



The Clinical Trials Action Group

(Of the Pharmaceutical Industry Working Group (PIWG))

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Novartis Pharmaceuticals Australia



The Clinical Trials Action Group

■ Agenda

• Background

- How did the CTAG come about?
 - Pharmaceuticals Industry Council (PIC)
 - » R&D Taskforce (RDTF)
 - Pharmaceutical Industry Strategy Group (PISG)
 - Pharmaceutical Industry Working Group (PIWG)
 - » Clinical Trial Action Group (CTAG)
- Changing face of global drug development
- What does Australia have to lose?

• CTAG

- Terms of Reference
- Submissions
- Process & Report

The Clinical Trials Action Group

■ My Background

- Hospital Pharmacist
 - Mid1980's - Oncology/BMTU Pharmacist, SVH, Sydney
- Global Clinical Drug Development
 - Late 1980's - CRA, global pharma then global CRO
 - Early 1990's - CRM, global CRO
 - Rest 1990's - Managing Director, global CRO, Australia and Asia
 - So far 2000's - CRM then Clinical Quality and Training, Novartis
- Industry advocate for clinical research in Australia
 - PIC RDTF founding Chair
 - Member NSW Health Reference group for streamlined ethical approval
 - Member PISG
 - Member CTAG

The Clinical Trials Action Group

- How did CTAG come about?
 - Pharmaceutical Industry Action Agenda (PIAA)
 - Commenced 2002 with 3 year life
 - Joint initiative
 - » Commonwealth Government (Industry & Health)
 - » “pharmaceutical industry”
 - “pharmaceutical industry”:
 - Medicines Australia, AusBiotech, GMiA
 - Innovative (pharma/biotech) & generic manufacturers
 - Research institutions
 - Biomedical research
 - Development firms & related services

The Clinical Trials Action Group

- How did CTAG come about?
 - Pharmaceuticals Industry Council (PIC)
 - Formed 2006 as follow-on from PIAA
 - “pharmaceutical industry” assume responsibility for agenda
 - Peak body of peak bodies + DIISR
 - PIC Aim
 - Double Australia’s share of the global pharmaceuticals industry by 2012 through the collaborative efforts of the industry, government and research

The Clinical Trials Action Group

- PIC Research & Development Taskforce (RDTF)
 - Established May 2004 under PIC predecessor
 - Ensure the regulatory & clinical trial environment in Australia is Globally Competitive
 - Key focus:
 - Four Pillar Model - Quality, Timeliness, Capacity (Recruitment), Value
 - National, streamlined approaches
 - Single ethics/scientific review – NSW, Vic, Qld, HoMER
 - simplify adverse event reporting to HRECs
 - simplify contracts - MA CTRA
 - Increase dialogue with key stakeholders
 - around Australia's global competitiveness, to facilitate change for the better
 - Gather data on value of clinical trials to Australia
 - Lobby for Government to lead coordinated & urgent action

The Clinical Trials Action Group

- Pharmaceutical Industry Strategy Group (PISG)
 - 2008 formed by Minister Carr and managed by DIISR
 - 23 mostly Managing Directors of MNC, Biotech, Generics, CSL
 - January 2009 PISG Report released: www.innovation.gov.au/pisg
 - Process highlighted need for greater transparency on value of trials to Australia

- Clinical trial recommendations:
 2. Accelerate implementation of national streamlined ethical approval process for multicentre clinical trials
 3. Accelerate implementation of e-health initiatives:
 - ensure electronic medical records in hospitals meet industry needs and
 - allow remote access for industry monitors
 4. Establish coordinated national patient referral networks, especially in therapeutic areas of high trial activity

The Clinical Trials Action Group

- **Pharmaceutical Industry Working Group (PIWG)**
 - PIC + Federal Ministers for Industry & Health + Others (eg NHMRC)
 - Established under previous federal government and continued
 - Meets approximately 3 times per year
 - Allows for direct dialogue over key issues
 - PIC, Industry or Health can put forward agenda items
 - PIC RDTF sought action to improve Australia's Global Competitiveness as follow on to PISG report

- **PIWG Clinical Trials Action Group**
 - Ministers Carr and Roxon announced following September 2009 PIWG meeting
 - Terms of reference related to increasing clinical trials in Australia
 - More details to follow

Global Clinical Trials

Making Australia More Competitive

Changing global environment for drug development

- Attrition of new drug candidates continues to increase
- More data needed to get drugs approved
 - Global tightening of regulatory policy
 - Society expectation of more effective and safer medicines
 - Increasing trend towards personalised medicine (biomarkers)
- Rapid escalation of the costs of R&D
- Companies face significant revenue cliffs on patent loss of block busters (GFC only one factor)
- Increasingly difficult environment for reimbursement

Global Clinical Trials

Making Australia More Competitive

Changing global environment for drug development

- **Impact:**

- Trial allocation driven by productivity metrics
 - Timeliness, Recruitment Capacity, Value (Cost), Quality
- Drive for productivity gains in clinical development
 - EDC, reduce SDV, streamline processes, reduce recruitment timelines
 - Target productivity gains in order of 10-20% per annum

Global Clinical Trials

Making Australia More Competitive

Changing global environment for drug development

■ Impact:

- Rising contribution of new markets/locations to global data pack
 - Rapid rise in less than 5 years (from less than 10% to 30-40% of patients)
 - Difficult to differentiate on basic quality (ICH GCP)
- Decreasing contribution of traditional markets/locations
 - Traditional contributors are now key competitors
 - Australia's competition is not China, India, Russia, Brazil
 - Example: Pfizer global rationalisation hits Australia, Western Europe

