trials Register (EU-CTR)	Primary registry, Data provider
German Clinical Trials Register (DRKS)	Primary registry, Data provider
Iranian Registry of Clinical Trials (IRCT)	Primary registry, Data provider
ISRCTN.org	Primary registry, Data provider
Japan Primary Registries Network (JPRN)	Primary registry, Data provider
Pan African Clinical Trial Registry (PACTR)	Primary registry, Data provider
Peruvian Clinical Trials Registry (REPEC)	Primary registry, Data provider
Sri Lanka Clinical Trials Registry (SLCTR)	Primary registry, Data provider
Thai Clinical Trials Registry (TCTR)	Primary registry, Data provider
The Netherlands National Trial Register (NTR)	Primary registry, Data provider
Clinical Trial Registry of the University Medical Center Freiburg. Affiliated registry: DRKS	Partner registry
DeReG – German Registry for Somatic Gene-Transfer Trials. Affiliated registry: DRKS	Partner registry
Centre for Clinical Trials, Clinical Trials Registry – Chinese University of Hong Kong. Affiliated registry: ChiCTR	Partner registry
ClinicalTrials.gov	Data provider

Registration of studies with Australian recruitment sites in other registries

The majority of registered studies recruiting in Australia are registered on the ANZCTR (approximately 60 per cent) or ClinicalTrials.gov (approximately 35 per cent). Only around 5 per cent of all registered studies recruiting in Australia are registered on other WHO primary registries.

Some studies counted are registered on multiple registries, and are thus duplicated in Table 31. The number of studies registered on both the ANZCTR and ClinicalTrials.gov is estimated to be approximately 110 as at December 2015, although this may be an underestimate as confirmed duplicates are only possible when a study cross-references both registration identification numbers in the records of both registries.

Table 31. Numbers of Australian studies registered 2005–2015 on different clinical trials registries, as of September 2016

REGISTRY	TOTAL
ANZCTR	8,075
ClinicalTrials.gov	4,775
ISRCTN.org	245
German CTR (DRKS)	211
EU-CTR	259
Sri Lanka CTR (SLCTR)	0
Brazilian CTR (ReBec)	1
Japan Primary Registries Network (JPRN)	1
Chinese CTR (ChiCTR)	0
Clinical Research Information Service (CRiS), Republic of Korea	0
Clinical Trials Registry – India (CTRI)	10
Cuban Public Registry of Clinical Trials (RPCEC)	0
Iranian Registry of Clinical Trials (IRCT)	0
The Netherlands National Trial Register (NTR)	0
Pan African Clinical Trials Register (PACTR)	0
Thai Clinical Trials Registry (TCTR)	0

Appendix 3: ANZCTR / ClinicalTrials.gov mapping tables

Study type

ANZCTR	CLINICALTRIALS.GOV	DISPLAY AS...
Interventional	Interventional Expanded access	Interventional
Observational	Observational	Observational

Purpose of the study/Primary purpose

ANZCTR	CLINICALTRIALS.GOV	DISPLAY AS...
Treatment	Treatment	Treatment
Prevention	Prevention	Prevention
Diagnosis	Diagnostic	Diagnosis
Educational/counselling/ training	Educational/counselling/ training (available only in 2005 and 2006)	Educational/counselling/training
-	Supportive care (n=30) Screening (n=6) Basic science (n=61) Health service research (n=16)	Other

Intervention code/Intervention type

ANZCTR	CLINICALTRIALS.GOV	DISPLAY AS...
Diagnosis/prognosis	-	Diagnosis/prognosis
Early detection/screening	-	Early detection/screening
Prevention	-	Prevention
Treatment: drugs	Drug	Treatment: drugs
Treatment: devices	Device	Treatment: devices
Treatment: surgery	Procedure/surgery	Treatment: surgery
Treatment: other	Radiation	Treatment: other
Lifestyle	-	Lifestyle
Behaviour	Behavioural	Behaviour
Rehabilitation	-	Rehabilitation
Other interventions	Other	Other interventions
None/not applicable	-	None/not applicable
-	Biological/vaccine (n=776) Genetic (n=14) Dietary supplement (n=57)	[NOT DISPLAYED]

Appendix 3 continued ...

Phase/Study phase

ANZCTR	CLINICALTRIALS.GOV	DISPLAY AS...
Not applicable	Not applicable	Not applicable
Phase 0	Phase 0	Phase 0
Phase 1 Phase 1/2	Phase 1 Phase 1/2	Phase 1
Phase 2 Phase 2/3	Phase 2 Phase 2/3	Phase 2
Phase 3 Phase 3/4	Phase 3	Phase 3
Phase 4	Phase 4	Phase 4

Primary sponsor type/Lead sponsor

ANZCTR	CLINICALTRIALS.GOV	DISPLAY AS...
Government body	NIH Other U.S. Federal agency	Government body
Hospital		Hospital
University		University
Commercial sector/industry	Industry	Commercial sector/industry
Charities/societies/foundations		Charities/societies/foundations
Other collaborative groups		Collaborative groups
Individual		Individual
Other	All others (individuals, universities, organizations)	Other

Assignment/Intervention model

ANZCTR	CLINICALTRIALS.GOV	DISPLAY AS...
Single group	Single group	Single group
Parallel	Parallel	Parallel
Crossover	Crossover	Crossover
Factorial	Factorial	Factorial
Other	-	Other

For all other fields direct matching was possible and no mapping was required.

Appendix 4: ANZCTR data field definitions

This table includes the definitions and explanation of the data fields to be completed when submitting a record for registration on the ANZCTR. The information requested is based on the definitions and set requirements for trial registration from the International Committee of Medical Journal Editors (ICMJE) and the World Health Organization (WHO) Trial Registration Data Set.

Mandatory data items for trial registration with the ANZCTR are marked in BOLD and with an asterisk (*).

The following are ANZCTR data field definitions V12 (November 2015).

