



THE GEORGE INSTITUTE  
for Global Health



# Research and Health Improvement Asking the hard questions

Professor Christine Jenkins, ARCS June 2014



*Affiliated with the University of Sydney*

# Medical Research and Health Improvement

## Asking the hard questions

- **Are science and research undervalued by our community and government?**
- **What is the value of medical research for**
  - health outcomes?
  - economic benefit?
- **Asking the hard questions to address public health needs**
  - end of life
  - health service delivery
  - self management strategies
- **Are the essential structures, skills and services in place to support the benefits of research**
  - For improving health outcomes of patients?
  - For illness prevention?
  - For access and equity for all Australians?



A decade of

DISCOVERY · INNOVATION · IMPACT

# Particular challenges for basic and clinical research

- **Undertaking studies that are inclusive of the population that is most likely to receive the intervention**
- **Developing, educating, rewarding and sustaining networks of skilled researchers**
- **Addressing common, serious health issues by testing affordable, accessible solutions with wide applicability**
- **Addressing health problems that do not require pharmacologic interventions, but would reduce the need for them**
- **Ensuring research findings are translated to improvements in healthcare for the general population**

# Medical research funding has been saved...now we need to spend wisely



**11<sup>th</sup> May 2011** The NHMRC budget escaped the threatened \$400 million cut in last night's Federal Government budget announcement. Instead, the 4% annual increase it has received in recent years will continue for another year



# Our science suffers from a national delusion

## How we compare

# 2.2%

of Australian GDP invested in research and development, placing us 13th out of all OECD countries. Japan spends 3.3 per cent while South Korea spends 4.4.

# 3%

of the world's scientific output is Australian.

\*

In Australia and the US there are nine researchers per 1000 people.

\*

# 60%

of Australian researchers are in universities compared with 20 per cent in the US where most are in private industry.

# 3.5%

of Australian businesses co-operate with universities compared with 31 per cent in UK universities.

\*

The problem facing Australia's scientists is not simply the lack of a science minister, but lack of a vision for the future.

Nicky Phillips, Science Editor

- Professor Ian Chubb, Chief Scientist ...says the budget cuts are a symptom of a much bigger problem
- ***We are a nation without a plan, he says. Nowhere does a policy or a strategy exist that sets out this country's vision for the future, and how science and innovation should help achieve that***
- As a consequence of not having a plan, it is easy for ministers to announce a program one year only to have the next government dismantle it
- Some people say the government declared its hand on Australian science when it decided not to appoint a dedicated minister for the first time in almost 80 years....
- *Without a science minister there is no one to take the lead on a national science strategy*



## Science going back to dark ages

May 28, 2014

*The Sydney Morning Herald*  
Comment

- **The Climate Commission has gone, the carbon tax is to be rescinded, the Australian Renewable Energy Agency is to be abolished....The Prime Minister has declared war on the Australian renewable energy industry, the environment and science itself**
- **A sceptic is someone who doubts accepted opinion; a denier is someone who refuses to accept fact. Scepticism is healthy, denial is dangerous.....**

Ian Berryman is reading for a DPhil in engineering science at the University of Oxford. His thesis is on solar thermal power. He is an Australian Student Prize Winner, a first-class honours graduate of Melbourne University and a Dean's Honours Recipient from Engineering ..... **"I have no future in Abbott's Australia"**

May 28, 2014

- **Cuts to ARENA, ANSTO, the CSIRO, and many other research bodies will severely damage our long-term economic health**
- **Perhaps then we will have a real deficit crisis**
- **Furthermore, the multidisciplinary nature of research means that the Medical Research Fund will be ineffective without adequate support from physics, engineering, chemistry and many other scientific areas the government is currently de-funding at research, doctorate and undergraduate level**