Global Clinical Trials

Making Australia More Competitive

Changing global environment for drug development

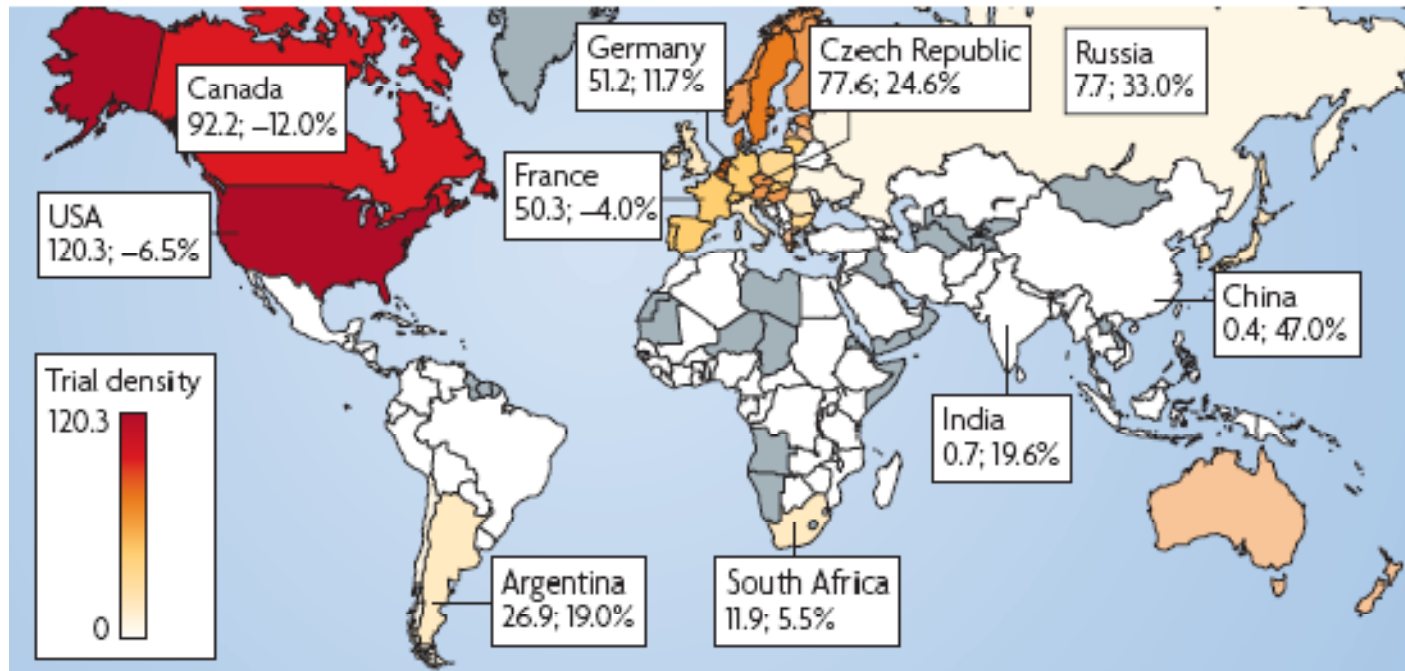


Figure 1 | Density of actively recruiting clinical sites of biopharmaceutical clinical trials worldwide. Density is in per country inhabitant (in millions; based on 2005 population censuses); darker orange/red denotes a higher density. The trial density and average relative annual growth rate in percent is shown for selected countries. The countries in grey had no actively recruiting biopharmaceutical clinical trial sites as of 12 April 2007.

Thiers et al, Nature Reviews Drug Discovery, Nov 2, 2007 (period 2005 – 2007)

Global Clinical Trials

Making Australia More Competitive

Changing global environment for drug development

- Decreased reliance on USA and Western Europe
 - *The proportion of principal investigators - the lead researchers on a trial - registered with the US Food & Drug Administration (FDA) but based outside the US and western Europe rose from 5 per cent in 1997 to 29 per cent last year (2007). The fastest growth in the past five years has come from India, China, Russia and Argentina.**
- Future R&D must see increased productivity
 - *Even allowing for inflation, the industry was investing twice as much in R&D in 2006 as it was a decade earlier but only producing two-fifths of the new medicines it then produced ***

* Financial Times (January 29, 2008)

** PriceWaterHouseCoopers (2008): The changing dynamics of pharma outsourcing in Asia: Are you readjusting your sights?

Global Clinical Trials

Making Australia More Competitive

Australia's Scorecard (X = under threat):

X Timeliness

- Rapid start up and rapid patient recruitment

X Recruitment Capacity

- Reliably recruit patients required for trials, size of patient contribution

X Value

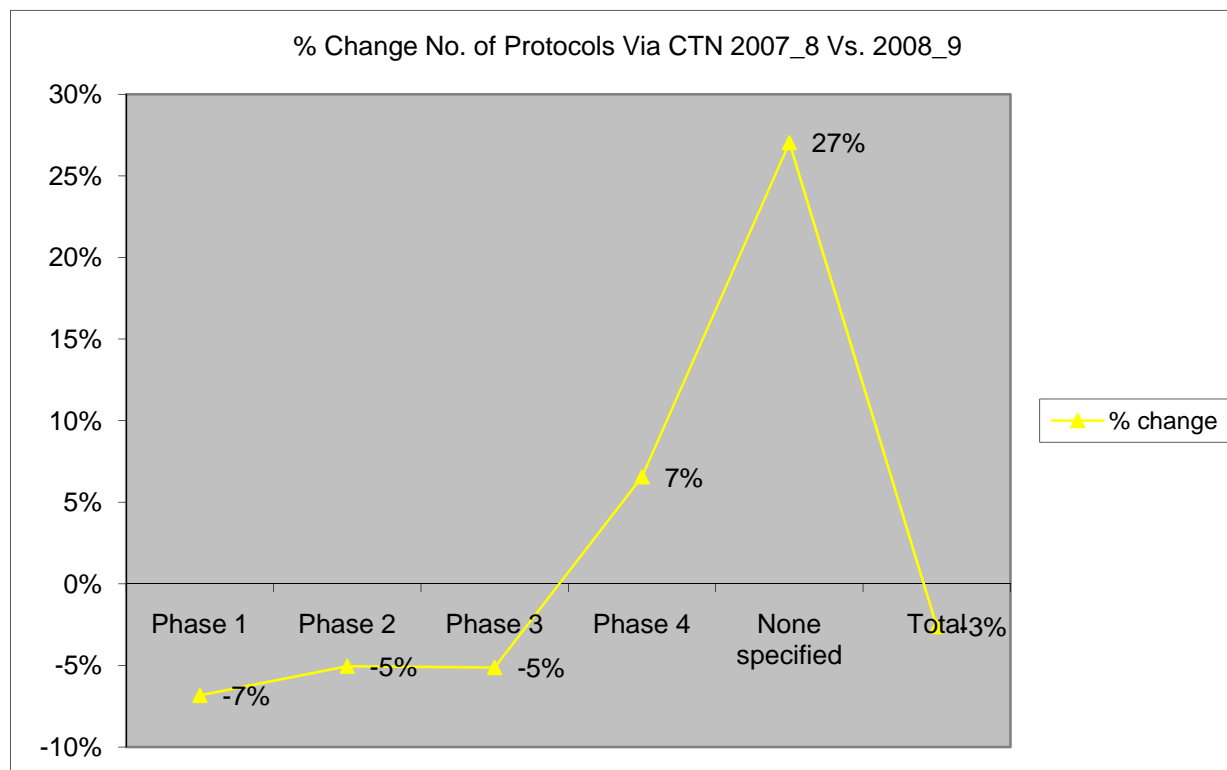
- cost (per patient including all labs), efficiency (pts/site; pts/CRA)

✓ Quality

- ICH Good Clinical Practice, medical expertise, translational expertise

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Making Australia More Competitive



Number of New Protocols Notified by Phase.