DATA ITEM	DEFINITION / EXPLANATION
STEP 1: TITLES & IDS	
1. Public title *	The public title of the study is intended for the lay public and should be in easily understood language. An informative public title should include at least 2 of the following components: participants, intervention/exposure, and main outcome of the study. Acronyms should be defined at first use. This field will be displayed on the main search page of the WHO ICTRP Search Portal.
2. Scientific title *	The scientific title is intended for use in grant and ethics applications. It should contain information on the participants in the study, the intervention(s) / exposure(s) and the primary outcome(s) to be assessed.
3. Secondary IDs *	Identifying numbers issued by authorities other than the ANZCTR if any. This includes: • Trial registration numbers issued by other registries (both Primary and Partner Registries in the WHO Registry Network, and other registries) • Identifiers assigned by the sponsor (record sponsor name and sponsor-issued trial number, e.g. protocol number) • Identifiers issued by funding bodies, collaborative research groups, etc. This does not include ethics identification numbers – these should be provided in the relevant Ethics section in Step 9. All secondary identifiers will have 2 elements: an identifier for the issuing authority (e.g. NCT, ISRCTN) plus a number. It is possible that the trial may not have a secondary ID. Please include the text 'Nil known' if you do not know of any secondary IDs. Enter only one secondary ID and issuing authority per box. Click 'Add new secondary ID' to add more boxes if necessary. There is no limit to the number of Secondary ID entries (boxes) that can be added.
4. UTN	The Universal Trial Number (UTN) is a unique number that aims to facilitate the unambiguous identification of clinical trials registered in Primary Registries in the WHO Registry Network and displayed on the WHO ICTRP Search Portal. A UTN should be obtained from http://apps.who.int/trialsearch/utn.aspx early in the history of a trial and should be used every time the trial is identified.
5. Trial acronym	A trial acronym is a word formed from the initial letters of the several words in the name, which identifies the specific trial, e.g. ACT (Angioplasty Compliance Trial). If there is no trial acronym then please leave this field blank.

DATA ITEM	DEFINITION / EXPLANATION
STEP 2: HEALTH CONDITION	
6. Health condition(s) or problem(s) studied *	Primary health condition(s) or problem(s) studied (e.g. depression, breast cancer, medication error). For studies conducted in healthy volunteers, enter the health area under investigation and/or the health condition(s) for which the intervention may be indicated and/or the health condition(s) being prevented.
	Enter only **one** health condition or problem per box. Click 'Add new health condition' to add more boxes. The form allows a maximum of 20 entries (boxes).
7. Condition category and condition code *	Choose the most appropriate condition category (1st level) and condition code (2nd level) from the list. *Note*: the full list is available at the end of this document.
	Click 'Add new condition category/code' to add more boxes if necessary. The form allows a maximum of 3 sets of entries.
STEP 3: INTERVENTION/EXPOSURE	
8. Study type *	Choose the appropriate study type from the list. ☐ Interventional: Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effect on outcomes. Interventions include, but are not restricted to, drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural approaches, process-of-care changes, preventive care, diagnostic procedures. ☐ Observational: A study in which no experimental intervention or treatment is applied. The investigator observes the effect of a risk factor, diagnostic test, or treatment on a particular outcome, e.g. the relationship between smoking and heart attacks. It involves observing without altering or influencing that which is being observed. For example, in an observational study the researchers examine and report on what is happening, without controlling the course of events. Certain outcomes are measured but no attempt is made to affect the outcome (i.e. no treatment or experimental intervention is given).
9. Patient registry (only available when **Observational** is selected for '**8. Study type**')	For observational studies only, check the 'Patient registry' box if this record describes a study that is considered to be a patient registry. A patient registry is an organised system that uses observational methods to collect uniform data (clinical and other) prospectively for a population defined by a particular disorder/disease, condition (including susceptibility to a disorder), or exposure (including products, health care services, and/or procedures) and that serves a predetermined scientific, clinical, or policy purpose. Patient registries may be single purpose or on-going data collection programs that address one or more questions.
10. Target follow-up duration * (only available when **Patient registry** is selected for 9.)	For patient registries, the anticipated time period over which each participant is to be followed. Provide a number and select a unit of time (weeks, months, years).

DATA ITEM	DEFINITION / EXPLANATION
11. Description of intervention(s) / exposure *	Briefly describe the specific intervention(s) being studied. If there are multiple intervention arms, please label with subheadings (e.g. Arm 1, Arm 2, etc.). (*Note*: there is a separate field below for details of comparator/control treatment(s)). Please provide sufficient detail so that information will be meaningful to ANZCTR users. For drug trials: Provide the International Non-proprietary Name (INN) of each drug (not brand/trade names). For an unregistered drug, the generic name, chemical name, or company serial number is acceptable. For each intervention drug, please also specify: • the dose administered, e.g. 5mg once daily; • the duration of administration, e.g. 4 weeks; • the mode of administration, e.g. oral tablet, intravenous infusion. For other non-drug trials: For each intervention, briefly describe: • what it involves; • the frequency and duration of administration, e.g. 1 x 1 hour session per week for 4 weeks; • the mode of administration, e.g. one-on-one consultation, group workshop, online program; • who will be administering the intervention, e.g. dietician, nurse. For all trials: A brief description of any strategies used to monitor adherence to the intervention needs to be included where applicable, e.g. drug tablet return, laboratory tests, daily food diary. Intervention names should be consistent throughout the form. Avoid using alternative intervention names for clarity. For observational studies: Provide a brief description of the condition observed and/or the exposure. The duration of observation must also be described.
12. Intervention code *	Choose the most appropriate intervention code(s) from the list. The form allows a maximum of 3 entries. Click 'Add new Intervention code' to add more boxes. **Note** that only the first 3 codes are available for observational studies. Not applicable: study in which no experimental intervention or treatment is applied. This selection is not available for interventional studies. Diagnosis / prognosis: study designed to evaluate one or more tests aimed at identifying a disease or health condition, or determining a patient's prognosis. Early detection / screening: study that involves the systematic examination of a group of participants, in order to separate well persons from those who have an undiagnosed pathologic condition or who are at high risk. It could also refer to the initial evaluation of an individual, intended to determine suitability for a particular treatment modality or to detect specific markers or characteristics that may require further investigation. Prevention: study designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition. Treatment: drugs: study designed to assess the effect(s) of one or more chemical or biological agents including vaccines.