Ian Berryman

# Australia's Health 2010

## Australian Institute of Health and Welfare

- The median age of the population (half is older and half is younger) was 36.9 years in June 2009
- Has increased by 5.1 years over last 20 years
- In 2009 > 2.9 million Australians (13.3% total pop) were aged  $\geq$  65 years, compared 1.1 million (8.3%) in 1971
- Increase in > 85 years has increased more than fivefold over the same period
- Centenarians have risen from 200 in 1971 to > 3,700 in 2009
- 1 in every 6,000 Australians is aged 100 years or older
- **Respiratory systems diseases are 3<sup>rd</sup> leading cause of death (behind CVD and cancer) for all > 65 yr old age groups**



A decade of

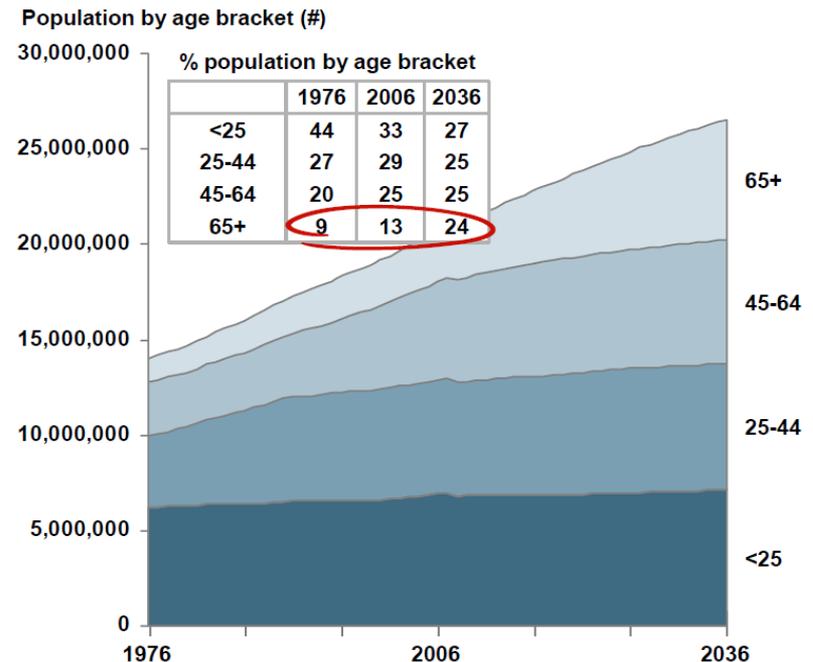
DISCOVERY · INNOVATION · IMPACT

# Australia's Health care challenges

- Australia faces unprecedented health and economic challenges in the next 3 decades
- Health & Ageing expenditure is currently  $> \frac{1}{4}$  of total Govt spend
- Will increase to almost  $\frac{1}{2}$  of total spend by 2049–50
- Total health and residential aged care expenditure is escalating from 9.3% GDP in 2003 to 12.4% GDP in 2033
- At least some of the burden of aged care is preventable

By 2036, it is projected that one quarter of Australians will be over 65

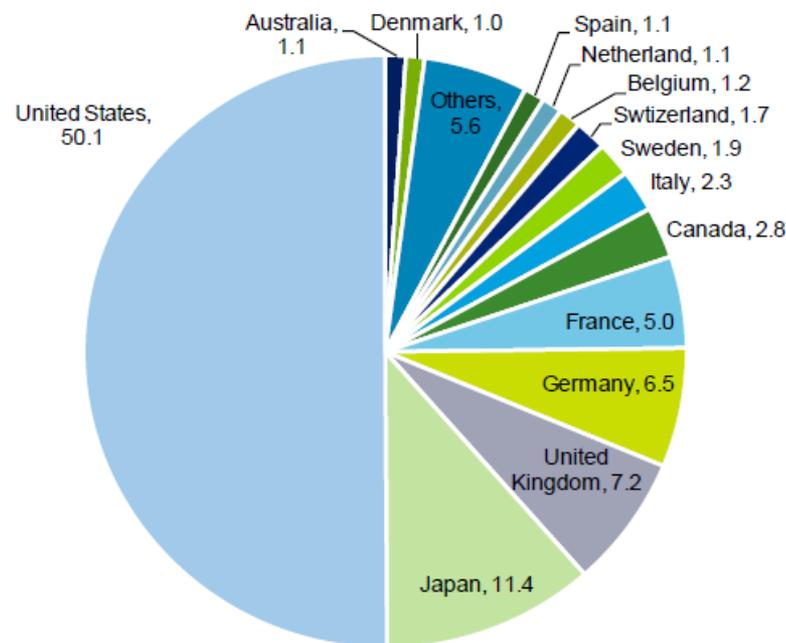
Australian population by age bracket: 1976-2036