	Phase 1	Phase 2	Phase 3	Phase 4	None specified	Total
Figures for 01/07/2007 to 30/06/2008:	117	198	273	61	37	686
Figures for 01/07/2008 to 30/06/2009:	109	188	259	65	47	668
% change	-7%	-5%	-5%	7%	27%	-3%

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- **Opportunities – not all doom and gloom !**
 - Early Phase (esp Phase I/II)
 - Translational medicine/biomarkers/tissue banks
 - E-Health (short term and long term)
 - Coordinated action for Phase II/III
 - to regain speed and reproducibility of start-up,
 - maximise recruitment with the population we have
 - can we find the answer in primary care setting?
 - include regional sites cost effectively?
 - make the most of the trial networks that exist?
 - niche populations eg paediatrics
 - improve cost competitiveness with like countries

Global Clinical Trials

Making Australia More Competitive

What value would Australia lose?

- Significant trial activity and investment
 - \$540 Million into health system per annum (best estimate)
 - ABS 2006-07 and MA Economic Survey*
 - More than 1,097 trials/projects
 - More than \$260 Million into health system per annum (only n=23)
 - PIC RDTF Benchmark Data 2008 Activity**

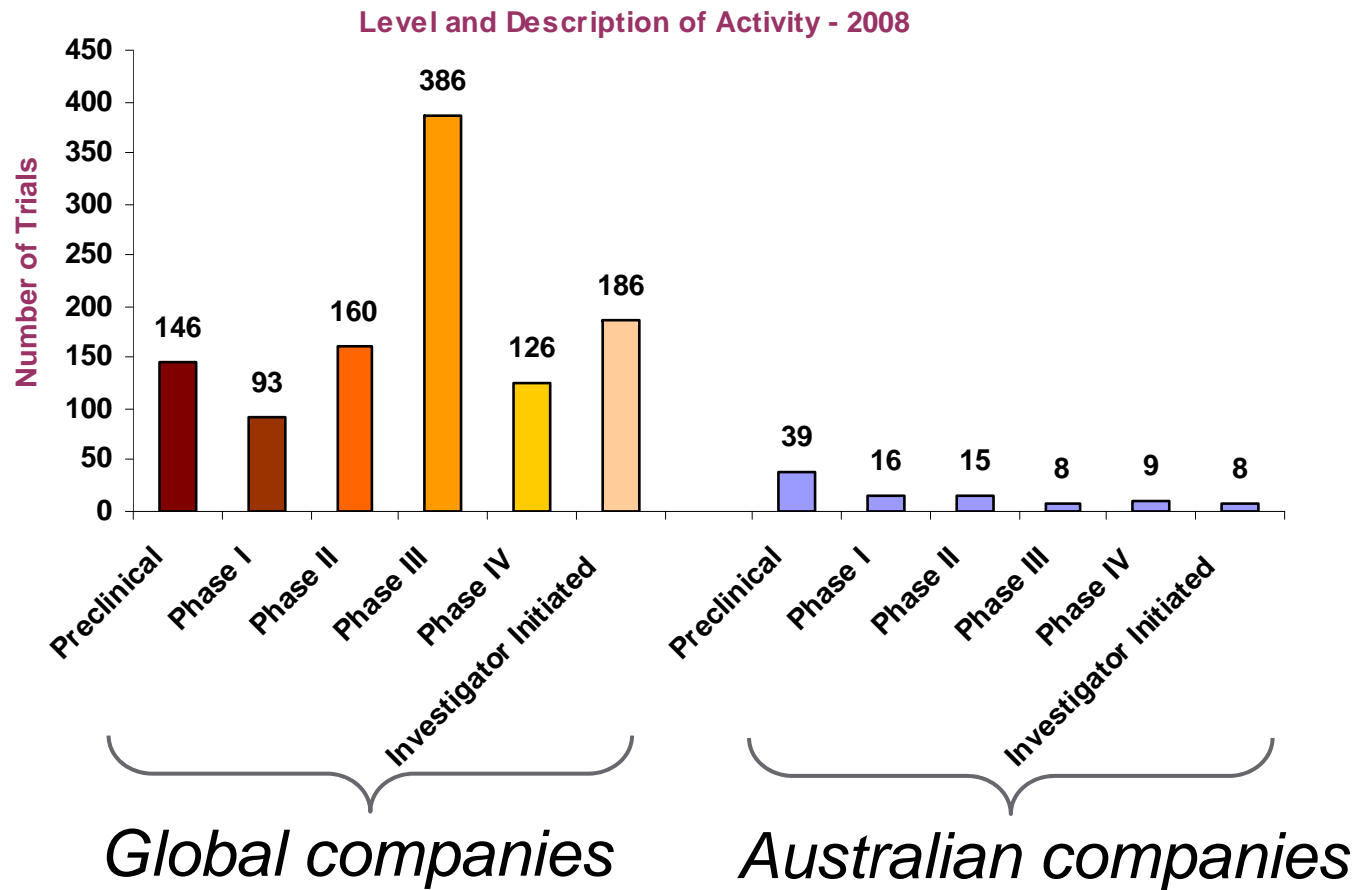
* ABS: \$587 million invested in 2006-07; MA Economic survey, 89% invested in clinical trials