DATA ITEM	DEFINITION / EXPLANATION
*Intervention code * continued*	Treatment: surgery: study designed to assess the effect(s) of one or more manual or operative surgical techniques, whether in the fields of cosmetic, elective, experimental, plastic, or replacement surgery (performed to diagnose, treat, or prevent disease or other abnormal conditions). Treatment: devices: study designed to evaluate the use of any physical item used in medical treatment whether it be an instrument, piece of equipment, machine, apparatus, appliance, material or other article, and whether it is used alone or in combination with the intention of preventing, diagnosing, treating, and curing a disease or condition. Examples include: artificial limbs, contact lenses, ventilators, catheters, implants, vibration therapy machines. Treatment: other: studies that do not fall under the broad definitions of drug, surgical, or device trials. Examples include interventions such as exercise, physiotherapy, cognitive therapy, special diets, herbal medicines, web-based treatments, motivational classes, music therapy, stem cell interventions. Rehabilitation: studies designed to evaluate one or more interventions which aim to restore the physical or mental health, function and quality of life in participants who have had or are currently suffering from an illness or injury. Rehabilitation may be performed through physical therapy (e.g. physiotherapy, chiropractic) and/or education (e.g. diet and exercise advice/ counselling). Lifestyle: studies designed to investigate the effect of interventions which relate to a way of life or style of living. Interventions may aim to alter the attitudes, habits and values of a person or group, and how these participants cope with their physical, psychological, social, and economic environments on a day-to-day basis. Examples include diet and nutrition plans, exercise or physical activity programs, quit smoking programs. Behaviour: studies designed to assess the effect of interventions which aim to elicit or modify mental or physical actions, responses or conduct in a person or group. Examples of behavioural interventions include cognitive behavioural therapy, exercise behaviour interventions, and breast feeding behavioural interventions. Other interventions: studies that do not fit under any of the above categories. This should only be selected when no other options are adequate. Examples include prayer, singing, driving.
13. Comparator / control treatment *	For controlled trials, the identity of the comparator/control arm should be clear. The comparator/control(s) is/are the treatments against which the study intervention is being compared (e.g. placebo, no treatment, active control). If an active control is used, be sure to provide the specific name of the treatment. For each comparator/control treatment, describe other details as applicable (dose, duration, mode of administration, etc). If the study is uncontrolled then please enter the text 'No control group' or similar.

DATA ITEM	DEFINITION / EXPLANATION
14. Control group *	A 'control' group is the type of treatment to which the intervention is being compared, also known as a 'comparator' group. Choose the most appropriate description of the study's control group from the list. Placebo: an inactive or sham treatment that has no treatment value is given to the control group, such as sugar pill or saline solution. Active: when the control treatment is active. This includes standard care, alternate forms of treatment, no treatment given, or if patients act as their own control (crossover study). Uncontrolled: when there is no control group, as in single group trials. The same intervention is applied to all subjects in the study. Historical: a group of people who received their care in the past, i.e. not at the same time as the people receiving the intervention. This selection is not applicable for randomised controlled trials. The source and time period that historical data was collected needs to be described in the 'Comparator / control treatment' field. Dose comparison: the comparator group receives the same treatment as the intervention group, but in a different dose.
STEP 4: OUTCOMES	
15. Primary outcome(s) and timepoint(s) *	Primary outcome(s) is the outcome(s) which provides the primary measure of the effectiveness (or lack of effectiveness) of the intervention. In many studies, more than one variable is used as a primary outcome measure. The primary outcome should be the outcome used in sample size calculations, or the main outcome(s) used to determine the effect of the intervention(s). Provide specific names of all primary outcomes, one at a time, e.g. '% with Beck depression score > 10' rather than just 'depression'. All outcomes should be provided in an objective form without indicating suspected or hypothesised results, e.g. 'Change in blood glucose' or 'proportion of participants with a reduction in blood glucose' rather than 'reduced blood glucose'. Instrument(s) to be used for the assessment/measurement need to be included / described, e.g. serum assay, MRI scan, 100mm visual analogue scale. If a questionnaire is used, the name of the questionnaire should be provided (if validated) or indicate whether it was designed specifically for the study. For adverse events provide examples of known/possible adverse reactions/events and how they will be assessed. For each outcome provide all timepoints at which it is assessed in the 'Timepoint' box. Timepoints should be specific, for example '7 days post commencement of intervention' rather than just '7 days'. Enter only one primary outcome per box. Click 'Add new primary outcome' to add more boxes if the study has multiple primary outcomes. The form allows a maximum of 3 sets of entries for the primary outcome and timepoint. Examples: *Primary Outcome 1:* all-cause mortality as assessed by data linkage to medical records *Timepoint:* at one year after randomisation *Primary Outcome 2:* mean Beck depression score *Timepoint:* Baseline, and at 6 and 12 weeks after intervention commencement

DATA ITEM	DEFINITION / EXPLANATION
16. Secondary outcome(s) and timepoint(s) *	Secondary outcomes are events, variables, or experiences that are of secondary interest or that are measured at timepoints of secondary interest. A secondary outcome may involve the same event, variable, or experience as the primary outcome, but measured at timepoints other than those of primary interest (e.g. primary outcome: all-cause mortality at 5 years; secondary outcome: all-cause mortality at 1 year, 3 years), or may involve a different event, variable, or experience altogether (e.g. Primary outcome: all-cause mortality at 5 years; Secondary outcome: hospitalisation rate at 5 years). Instrument(s) to be used for the assessment/measurement need to be included / described. For each outcome, also provide all timepoints at which it is assessed in the 'Timepoint' box. Enter only **one** secondary outcome per box. Click 'Add new secondary outcome' to add more boxes if the study has multiple secondary outcomes. The form allows a maximum of 40 sets of entries for the secondary outcome(s) and timepoint(s). Examples: *Secondary Outcome 1:* knee pain assessed using a 100mm Visual Analogue Scale (VAS) *Timepoint:* at 6 months after randomisation *Secondary Outcome 2:* quality of life assessed using the SF-36 Quality of Life Questionnaire *Timepoint:* Baseline, and at 4 and 8 weeks after intervention commencement
STEP 5: ELIGIBILITY	
17. Key inclusion criteria *	Summary of key inclusion criteria of patient characteristics that determine eligibility for participation in the study.
18. Minimum age *	Specify minimum age of eligible study participants. \ Enter the number and choose the appropriate unit from the list. If there is no minimum age limit leave the box for the number blank and select 'No limit' from the unit of measurement list. ☐ Years ☐ Months ☐ Weeks ☐ Days ☐ Hours ☐ No limit
19. Maximum age *	Specify maximum age of eligible study participants. Enter the number and choose the appropriate unit from the list. If there is no maximum age limit leave the box for the number blank and select 'No limit' from the unit of measurement list. ☐ Years ☐ Months ☐ Weeks ☐ Days ☐ Hours ☐ No limit