# Does investment in health research have commercial benefit?

- **In UK**, R&D is recognised as the path to future economic prosperity and not a burden on the present
- The value added to British GDP by research is conservatively estimated at £30 billion (\$55 billion), from a total research budget of £3.5 billion
- **In the US**, For every USD spent on global health research and development, 64 cents go directly to domestic-based researchers and product developers, generating jobs, research and technological capacity, and additional investment (NIH 2012)

Chart 4.12 Global distribution of R&D for health expenditure, 2003 (%)



Source: Burke and Monot, 2006

# Australia's urgent need for improved health and medical research funding

- **Health system expenditure predicted to grow from \$113 billion in 2012 to \$3.3 trillion by 2062**
- Almost 2/3 of the projected increase in Australian government spending to 2049-50 is expected to be on health
- **Economic benefit of health and medical research**
  - ❖ Health and medical research 1993-2005 is estimated to have returned a net benefit of \$29.5 billion
  - ❖ Every dollar invested in HMR returns on average \$2.17 in health benefits
  - ❖ Australian HMR returns 117%, exceeded only by mining (159%) and wholesale/retail (438%) sectors

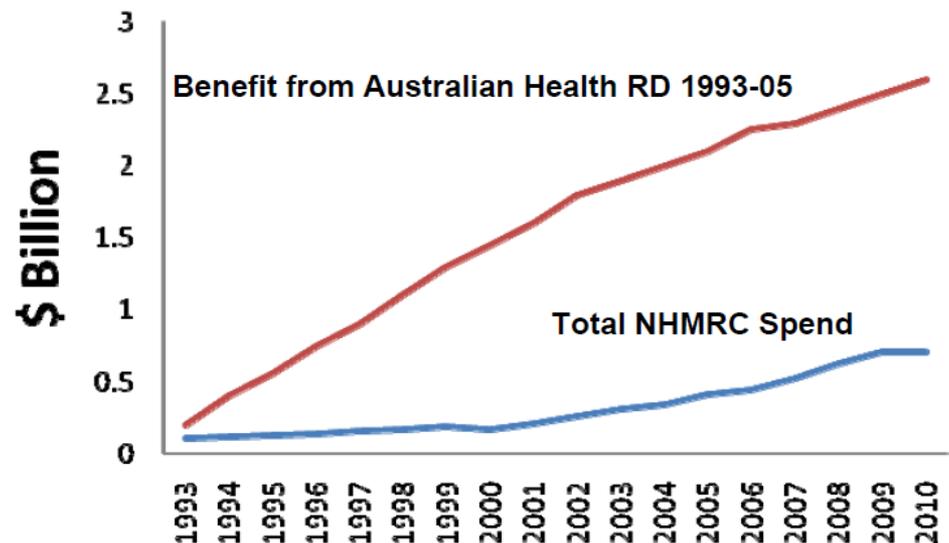


# Returns on NHMRC funded Research and Development

Deloitte Access Economics

Australian Society for Medical Research

- In wellbeing terms, NHMRC funded R&D between 2000 and 2010 is estimated to return a benefit between the years 2040 and 2050 of approximately:
  - ❖ \$4 billion for CVD
  - ❖ \$2 billion for cancer
  - ❖ \$2 million for SIDS
  - ❖ \$60 million for asthma



Adapted from Access Economics 2008 and NHMRC Statistics  
<http://www.nhmrc.gov.au/grants/dataset/index.htm>