** n = 23 global companies 2008 PIC RDTF Benchmarking Data – global trials/projects

Global Clinical Trials

Making Australia More Competitive

What value would Australia lose? Significant level of trial activity



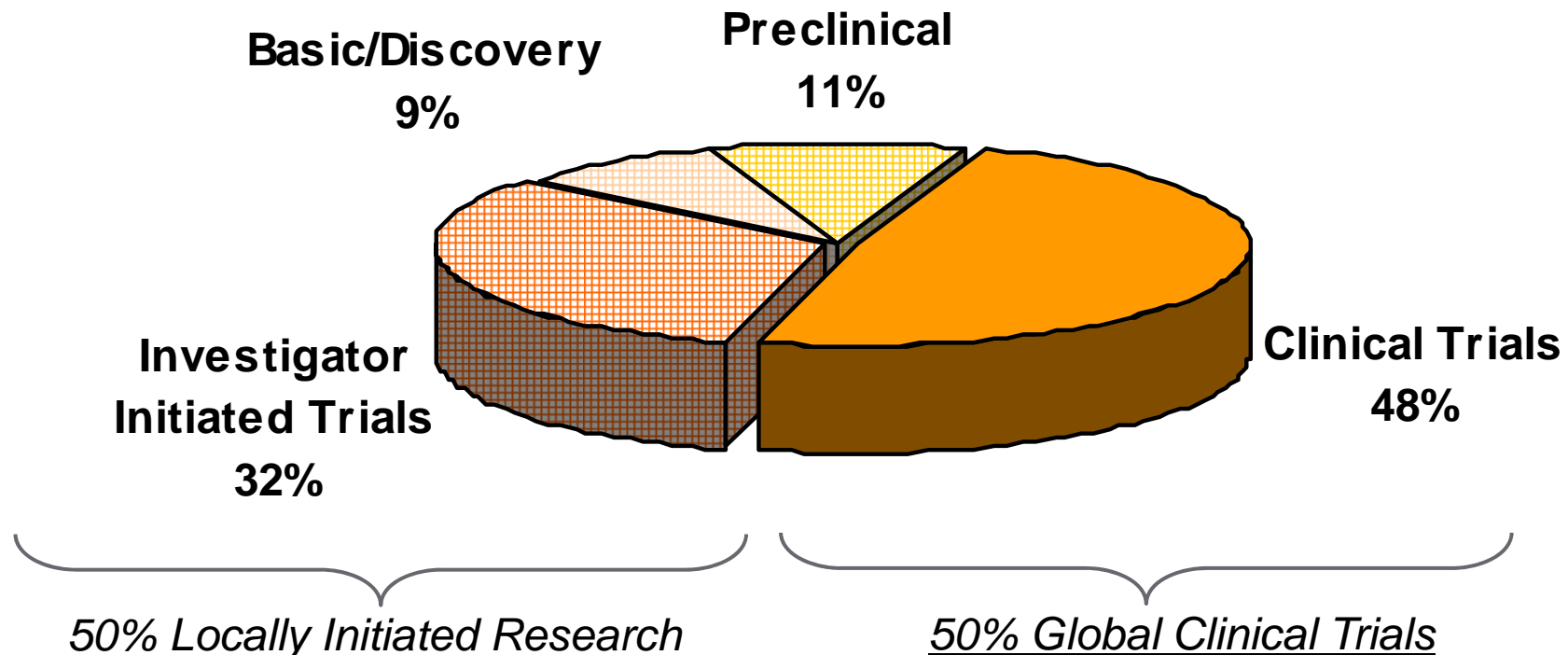
* n = 23 global companies; n = 10 Australian companies 2008 PIC RDTF Benchmarking Data – global trials/projects*

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Making Australia More Competitive

What value would Australia lose? Local and Global Research

Global Companies: Type of R&D in Australia During 2008



* n = 23 global companies 2008 PIC RDTF Benchmarking Data – global trials/projects

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Making Australia More Competitive

What value would Australia lose?

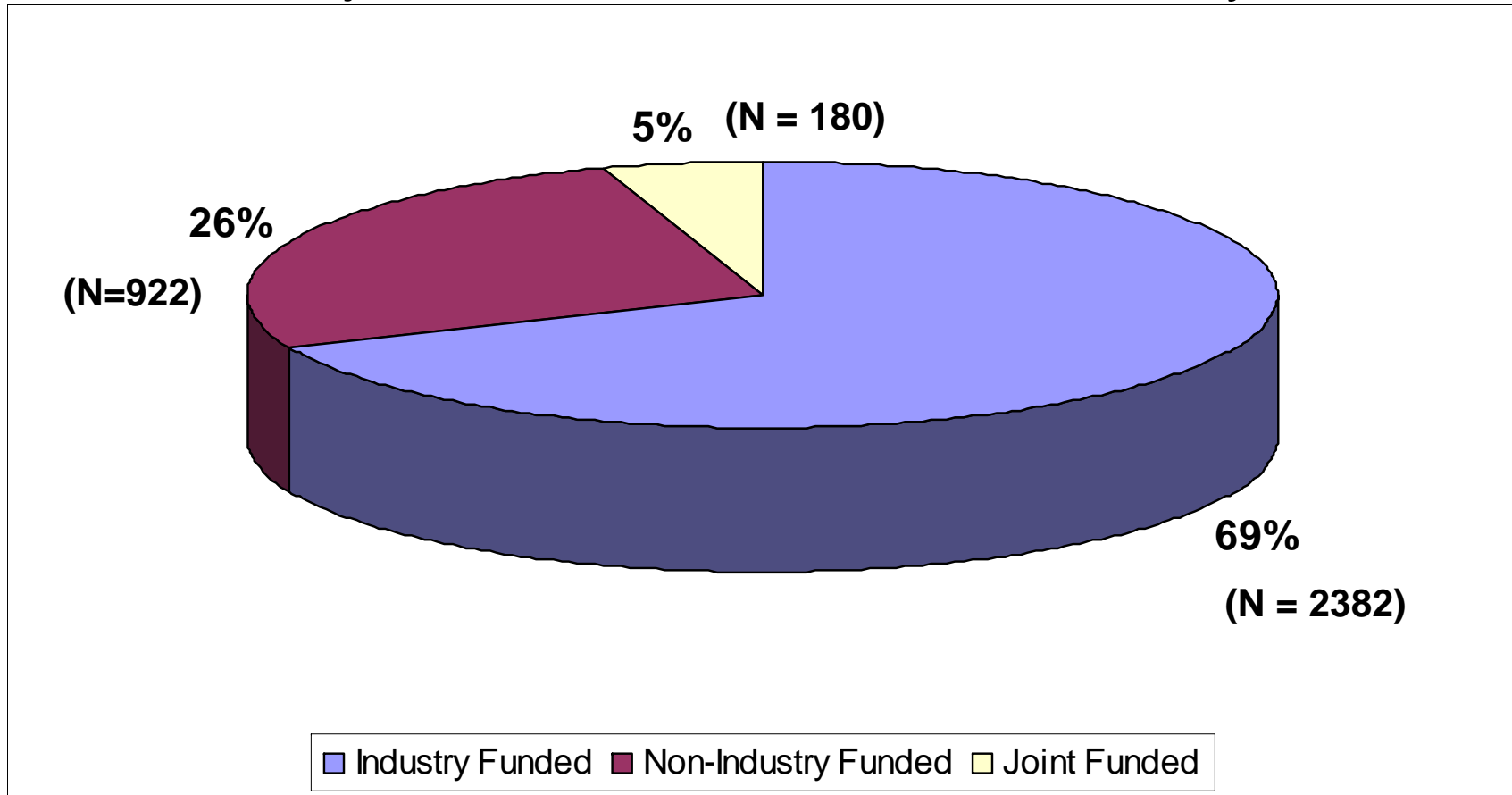
- 70% of trials/projects at typical study site*
- 50% of positions at typical study site*
 - 16% investigator
 - 72% study coordinator/other roles
 - (across just 187 sites this was 828 positions)