DATA ITEM	DEFINITION / EXPLANATION
20. Gender *	Choose the appropriate selection for gender of the study's participants. ☐ Males ☐ Females ☐ Both males and females
21. Can healthy volunteers participate? *	Indicate whether healthy volunteers may participate in this study. ☐ Yes ☐ No
22. Key exclusion criteria *	Summary of key exclusion criteria of patient characteristics that determine eligibility for participation in the study. These should not simply be the opposite of the inclusion criteria.
STEP 6: STUDY DESIGN	
23. Purpose of the study * (only available when Interventional is selected for '8. Study type')	Choose the most appropriate purpose of the study from the list. Treatment: study designed to evaluate one or more interventions for treating a disease, syndrome or other health condition(s). Prevention: study designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition. Diagnosis: study designed to evaluate one or more interventions aimed at identifying a disease or health condition. Educational / counselling / training: study designed to assess one or more interventions in an educational, counselling or training environment.
24. Allocation to intervention * (only available when Interventional is selected for '8. Study type')	Choose the appropriate type of allocation to intervention. Randomised controlled trial means that allocation of subjects into different groups (i.e. intervention and control) was random or by a method based on chance. Non-randomised trial means that allocation of subjects into different groups (i.e. intervention and control) is expressly or deliberately done, and is not random or by chance. *Note:* Trials with quasi-randomisation allocation procedures such as allocation by hospital record number, birth date or alternate days of the week, do not qualify as a randomised trial. Therefore, these studies should be classified as non-randomised trials.
25. Allocation concealment (only available when Interventional is selected for '8. Study type')	Only applicable for randomised controlled trials. Allocation concealment means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, to which group the subject would be allocated. Allocation was concealed if it was done by, for example: 1. sealed opaque envelopes 2. numbered containers 3. central randomisation by phone/fax/computer 4. allocation involved contacting the holder of the allocation schedule who was 'off-site' or at central administration site. If concealment was not carried out, the text 'Allocation is not concealed' should be stated for this section.

DATA ITEM	DEFINITION / EXPLANATION
26. Sequence generation (only available when **Interventional** is selected for '**8. Study type**')	Only applicable for randomised controlled trials. This is the method used to create the random order for the allocation of subjects into different groups. Examples of the random order generation include (but are not limited to): 1. Simple randomisation using a randomisation table from a statistic book 2. Simple randomisation using a randomisation table created by computer software (i.e. computerised sequence generation) 3. Simple randomisation using procedures like coin-tossing and dice-rolling 4. Permuted block randomisation 5. Dynamic (adaptive) random allocation methods such as Minimisation If stratified allocation was employed in the study, specify factor(s) used for the stratification. Examples of factors that can be used for stratification include centre, age, gender or previous treatment. Quasi-randomisation allocation procedures or inappropriate randomisation methods such as allocation by hospital record number, birth date or alternate days of the week, do not qualify as a random order generation.
27. Masking / blinding (only available when **Interventional** is selected for '**8. Study type**')	Masking / blinding is when the person in question (participant, therapist/clinician, assessor or data analyst) did not know which group the participant had been allocated to. For trials in which key outcomes are self-reported (e.g. visual analogue scale, pain diary), the assessor is considered to be blinded if the subject was blinded. Open (masking not used) – all involved in the study know the identity of the intervention assignment. Participant, therapist/clinician, assessor and data analyst are not blinded. Blinded (masking used) – when one or more of the parties (participants, therapist/clinician, assessor or data analyst) is/are blinded or unaware of the intervention assignment. If 'Blinded (masking used)' option was chosen above, please tick who is/are blinded (choose all that apply), from the list. ☐ the people receiving the treatment/s (participants) ☐ the people administering the treatment/s (therapist/clinician) ☐ the people assessing the outcomes (assessor) ☐ the people analysing the results/data (data analyst)
28. Assignment (only available when **Interventional** is selected for '**8. Study type**')	Choose the most appropriate description of the study's assignment from the list. Single group: all participants receive the same intervention throughout the study. Trials in which participants are assigned to receiving one of two or more interventions are not single group studies. Crossover trials are not single group studies. Parallel: different groups of participants receive different interventions during the same time span of the study. Crossover: all participants receive all the interventions in random order or in a specific sequence (non-randomised) during the study. They act as their own control. Factorial: participants are randomly allocated to receive either no intervention, one or some interventions, or all interventions combined. For example in a 2x2 factorial trial of diet and exercise for weight loss, participants would be allocated to: diet alone, exercise alone, both diet and exercise, or neither. In this way it is possible to test the independent effects of diet and exercise on the outcome, i.e. weight loss. Other: None of the selections provide an appropriate description of the study's assignment. If 'Other' is selected for the study's assignment, please give a brief description of the study's assignment in the 'Other design features' field below.

DATA ITEM	DEFINITION / EXPLANATION
29. Other design features (only available when **Interventional** is selected for '**8. Study type**')	Briefly describe other design features if 'Other' is selected for Assignment above.
30. Phase	Phases of investigation, usually applied to a drug trial. Not applicable: this selection is for a non-drug trial. Phase 0: includes exploratory, first-in-human trials. Phase 0 trials are also known as human micro-dosing studies and are designed to speed up the development of promising drugs or imaging agents by establishing very early on whether the drug or agent behaves in human subjects as was anticipated from preclinical studies. Exploratory trials are conducted before traditional dose escalation and safety studies and gives no data on safety or efficacy, being by definition a dose too low to cause any therapeutic effect. Phase 1: includes initial study to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients. Trials are often dose ranging/escalating trials which are done to determine the maximum dose of a new medication that can be safely given to a patient. Phase 1/Phase 2: for trials at a combined stage of phases 1 and 2. Phase 2: includes controlled clinical studies conducted to evaluate/test the effectiveness of a new drug/medication or intervention for a particular indication or indications in patients with the disease or condition being studied and to determine the common short-term side effects and risks. Phase 2/Phase 3: for trials at a combined stage of phases 2 and 3. Phase 3: includes expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of a new drug/medication or intervention, including possible adverse reactions. It is also to provide an adequate basis for physician labelling. Phase 3/Phase 4: for trials at a combined stage of phases 3 and 4. Phase 4: post-marketing study to delineate additional information. Trials are done to monitor the toxicity, risks, utility, benefits and optimal use after the efficacy of the drug/medication or intervention has been proven.
31. Type of endpoint(s) (only available when **Interventional** is selected for '**8. Study type**')	Choose the most appropriate study endpoint(s) from the list. Safety: to show if the intervention is safe under conditions of proposed protocol/use Efficacy: to measure an intervention's influence on a disease or health condition Safety/efficacy: combination of safety and efficacy Bio-equivalence: scientific basis for comparing generic and brand name drugs Bio-availability: rate and extent to which a drug is absorbed or otherwise available to the treatment site in the body Pharmacokinetics: the action of a drug in the body over a period of time including the process of absorption, distribution and localisation in tissue, biotransformation, and excretion of the compound Pharmacodynamics: action of drugs in living systems Pharmacokinetics / pharmacodynamics: combination of pharmacokinetics and pharmacodynamics