A decade of

DISCOVERY · INNOVATION · IMPACT

# Health and Medical Research

- ✓ Saves lives and reduces suffering
- ✓ Develops critical public health, preventative screening strategies and interventions
- ✓ Maintains healthier and more productive lives
- ✓ Decreases hospital stays, Medicare and PBS costs
- ✓ Delivers significant economic benefits : hard and soft capital
- ✓ Delivers social, intellectual and cultural returns to benefit Australia's capacity to address a wide range of social and health related problems
- ✓ Builds collaboration and capacity across multiple sectors in education, science, technology and service delivery
- ✓ Enables us to train our best and brightest, prevent loss of brainpower and talent overseas, and attract international researchers and funding



A decade of

DISCOVERY · INNOVATION · IMPACT

# New \$20B Medical Research Future Fund

## Budget 2014: New medical research future fund as apprentices lose handouts

May 13, 2014

☆ Read later

Heath Aston and Fergus Hunter

Tweet f g+ in submit

Email article Print Reprints & permissions



Medical research future fund: Government to announce plans in budget announcement. Photo: Peter Braig

### Most popular

1 Frank Lowy's Westfield threat makes corporate history



2 Fixing Ten was just too hard, says programmer John ...



3 Markets Live: Capex data cheers 159



4 The world's most expensive street



5 \$1b revamp in store for Wynyard area



### Most Searched Shares

1. TLS - TELSTRA CORPORATION LIMITED.
2. CBA - COMMONWEALTH BANK OF AUSTRALIA.
3. BHP - BHP BILLITON LIMITED

# “Double the funding in rare win”

Amy Corderoy SMH 14<sup>th</sup> May

A \$20 billion medical research future fund for cutting-edge research will be the largest of its kind in the world, the government says.

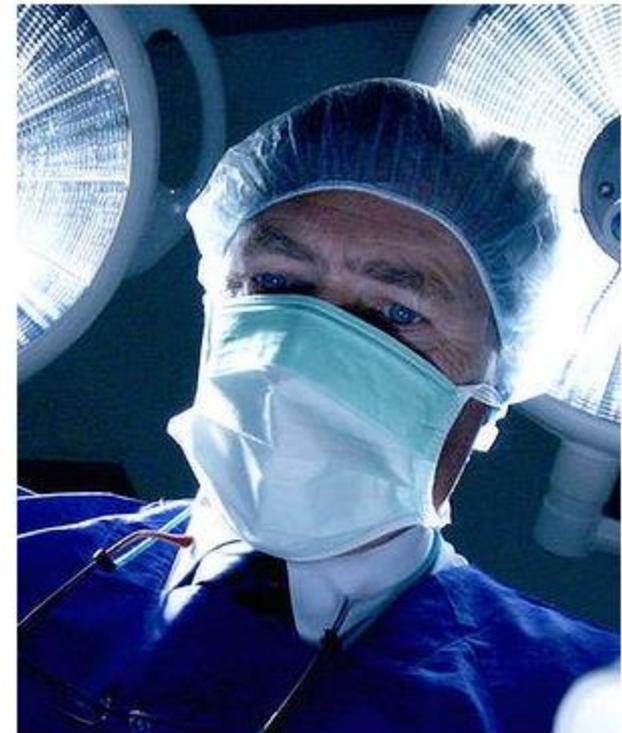
Medical research is one of the few winners in a budget that makes massive cuts to health and hospital funding - much of which will be reinvested in the fund until it reaches its \$20 billion target in 2020.

The fund could change the way medical research is done in Australia, with interest from the capital able to fund \$1 billion a year in new research projects through the National Health and Medical Research Council.

"The additional \$1 billion a year in funding will roughly double the government's direct funding to medical research," it said in its budget overview.

"This investment, to be managed by the Future Fund Board of Guardians, will help to ensure Australia can continue to advance world leading medical research projects, attract and retain first-class researchers and deliver improved health and medical outcomes for all Australians."

The government will also spend \$200 million over five years on dementia research, and \$18 million over four years on the Orygen Youth Health Research Centre to establish and operate a National Centre for Excellence in Youth Mental Health.