* Inaugural Survey of Investigator Perceptions on the Value of Industry Funded Clinical Research: March 2009

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Source of Project Funds: Pharmaceutical Industry > 70%

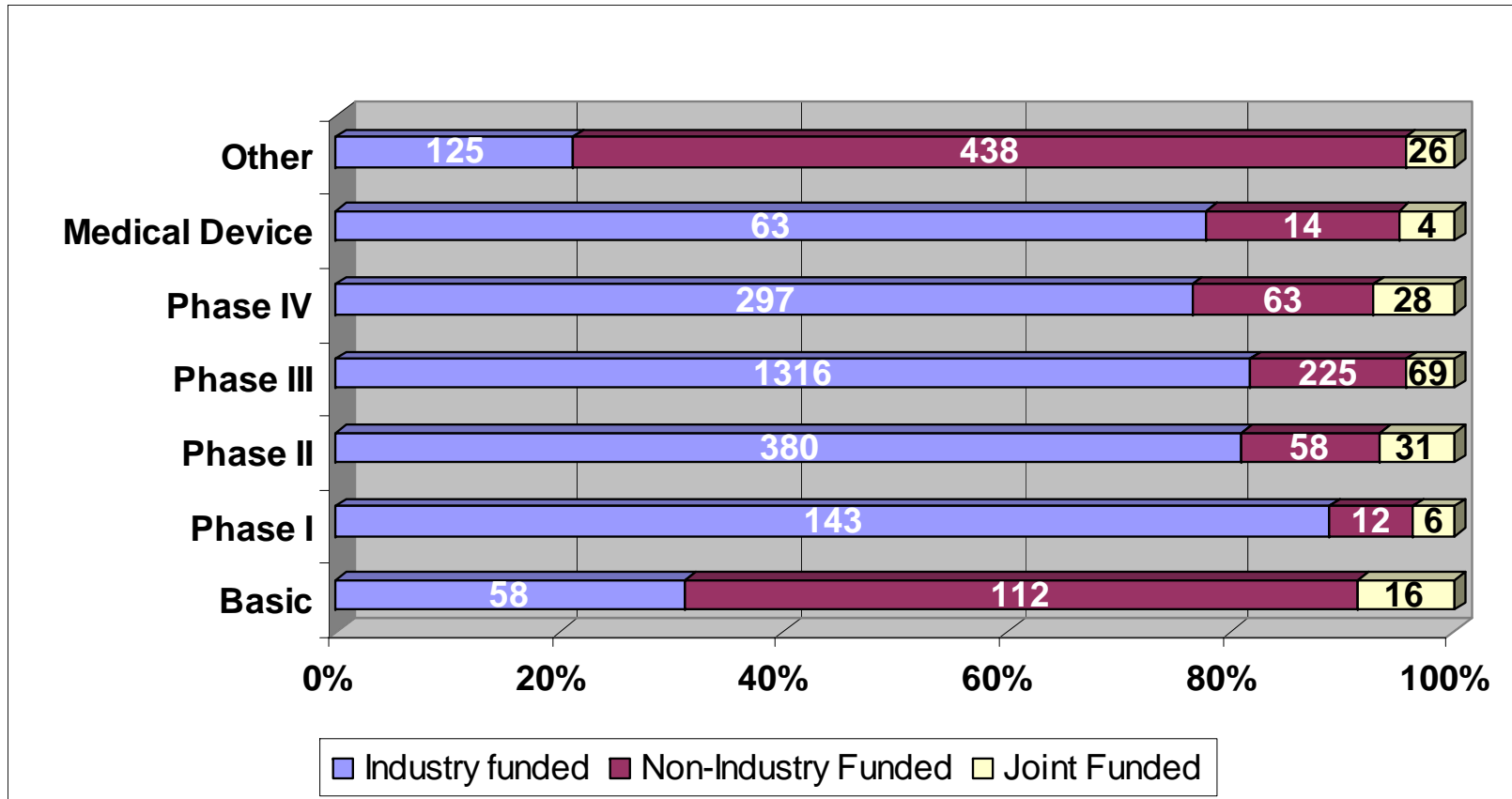


* Inaugural Survey of Investigator Perceptions on the Value of Industry Funded Clinical Research: March 2009

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Source of Funds: Cumulative # of Trials / Research Projects



* Inaugural Survey of Investigator Perceptions on the Value of Industry Funded Clinical Research: March 2009

N = 170 (NB: #'s may include the same trial at multiple sites)

Global Clinical Trials

Making Australia More Competitive

Employment at Sites: ~ 50% positions via industry trials

	# Positions* Reported at Site		# Positions* Funded via Industry Trials		% Positions* Funded via Industry Trials
	Average/ Site	Total	Average/ Site	Total	
Investigators	4.5	807	0.8	129	16%
Study Coordinators	5.6	972	4.1	699	72%
Total		1779		828	47%

N = 178 * Headcount positions not FTEs

* Inaugural Survey of Investigator Perceptions on the Value of Industry Funded Clinical Research: March 2009

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Making Australia More Competitive

What value would Australia lose?