DATA ITEM	DEFINITION / EXPLANATION
32. Statistical methods / analysis	Provide a brief description of how the number of participants needed to achieve study objectives was determined, including clinical and statistical assumptions supporting any sample size calculations. A brief summary of the statistical methods and/or analysis plan to be used to evaluate the data also need to be provided.
33. Purpose (only available when **Interventional** is selected for '**8. Study type**')	If the study is an observational study, choose the most appropriate purpose of the study from the list. Natural history: study designed to investigate a disease or condition through observation under natural conditions (i.e. without intervention) Screening: study designed to assess or examine persons or groups in a systematic way to identify specific markers or characteristics (e.g. for eligibility for further evaluation) Psychosocial: study designed to observe the psychosocial impact of natural events
34. Duration (only available when **Interventional** is selected for '**8. Study type**')	If the study is an observational study, choose the most appropriate duration of the study from the list. Longitudinal: study in which participants are evaluated over long period of time, typically months or years. Cross-sectional: study in which participants are evaluated at a particular point in time.
35. Selection (only available when **Interventional** is selected for '**8. Study type**')	If the study is an observational study, choose the most appropriate sample selection of the study from the list. Convenience sample: participants or populations are selected at the convenience of the investigator or primarily because they were available at a convenient time or place. The investigators make little or no effort to ensure that the sample is an accurate representation of some larger group or population. Defined population: participants or populations are selected based on predefined criteria. Random sample: participants or populations are selected by chance in a manner such that all samples of a population have an equal chance of being selected. Case control: participants or populations are selected to match control participants or populations in all relevant factors except for the disease; only the case participants or populations have the disease.
36. Timing (only available when **Interventional** is selected for '**8. Study type**')	If the study is an observational study, choose the most appropriate timing of the study from the list. Retrospective: study that observes events in the past Prospective: study that observes events in real time (may also occur in future) Both: study that combines retrospective and prospective observation

DATA ITEM	DEFINITION / EXPLANATION
STEP 7: RECRUITMENT	
37. **Recruitment status** *	Choose the most appropriate description of the study's recruitment status at the time of registration from the list. Not yet recruiting: participants are not yet being recruited Recruiting: open for recruitment and the first participant has been enrolled Enrolling by invitation: participants were/are being/will be invited to participate from a predetermined population Active, not recruiting: study is ongoing (i.e. participants are being treated or examined), but participants are not currently being recruited or enrolled Closed: follow-up continuing: closed to recruitment of participants and follow-up is still continuing Closed: follow-up complete: closed to recruitment of participants and follow-up is complete Completed: closed to recruitment of participants and data analysis complete Withdrawn: study halted prematurely, prior to enrolment of first participant Suspended: there is a temporary halt in recruitment and enrolment but potentially will resume Terminated: recruiting or enrolling participants has halted prematurely and will not resume; participants are no longer being examined or treated
38. **Anticipated date of first participant enrolment** *	Estimated enrolment date (dd/mm/yyyy) of the first participant. For studies involving secondary analysis of data (e.g. meta-analysis), please specify the anticipated start date of data collection.
39. Date of first participant enrolment	Actual enrolment date (dd/mm/yyyy) of the first participant. For studies involving secondary analysis of data (e.g. meta-analysis), please specify the actual start date of data collection.
40. Anticipated date of last participant enrolment	The anticipated date (dd/mm/yyyy) that recruitment into the study will cease. For studies involving secondary analysis of data (e.g. meta-analysis), please specify the anticipated date that data collection will cease.
41. Actual date of last participant enrolment	The actual date (dd/mm/yyyy) that the final participant was enrolled into the study. For studies involving secondary analysis of data (e.g. meta-analysis), please specify the actual date that data collection ceased.
42. **Target sample size** *	The total number of participants the investigators plan to enrol before closing the trial to new participants. *Note:* This is a 'number only' field.
43. Actual sample size	The total number of participants actually enrolled into the study. This is mandatory for studies which have completed recruitment. *Note:* This is a 'number only' field.
44. Recruiting in Australia	Tick this box if your study is/was or will be recruiting from within Australia.
45. **Recruitment states** * **(mandatory when 'Recruiting in Australia' is selected for 44)**	Tick the boxes corresponding to all recruiting states within Australia. ☐ NSW ☐ VIC ☐ QLD ☐ ACT ☐ NT ☐ SA ☐ TAS ☐ WA

DATA ITEM	DEFINITION / EXPLANATION
46. Recruitment hospitals (only available when '**Recruiting in Australia**' is selected for **44**)	Type the full name of the recruiting hospital(s), and click on the matching option that appears on the list to add it to this form (e.g. instead of 'RPA', please enter 'Royal Prince Alfred Hospital'). If the site you wish to enter does not appear, then please email us at info@actr.org.au.
47. 47. Recruitment postcode(s) (only available when '**Recruiting in Australia**' is selected for **44**)	Type the four-digit postcode for the suburb where recruitment will occur, and click on the matching option that appears on the list to add it to this form.
48. Recruitment countries outside Australia	Tick this box if your study is/was or will be recruiting from countries outside Australia. Select the appropriate recruitment country from the drop-down list and enter the state/ province of recruitment (free text). If there is more than one country of recruitment outside Australia, please click on the 'Add new country' button.
STEP 8: FUNDING & SPONSORS	
49. Funding source(s) *	Major source(s) of monetary or material or infrastructure support for the study. Funding type: choose the most appropriate type from the list. ☐ Government body ☐ Hospital ☐ University ☐ Commercial sector/industry ☐ Charities/societies/foundations ☐ Other collaborative groups ☐ Self funded/unfunded ☐ Other *Note:* The selection 'Self funded/ unfunded' applies to studies which are either funded by an individual person or not funded at all. Name of funding source: enter only one per box. Address of funding source: enter the full address of the named funding source, including street number and name, suburb/town/ city, postcode and state/province (where applicable). Alternatively PO Box/Locked Bag/Private Bag addresses are also permitted. Country of funding source: choose the appropriate country from list. Click 'Add new funding source' to add more boxes if the study has multiple funding sources. The form allows maximum of 20 sets of entries.