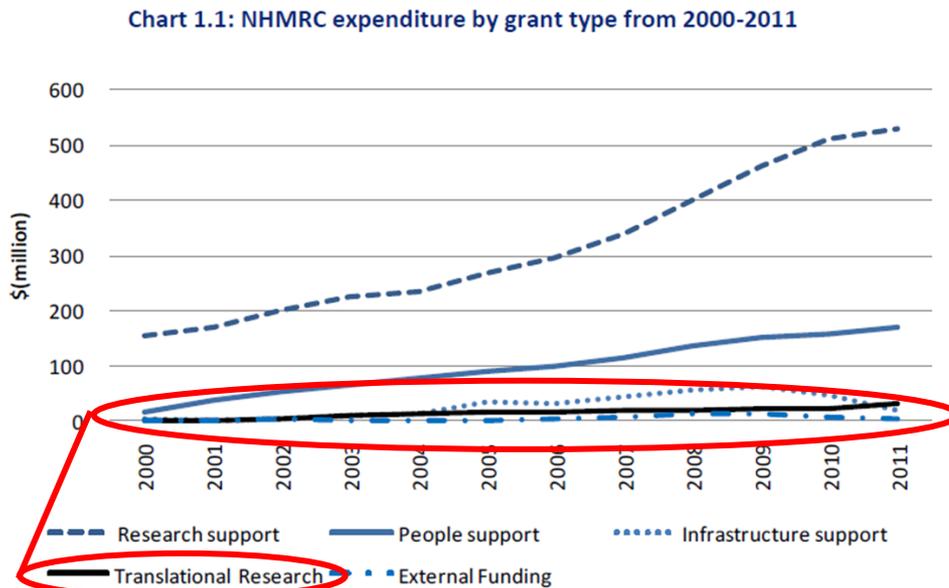


While the project could deliver huge growth in innovative medical treatments, it is unclear who will pay for them to be implemented in Australia's hospitals and GP rooms.

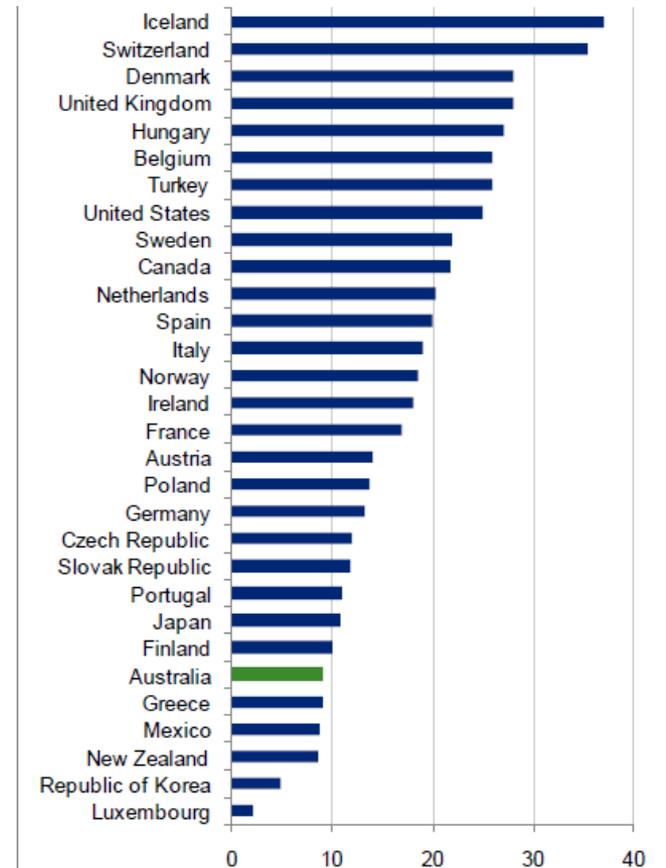
The Medical Research Fund is expected to reach \$20 billion in size by 2020. Photo: Nicolas Walker

# National Health & Research funding

OECD countries (2005) and Australian (2009) national health R&D: proportion of total R&D (%)



Source: NHMRC.



Source: Adapted from Landriault and Matlin, 2009; Deloitte Access Economics calculations.