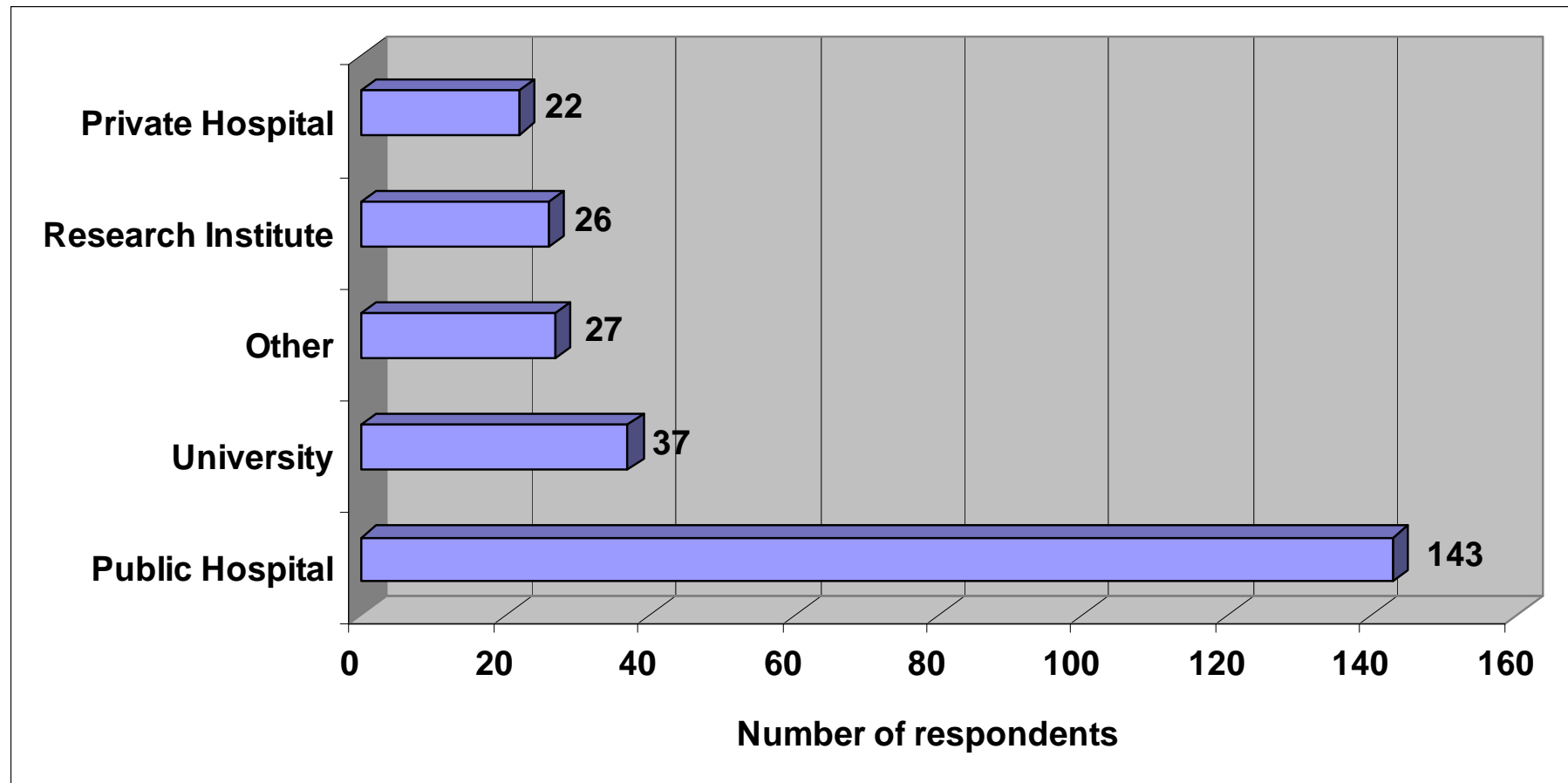
- Inaugural Survey of Investigator Perceptions on the Value of Industry Funded Clinical Research:
 - Commissioned by Pharmaceutical Industry Council R&D Taskforce
 - Conducted March 2009
 - Results available www.clinicaltrials.org.au

- Demographics (n=187)
 - Investigators: 88% (n=165)
 - Study Coordinators: 8% (n=15)
 - Other: 4% (n=7)

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Making Australia More Competitive

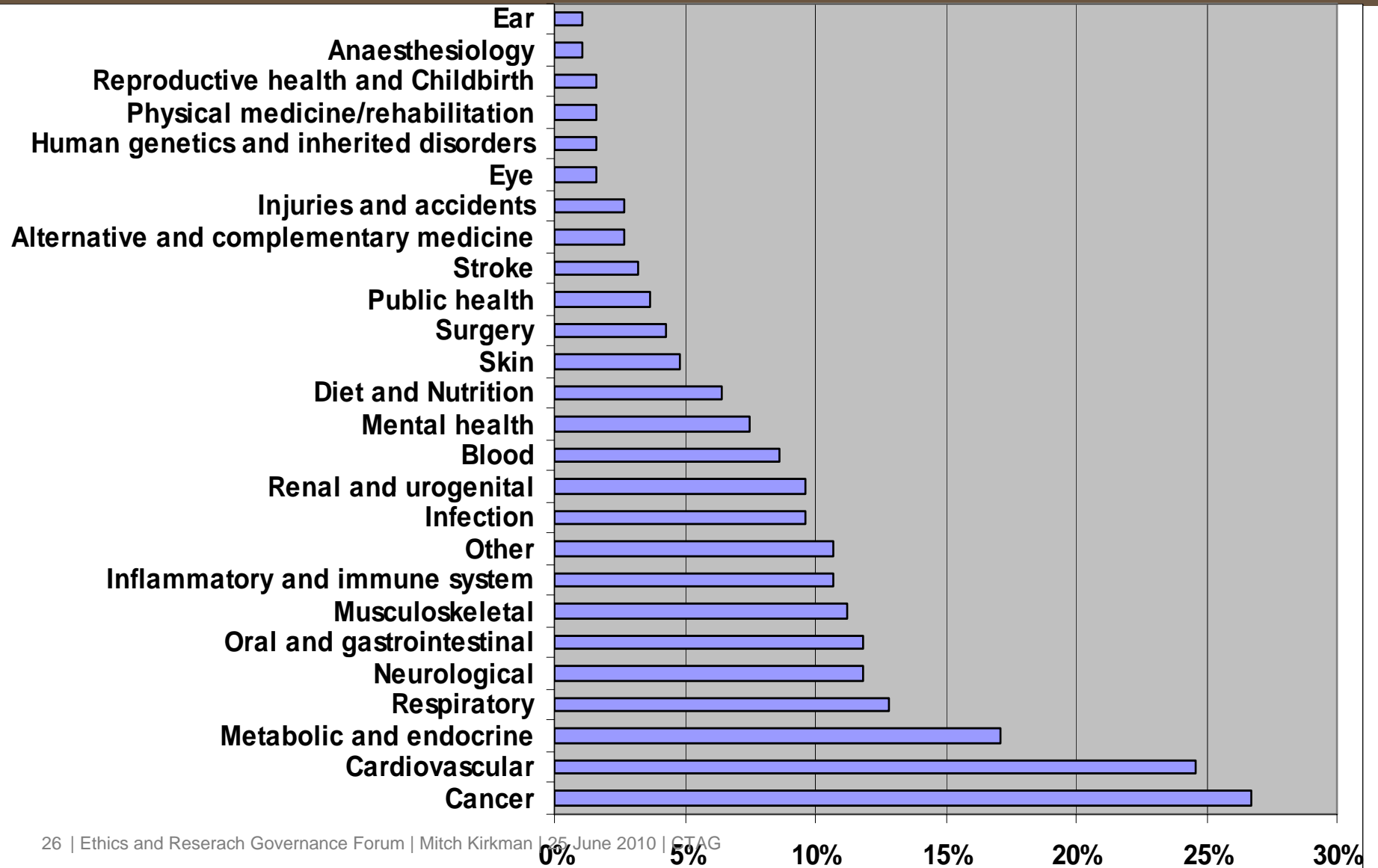
Demographics: Type of Study Centre



2009 PIC RDTF Investigator Survey

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What value would Australia lose?