DATA ITEM	DEFINITION / EXPLANATION
50. Primary sponsor *	The individual, organisation, group or other legal person taking on responsibility for securing the arrangements to initiate and/or manage a study, including arrangements to ensure that the design of the study meets appropriate standards and to ensure appropriate conduct and reporting. The primary sponsor is normally the main applicant or principle investigator for regulatory authorisation or funding to begin the study. The primary sponsor is responsible for ensuring that the trial is properly registered. It may or may not be the main funder. Primary sponsor type: choose the most appropriate type from the list. ☐ Government body ☐ Hospital ☐ University ☐ Commercial sector/industry ☐ Charities/societies/foundation ☐ Other collaborative groups ☐ Individual ☐ Other Name of primary sponsor: enter only one name of the study's primary sponsor. Address of primary sponsor: enter the full address of the primary sponsor, including work organisation/affiliation, street number and name, suburb/town city, postcode and state/province (where applicable). Alternatively PO Box/Locked Bag/Private Bag addresses are also permitted. Country of primary sponsor: choose the appropriate country from list. The form allows only one entry for primary sponsor. For additional sponsors, please refer to the secondary sponsor(s) section.
51. Secondary sponsor(s) *	Additional individuals, organisations or other legal persons, if any, that have agreed with the primary sponsor to jointly take on responsibilities of sponsorship. A secondary sponsor may have agreed to form a group with the primary sponsor in which the responsibilities of sponsorship are allocated among the members of the group and/or to act as the sponsor's legal representative in relation to some or all of the trial sites. A secondary sponsor may take responsibility for the accuracy of trial registration information submitted. *Note:* The primary and secondary sponsors should not be the same. Secondary sponsor type: choose the most appropriate type from the list. ☐ Government body ☐ Hospital ☐ University ☐ Commercial sector/industry ☐ Charities/societies/foundations ☐ Other collaborative groups ☐ Individual ☐ Other Name of secondary sponsor: enter only one name of the study's secondary sponsor per box. Address of secondary sponsor: enter the full address of the named sponsor, including work organisation/affiliation, street number and name, suburb/town city, postcode and state/province (where applicable). Alternatively PO Box/Locked Bag/Private Bag addresses are also permitted. Country of secondary sponsor: choose the appropriate country from list. Click 'Add new secondary sponsor' to add more boxes if the study has multiple secondary sponsors. The form allows maximum of 20 sets of entries for the secondary sponsor(s).

DATA ITEM	DEFINITION / EXPLANATION
52. Other collaborator(s)	Additional individuals, organisations or other legal persons, if any, that have agreed with the primary sponsor to jointly take on responsibilities of sponsorship. A collaborator may have agreed to form a group with the primary sponsor in which the responsibilities of sponsorship are allocated among the members of the group and/or to act as the sponsor's legal representative in relation to some or all of the trial sites. Collaborator type: choose the most appropriate type from the list. ☐ Government body ☐ Hospital ☐ University ☐ Commercial sector/industry ☐ Charities/societies/foundations ☐ Other collaborative groups ☐ Individual ☐ Other Name of collaborator: enter only one name of the study's collaborator per box. Address of collaborator: enter the full address of the named collaborator, including work organisation/affiliation, street number and name, suburb/town city, postcode and state/province (where applicable). Alternatively PO Box/Locked Bag/Private Bag addresses are also permitted. Country of collaborator: choose the appropriate country from list. Click 'Add new other collaborator' to add more boxes if necessary. The form allows maximum of 20 sets of entries.
STEP 9: ETHICS & SUMMARY	
53. Ethics application status *	Select the appropriate option from the list. Not yet submitted: You intend to submit to at least one ethics committee, but have not yet done so. *Note:* If this option is selected it is mandatory to provide the date which the trial's primary sponsor or their representatives intend to submit an ethics application in the 'Submit date' field. Submitted, not yet approved: You have submitted an application to at least one ethics committee, but have not yet received approval. *Note:* If this option is selected it is mandatory to provide the date when the ethics application was submitted in the 'Submit date' field. Approved: You have received full ethical approval for this study from at least one ethics committee. *Note:* If this option is selected it is mandatory to provide the date when the ethics approval was granted in the 'Approval date' field. Not required: Ethics approval not required for this study. *Note:* If this option is selected it is mandatory to provide the reason(s) why ethics approval is not required in the 'Public notes' field on page 9 of the form.

DATA ITEM	DEFINITION / EXPLANATION
54. Ethics committee details	Please also provide the following information: Name of ethics committee: enter only one per box. Address of ethics committee: enter the full address of the named ethics committee, including work organisation/affiliation, street number and name, suburb/town city, postcode and state/province (where applicable). Alternatively PO Box/Locked Bag/Private Bag addresses are also permitted. Country of ethics committee: choose the appropriate country from list. Submit date: enter the date that the ethics committee application was submitted, or is planned to be submitted. *Note:* This field is mandatory when either 'Not yet submitted' or 'Submitted, not yet approved' has been selected for ethics application status above. Approval date: enter the date that the ethics committee application was approved. *Note:* This field is mandatory when 'Approved' has been selected for ethics application status above. Approval ID: enter the approval ID assigned to the ethics application by the ethics committee at the time of granting approval. Click 'Add new ethics committee' to add more boxes if the study has received approval from multiple ethics committees. The form allows a maximum of 50 sets of entries.
55. Brief summary *	Short description of the primary purpose of the study, including a brief statement of the study hypothesis, intended for the lay public. Ensure that the information provided in the brief summary is consistent with study design, intervention description and study outcomes provided in the form.
56. Trial website	If the study has a trial website, enter the web address/URL (Uniform Resource Locator) in this section. Otherwise, please leave blank.
57. Trial related presentations / publication list	If the study has a list of presentations/publications, enter the full citations in this section. Otherwise please leave blank. Example: Smith J. (2012) The effect of a very low energy diet on weight loss in obese women. *JAMA 3(12) 44-52.*
58. Public notes	This field is for any extra, miscellaneous text you'd like included within this trial registration which is not relevant elsewhere on this form. Anything placed here WILL be publicly viewable.
59. Private notes	This field is for any extra, miscellaneous text to be included within this trial registration not relevant elsewhere on this form. Anything placed here will NOT be publicly viewable, but will be available to ANZCTR staff.
60. 60. Attachments	Use this optional section to upload any relevant documents (e.g. trial protocol, ethics approval forms, blank clinical record forms). Files must be in PDF or Word format and clearly labelled. Maximum size is 15MB per file. It is the responsibility of the registrant to ensure that any uploaded documents comply with copyright regulations. *Please note* that any files attached WILL be publicly available via your trial's ANZCTR registration record.