A decade of

DISCOVERY · INNOVATION · IMPACT

# Making Medical Research Effective and Relevant

- ❖ **The value of medical research**
- ❖ **How clinical trials address gaps in health care**
- ❖ **Developing and up-skilling networks for multicentre multi-country trials**
- ❖ **Benefits to health research capacity building in our region**
- ❖ **Addressing issues for at risk populations**
- ❖ **Identifying eligible populations and ensuring representativeness**
- ❖ **Some George Institute and George Clinical success stories**

# Stating the obvious.....

- **Research to improve health outcomes is NOT just**
  - ❖ About drugs
  - ❖ About longevity
  - ❖ About “on average” changes in outcomes
  - ❖ About expensive interventions
- **Research to improve health outcomes IS**
  - ❖ About self care
  - ❖ About prevention
  - ❖ About strategic, cost effective interventions
  - ❖ About targeting susceptible, responsive populations
  - ❖ About meaningful improvements in quality of life

# Asking the right research questions to facilitate research Translation

## Requires

- Awareness & Relevance
  - ❖ Current state of knowledge
    - ✓ Current studies
    - ✓ Gaps in care
    - ✓ Sub-optimal outcomes
- Robust design: clinical trials must start with a hypothesis
- Minimising exclusion criteria to enable generalisability
- Strategic attempts to avoid clinical trials effect
- Excellence in trial conduct
- Appropriate interpretation and application : for whom are the results of this clinical trial important?

# Prevention IS better than cure



# Breathlessness and Ageing in Australia

- Shortness of breath is low on the radar of older people and their health providers but significantly impacts Quality of life & wellbeing
- **It is becoming “normal” (common) to be breathless but it is not healthy**
- Prevalence of dyspnea (short of breath/breathless walking on the flat or having to stop after 100m) in the Australian community is around 10% in > 55 yr olds, and increases with age

Dyspnea can be addressed : much of it is **NOT** due to heart or lung disease

**Strong associations with preventable, addressable lifestyle factors**

- Physical activity
- Anxiety and depression
- Obesity
- Social disadvantage



A decade of

DISCOVERY · INNOVATION · IMPACT

# Fat nation in need of a dietitian

Australia is 25th in obesity rankings and is getting fatter, write **Amy Corderoy** and **Lucy Carroll**

**P**icture a typical Australian in 2025. Beer in hand, playing on the latest smart device, probably working in healthcare or finance. And one more thing: they are almost definitely obese, or overweight (and quite possibly researching the latest fad diet on that smart device).

According to a study published this week in *The Lancet*, about two-thirds of adults – about 11 million people – are overweight or obese, placing Australia 25th in a global obesity ranking of almost 200 countries.

Rates of the most dangerous of the two diseases, obesity, have skyrocketed faster in Australia and New Zealand than almost anywhere else.

And if predictions are correct, we will only get heavier.

Data published in the journal, *Health Promotion International*, shows almost 80 per cent of adults and more than one in three children will be obese or

taking up cycling and that's obviously very good for them ... but on the other hand, some people don't exercise as much as they ought and probably don't eat as well as they ought," he said. "I'm not going to become a kind of dietitian to the nation."

It's a shame, because if we all followed the Prime Minister's diet and exercise regime, we would probably be the healthier for it.

The food and diet industries have been happy to step in to fill the void of political leadership – helping our waistlines become a growth industry in more ways than one.

Market research firm IBIS World estimates during the past financial year we spent nearly \$644 million on weight-calorie

Yet A fatter.

"Aus

**2/3 Australian adults are overweight**

**'There is no pill to fix obesity.'**

Jane Martin



15 % of Australians worked more than 50 hours/week in 2010, 13 % worked 40 - 50 hours. The longer your work hours, the more likely you are to gain weight.