- As reported by Investigators* -
 - Early patient access to new medicines
 - Enhanced uptake of new evidence into clinical practice
 - Improved standard of care - better health outcomes
 - Source of funds to supplement academic projects
 - Practical experience for researchers/study staff
 - Global recognition for Australian researchers
 - Retaining researchers in Australian health system

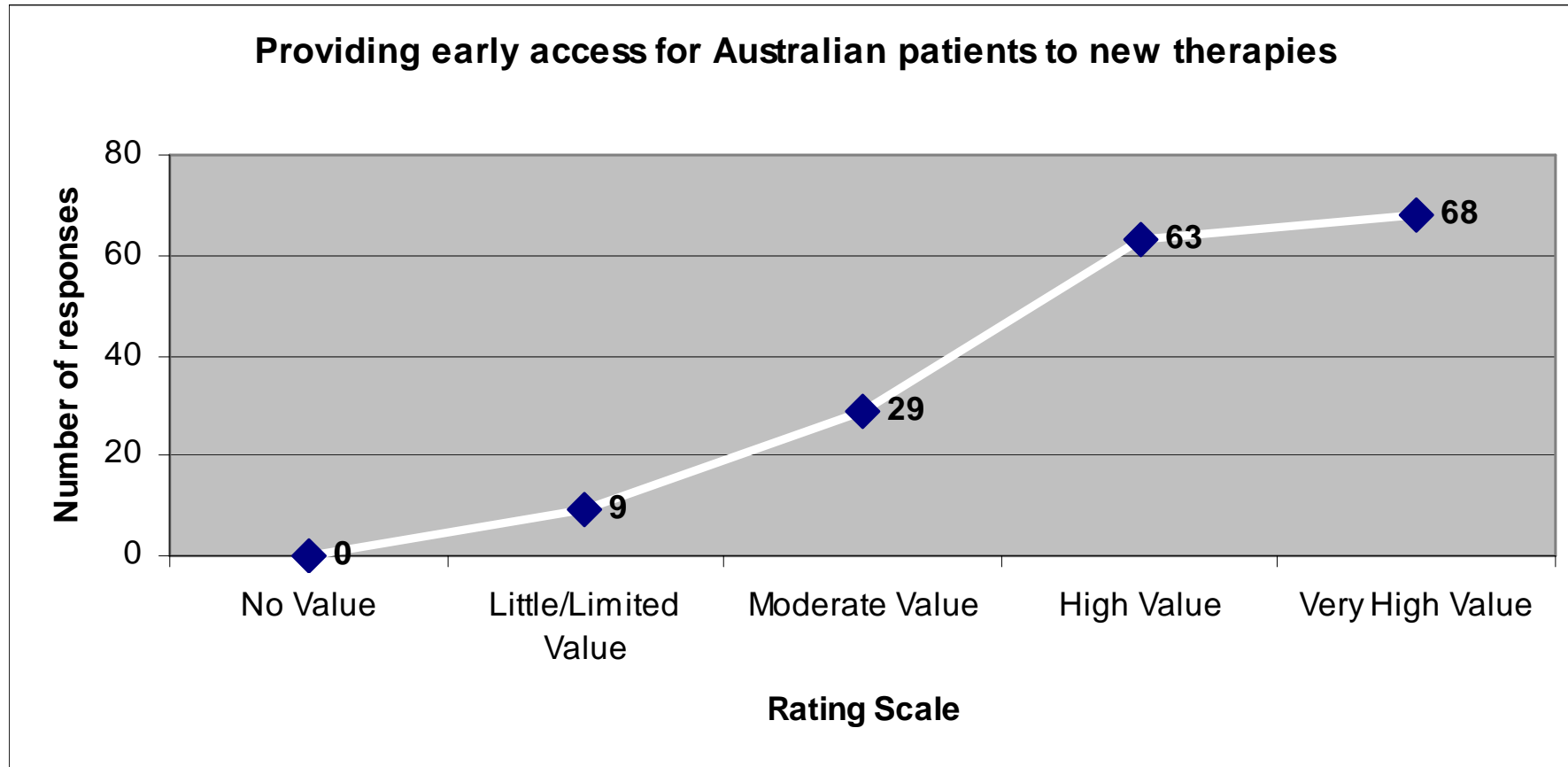
• Inaugural Survey of Investigator Perceptions on the Value of Industry Funded Clinical Research: March 2009