DATA ITEM	DEFINITION / EXPLANATION
STEP 10: CONTACTS	
Note: For each of the contact sections below: Address should include work organisation/affiliation, street number and name, suburb/town city, postcode and state/province (where applicable). Alternatively PO Box/Locked Bag/Private Bag addresses are also permitted. Telephone and fax numbers should be entered in the format +country code, area code, number, for example: +61 2 9562 5333 (for Sydney, Australia) +1 310 8298781 (for Santa Monica CA, USA)	
61. Principal investigator *	Title, name, address, country, telephone number and email address of the principal investigator of the study. Professional contact details should be provided.
62. Contact person for public queries *	Title, name, address, telephone number and email address of the contact person who will respond to general queries, including information about current recruitment status. Only professional contact details should be provided.
63. Contact person for scientific queries *	Title, name, address, telephone number and email address of the contact person for scientific inquiries about the trial (e.g. principal investigator, medical director for the study). For a multi-centre study, enter the contact information for the lead principal investigator or overall medical director. Only professional contact details should be provided.
64. Contact person responsible for updating information	Title, name, address, telephone number and email address of the person to contact for updating trial information after registration with the ANZCTR. Only professional contact details should be provided.

Appendix 5. ANZCTR condition categories and codes

Categories and codes have been adapted to suit Australian needs from the Health Research Classification System developed by the UK Clinical Research Collaboration (see www.ukcrc.org/research-coordination/health-research-classification-system/).

CONDITION CATEGORY (LEVEL 1)	CONDITION CODE (LEVEL 2)
Alternative and complementary medicine	Spiritual care
	Herbal remedies
	Other alternative and complementary medicine
Anaesthesiology	Anaesthetics
	Pain management
	Other anaesthesiology
Blood	Haematological diseases
	Anaemia
	Clotting disorders
	Normal development and function of platelets and erythrocytes
	Other blood disorders
Cancer	Any
	Biliary tree (gall bladder and bile duct)
	Bladder – transitional cell cancer
	Bone
	Bowel – anal
	Bowel – back passage (rectum) or large bowel (colon)
	Bowel – small bowel (duodenum and ileum)
	Brain
	Breast
	Cervical (cervix)
	Children's – brain
	Children's – leukaemia & lymphoma
	Children's – other
	Head and neck
	Hodgkin's
	Kidney
	Leukaemia – acute leukaemia
	Leukaemia – chronic leukaemia
	Liver
	Lung – mesothelioma
	Lung – non small cell

CONDITION CATEGORY (LEVEL 1)	CONDITION CODE (LEVEL 2)
Cancer continued	Lung – small cell
	Lymphoma (non Hodgkin's lymphoma) – high grade lymphoma
	Lymphoma (non Hodgkin's lymphoma) – low grade lymphoma
	Malignant melanoma
	Myeloma
	Neuroendocrine tumour (NET)
	Non-melanoma skin cancer
	Oesophageal (gullet)
	Ovarian and primary peritoneal
	Pancreatic
	Penile (penis)
	Prostate
	Sarcoma (also see 'Bone') – soft tissue
	Stomach
	Testicular
	Thrombocythaemia
	Thyroid
	Womb (uterine or endometrial cancer)
	Other cancer types
Cardiovascular	Coronary heart disease
	Diseases of the vasculature and circulation including the lymphatic system
	Hypertension
	Other cardiovascular diseases
	Normal development and function of the cardiovascular system
Diet and nutrition	Obesity
	Other diet and nutrition disorders
Ear	Deafness
	Other ear disorders
	Normal ear development and function
Eye	Diseases / disorders of the eye
	Normal eye development and function
Infection	Acquired immune deficiency syndrome (AIDS / HIV)
	Sexually transmitted infections
	Other infectious diseases
	Studies of infection and infectious agents

CONDITION CATEGORY (LEVEL 1)	CONDITION CODE (LEVEL 2)
Inflammatory and immune system	Rheumatoid arthritis
	Connective tissue diseases
	Autoimmune diseases
	Allergies
	Other inflammatory or immune system disorders
	Normal development and function of the immune system
Injuries and accidents	Fractures
	Poisoning
	Burns
	Other injuries and accidents
Human genetics and inherited disorders	Down's syndrome
	Cystic fibrosis
	Other human genetics and inherited disorders
Mental health	Depression
	Schizophrenia
	Psychosis and personality disorders
	Addiction
	Suicide
	Anxiety
	Eating disorders
	Learning disabilities
	Autistic spectrum disorders
	Other mental health disorders
	Studies of normal psychology, cognitive function and behaviour
Metabolic and endocrine	Diabetes
	Thyroid disease
	Metabolic disorders
	Other metabolic disorders
	Other endocrine disorders
	Normal metabolism and endocrine development and function
Musculoskeletal	Osteoporosis
	Osteoarthritis
	Other muscular and skeletal disorders
	Normal musculoskeletal and cartilage development and function

CONDITION CATEGORY (LEVEL 1)	CONDITION CODE (LEVEL 2)
Neurological	Dementias
	Transmissible spongiform encephalopathies
	Parkinson's disease
	Neurodegenerative diseases
	Alzheimer's disease
	Epilepsy
	Multiple sclerosis
	Other neurological disorders
	Studies of the normal brain and nervous system
Oral and gastrointestinal	Inflammatory bowel disease
	Crohn's disease
	Other diseases of the mouth, teeth, oesophagus, digestive system including liver and colon
	Normal oral and gastrointestinal development and function
Physical medicine / rehabilitation	Physiotherapy
	Speech therapy
	Occupational therapy
	Other physical medicine / rehabilitation
Public health	Epidemiology
	Health promotion/education
	Health service research
	Other public health
Renal and urogenital	Kidney disease
	Pelvic inflammatory disease
	Other renal and urogenital disorders
	Normal development and function of male and female renal and urogenital system