# Sufficient physical activity, by gender and age group, 2007–08 (%)

Characteristic	Sufficient			Insufficient		
	Males	Females	Persons	Males	Females	Persons
Age group						
18–24				.2		11.4
25–34				.2		17.0
35–44				.4		19.6
45–54				.5		18.9
55–64				.0		15.1
65–74				.4		8.9
75–84				.7		7.2
85 and over				.6		1.9

NHMRC Guidelines for minimum time spent doing physical activity

Sufficient time = at least 150 minutes per week of moderate-intensity physical activity

# Clinical trials and Clinical research

## Are they different?

- Historically in Australia, too little money in clinical trials through independent funding bodies
- Maybe changing now...Wills report , FFMR
- Belief that the pharmaceutical industry will fund clinical research
- Somewhat schizoid...investigators told
  - Seek funding from industry
  - Compromised for doing sponsored studies
- Now recognised that clinical departments can undertake good clinical research and there are benefits for clinical-academic units
- Difficult to undertake clinical trials in a setting away from patients, or where some infrastructure costs are supported by a university or hospital

# Industry sponsored versus Investigator initiated trials

## Industry sponsored

- Usually initiated to answer a comparative question → build new treatment approaches
- Designed with a primary outcome that identifies either
  - A new indication
  - A cost advantage
- May align with regulators' outdated ideas about a disease
- Well resourced, excellent oversight when multicentre
- Highest quality data collection, QA, verification and storage

## Investigator initiated

- Usually address disease causes, evolution, mechanisms → Build new disease knowledge
- Often focused on new disease understanding
- Include “usual” clinic subjects with the disease
- Not necessarily representative of true population with the disease
- Poorly resourced, oversight & QA are challenging if multicentre
- May seek to answer too many questions



A decade of

DISCOVERY · INNOVATION · IMPACT

# Consequences

## If too few sponsored or investigator initiated clinical trials

- Erosion of intellectual and technical skills in clinical research
- Limits sector's capacity to conduct and run trials efficiently
- Reduces familiarity with best practice data collection & entry
- Reduces community awareness about process of new drug discovery
- Clinicians less aware of new opportunities for patient care
- Innovation goes off-shore
- Fellows go off-shore
- Profile of Australian research suffers : fewer people attracted to work in clinical research and science in Australia
- Studies conducted overseas are not all relevant to Australian setting



A decade of

# New drug buddies: Pharma turns to academia for medicines pipeline

Guy Krippner, Head of Medical Chemistry at Baker IDI Heart & Diabetes Institute

15<sup>th</sup> February 2012

- **Pharmaceutical industry recognises that a sustainable product pipeline might be achieved by nurturing talented academic partners**
- **Academia is aware that getting funding of research is continually becoming more competitive**
- **An industry partner with deep(er) pockets is an effective way to**
  - Advance fundamental research
  - Facilitate research translation into patient care
- **Next few years will see a vastly different pharmaceutical industry : addressing change, sustainability & an increased ability to meet medical need**
- **New opportunities for public-private partnerships in clinical research**

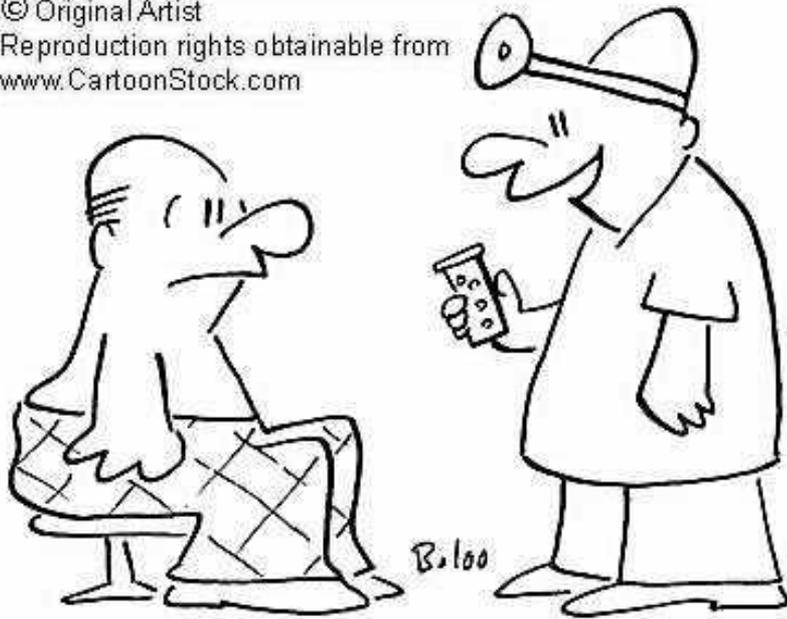


A decade of

DISCOVERY · INNOVATION · IMPACT

# Medicines and Interventions : The Yin and Yang of Clinical Trials

© Original Artist  
Reproduction rights obtainable from  
[www.CartoonStock.com](http://www.CartoonStock.com)



"The FDA hasn't approved these pills yet, but the CIA swears by them!"