• Full Report www.pharmacouncil.com.au/resources or www.clinicaltrials.org.au

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Typical score for responses

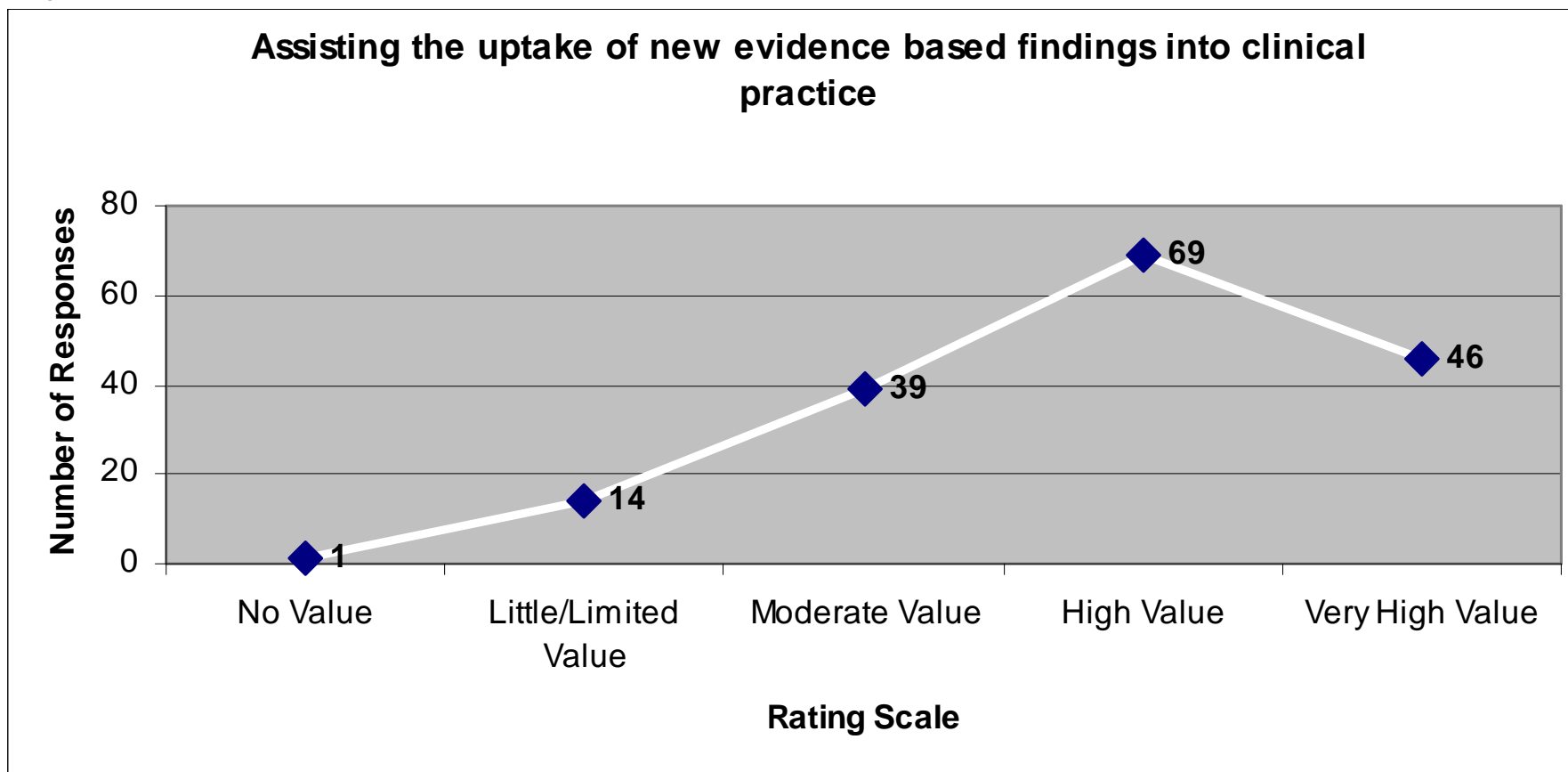


* Instructions – “Please use this scale to rate the value of Australian involvement in industry sponsored research in the following areas: ...”

Global Clinical Trials

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Typical score for responses



* Instructions – “Please use this scale to rate the value of Australian involvement in industry sponsored research in the following areas: ...”

Clinical Trial Action Group

- Improving the environment for clinical trials in Australia benefits not just industry trials

A rising tide lifts all boats....

Clinical Trial Action Group

- Jointly established by
 - Hon Nicola Roxon MP, Health
 - Senator the Hon Kim Carr, Innovation
- Subgroup of PIWG
- Boost Australia's profile as a preferred destination of conducting clinical trials
- In response to PISG calls for priority reforms
- Announced 27 October 2009, report by end March 2010

Clinical Trial Action Group

Membership

Co-Chairs:

- Parliamentary Secretary for Innovation, Industry, Science and Research, the Hon Richard Marles, MP
- Parliamentary Secretary for Health, the Hon Mark Butler, MP

Others:

- Prof. Jim Bishop AO, Australian Government Chief Medical Officer
- Dr Tim Dyke, Executive Director, Quality and Regulation Branch, NHMRC
- Mr Mitch Kirkman, Novartis and former PISG member
- (Prof Warwick Anderson AM, CEO NHMRC)

Clinical Trial Action Group

Terms of Reference

Work in consultation with relevant stakeholders...

1. National clinical trials roadmap to prioritise and coordinate initiatives to best leverage varied public investments in clinical research
2. Investigate the development of appropriate performance measures for clinical trials for inclusion in Australian Government funding agreements with states and territories

Clinical Trial Action Group

Terms of Reference (Cont'd)

3. Investigate how to ensure rapid uptake of HoMER and adoption of best practice in research governance approval
4. Development of strategies to increase patient recruitment for clinical trials
5. Development of clinical trials ICT strategic plan to maximise efficiency in feasibility, approval, establishment and conduct of clinical trials

Clinical Trial Action Group

Methodology

- Established five expert Reference Groups
 - Industry, institutions, hospitals, patients and consumers, federal and state governments, academia, private researchers
 - Each tasked with 1 term of reference
 - Each group to produce written submission to CTAG
 - Chairs
 - Clinical Trials Road Map – Prof Jim Bishop
 - Key Performance Measures – Prof Richard Fox, SVH, Melb
 - National Ethics & Governance – Prof John Funder, Prince Henry RI
 - Patient Recruitment – Mr John Stubbs, CEO, Cancer Voices Australia
 - ICT Strategy – Ms Carol Bennett, CEO, Consumer Health Forum

Clinical Trial Action Group

Methodology

- Call for public submissions
 - Published five discussion papers on DIISR website each term of reference
 - 54 public submission – strong interest!
 - State government departments
 - Medical and industry associations
 - Researchers, study staff
 - Consumer groups, private persons
 - Pharmaceutical companies, CRO
 - Most submissions public – see DIISR website

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Methodology

Discussion Paper	Number of submissions addressing
Roadmap	24
Performance measures	23
HoMER/research governance	30
Patient recruitment	34
ICT plan	15

Clinical Trial Action Group

CTAG

- met on six occasions
- DIISR acted as secretariat
- considered public submissions
- considered reference group submissions
 - ~80 recommendations alone
- National Health and Hospital Network announced
- sought and granted extension from Ministers for report
- CTAG Report submitted 18 June 2010

Clinical Trial Action Group

CTAG Report

- Contains recommendations to the terms of reference:
 - Road map for future for clinical trials in Australia
 - Performance measures
 - Streamlined national ethical approval & best practice research governance
 - Increase patient recruitment
 - ICT strategy
- Encourage ongoing communication from all stakeholders to the Ministers re the urgency of action and of the Government's response to the CTAG Report

Global Clinical Trials

Making Australia More Competitive

- Make every trial count -
 - Timeliness:
 - Ensure timely ethical and governance approval
 - Be ready to start as soon as approvals are through
 - Propose and support changes to streamline processes

 - Recruitment Capacity
 - Reliable feasibility (even the bad news is “not feasible”)
 - Ensure detailed planning for recruitment before study starts
 - Start identifying possible patients as early as possible
 - Meet or exceed your patient commitment in shortest timelines possible

Global Clinical Trials

Making Australia More Competitive

- Make every trial count -
 - Value
 - Promote the full value of global trials in the health system (not “cash cow”)
 - Ensure trial costs are transparent and relate to activity
 - Propose and support changes to streamline processes
 - Facilitate CRA direct access to e-medical records (efficiency)
 - Quality
 - Ensure data is entered on time and is clean first time (build quality in)
 - Differentiate Australia through scientific excellence: especially translational medicine

Global Clinical Trials

Making Australia More Competitive

How can Australia be more competitive?

- Play to our strengths and be smart
- All stakeholders need to work together
- Need national leadership and coordinated action
 - Natural ability no longer good enough