CONDITION CATEGORY (LEVEL 1)	CONDITION CODE (LEVEL 2)
Reproductive health and childbirth	Fertility including in vitro fertilisation
	Contraception
	Abortion
	Fetal medicine and complications of pregnancy
	Normal pregnancy
	Mammary gland development
	Menstruation and menopause
	Breast feeding
	Antenatal care
	Childbirth and postnatal care
	Complications of newborn
	Other reproductive health and childbirth disorders
Respiratory	Asthma
	Chronic obstructive pulmonary disease
	Sleep apnoea
	Other respiratory disorders / diseases
	Normal development and function of the respiratory system
Skin	Dermatological conditions
	Normal skin development and function
	Other skin conditions
Surgery	Surgical techniques
	Other surgery
Stroke	Ischaemic
	Haemorrhagic
Other	Conditions of unknown or disputed aetiology (such as chronic fatigue syndrome/ myalgic encephalomyelitis)
	Research that is not of generic health relevance and not applicable to specific health categories listed above

References

1. MTPConnect. Clinical Trials in Australia: The economic profile and competitive advantage of the sector. 2017: available at https://www.mtpconnect.org.au/clinicaltrials [accessed 6 December 2017].
2. Austrade. Clinical Trials Capability Report. 2015: available at https://www.austrade.gov.au/ArticleDocuments/2814/Clincal-Trials-Capability-Report.pdf.aspx [accessed 6 December 2017].
3. Medicines Australia. Keeping clinical trials in Australia: why action is needed now. 2011: available at http://medicinesaustralia.com.au/files/2011/02/Occasional-Paper-3-Clinical-Trials.pdf [accessed 6 December 2017].
4. Australian Commission on Safety and Quality in Health Care. Economic evaluation of investigator-initiated clinical trials conducted by networks: Final report. 2017: available at https://www.safetyandquality.gov.au/publications/economic-evaluation-of-investigator-initiated-clinical-trials-conducted-by-networks/ [accessed 6 December 2017].
5. KPMG. NIHR Clinical Research Network: Impact and Value Assessment, Final Report. 2016: available at https://www.nihr.ac.uk/life-sciences-industry/documents/NIHR%20CRN%20Impact%20and%20Value%20FINAL%20REPORT_vSTC_160908_FOR%20EXTERNAL%20USE.pdf [accessed 6 December 2017].
6. Downing A, Morris EJ, Corrigan N, Sebag-Montefiore D, Finan PJ, Thomas JD, et al. High hospital research participation and improved colorectal cancer survival outcomes: a population-based study. Gut 2017;66(1):89-96.
7. Majumdar SR, Roe MT, Peterson ED, Chen AY, Gibler W, Armstrong PW. Better outcomes for patients treated at hospitals that participate in clinical trials. Archives of Internal Medicine 2008;168(6):657-62.
8. Ozdemir BA, Karthikesalingam A, Sinha S, Poloniecki JD, Hinchliffe RJ, Thompson MM, et al. Research Activity and the Association with Mortality. PLoS One 2015;10(2):e0118253.
9. Krzyzanowska MK, Kaplan R, Sullivan R. How may clinical research improve healthcare outcomes? Annals of Oncology 2011;22(Suppl_7):vii10-vii5.
10. Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. The Lancet 2009;374(9683):86-9.
11. Ghersi D, Berlin J, Askie L. Chapter 19: Prospective meta-analysis. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. Available from http://handbook.cochrane.org.
12. Song F, Parekh-Bhurke S, Hooper L, Loke YK, Ryder JJ, Sutton AJ, et al. Extent of publication bias in different categories of research cohorts: a meta-analysis of empirical studies. BioMed Central Medical Research Methodology 2009;9(1):79.
13. Simes RJ. Publication bias: the case for an international registry of clinical trials. Journal of Clinical Oncology 1986;4(10):1529-41.
14. Chan A, Hrobjartsson AH, Haahr MT, Gotzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials. Comparison of protocols to published articles. Journal of the American Medical Association 2004;291(20):2457-65.
15. Dear RF, Barratt AL, Askie LM, Butow PN, McGeechan K, Crossing S, et al. Impact of a cancer clinical trials web site on discussions about trial participation: a cluster randomized trial. Annals of Oncology 2012;23(7):1912-8.
16. Lam J, Lord SJ, Hunter KE, Simes RJ, Vu T, Askie LM. Australian clinical trial activity and burden of disease: an analysis of registered trials in National Health Priority Areas. Medical Journal of Australia 2015;203(2):97-101.
17. The Reward Alliance. Funders roles in implementation: A workshop held at the EVIR meeting June 1st 2017: available at https://publicaties.zonmw.nl/health-funders-forum/ [accessed 5 December 2017].
18. World Medical Association. Declaration of Helsinki: Ethical principles for medical research involving human subjects. 2013: available at https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ [accessed 6 December 2017].
19. DeAngelis C, Drazen J, Frizelle F, Haud C, Hoey J, Horton R. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. New England Journal of Medicine 2004;351:1250-1.
20. Taichman DB, Sahni P, Pinborg A, Peiperl L, Laine C, James A, et al. Data Sharing Statements for Clinical Trials – A Requirement of the International Committee of Medical Journal Editors. New England Journal of Medicine 2017;376(23):2277-9.
21. Australian Government. 2016 National Research Infrastructure Roadmap. 2016: available at https://www.education.gov.au/2016-national-research-infrastructure-roadmap [accessed 3 December 2017].
22. Australian Institute of Health and Welfare and Commonwealth Department of Health and Family Services 1997. First report on National Health Priority Areas 1996. AIHW Cat. No. PHE 1. Canberra: AIHW and DHFS.
23. Begg S, Vos T, Barker B, Stevenson C, Stanley L, Lopez AD. The burden of disease and injury in Australia 2003. PHE 82 Canberra: AIHW: 2007.
24. World Health Organization: International Clinical Trials Registry Platform (ICTRP). WHO Registry Criteria, VersioN 2.1 APRIL 2009: available at http://www.who.int/ictrp/network/criteria_summary/en/ [accessed 14 November 2017].