"They're not testing any drugs on me. Instead they're providing spiritual advisers."

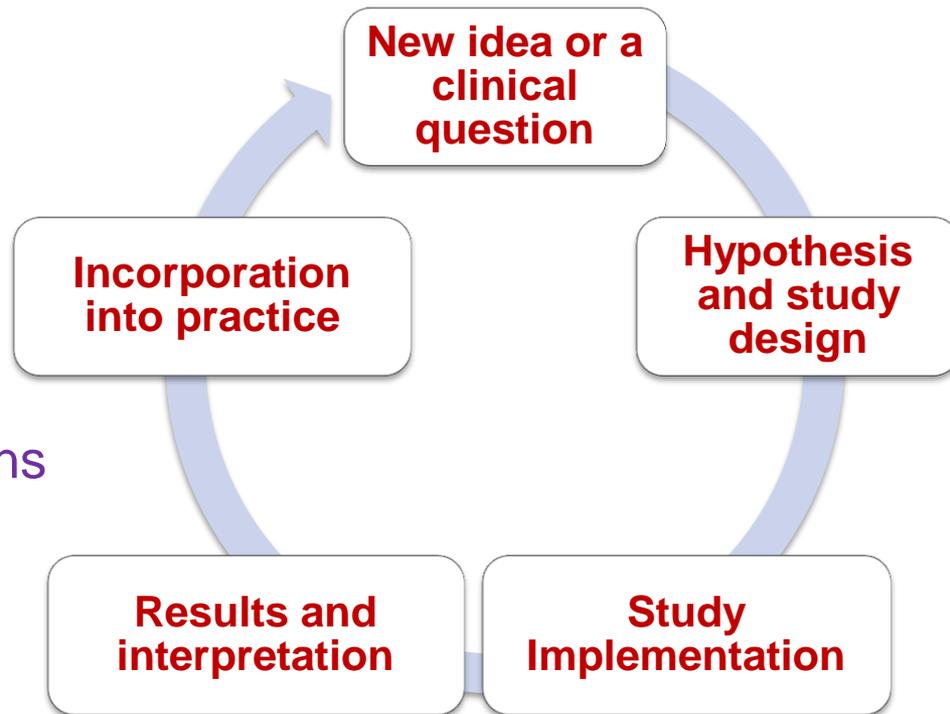
# The best part of clinical trials

- Last patient out
- Data cleaning
- All patients followed up
- Statistical Analysis

## RESULTS

- ✓ Interpretation
- ✓ Surprises
- ✓ Understanding design limitations
- ✓ Writing up, publication
- ✓ Translation
- ✓ Implementation

→ NEW IDEAS



# Two examples : meeting the challenge of relevant clinical research

## 1. Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage : INTERACT2

- Investigator initiated, NHMRC funded
- study to determine the safety and effectiveness of early intensive lowering of blood pressure in patients with intracerebral hemorrhage
- significantly lower disability scores with intensive treatment (OR for disability, 0.87,  $p = 0.04$ ). Mortality was 11.9% vs 12% ( $p = \text{NS}$ )

## 2. Theophylline and Steroids in COPD (TASCS)

- NHMRC funded investigator initiated study in COPD
- Building respiratory research networks and capacity in China

# The George Institute for Global Health

To improve the health of millions of people worldwide by:

- ✓ Providing best evidence to guide critical health decisions
- ✓ Engaging with decision makers to enact real change
- ✓ Targeting global epidemics particular of chronic diseases and injury
- ✓ Focusing on vulnerable populations in both rich and poor countries



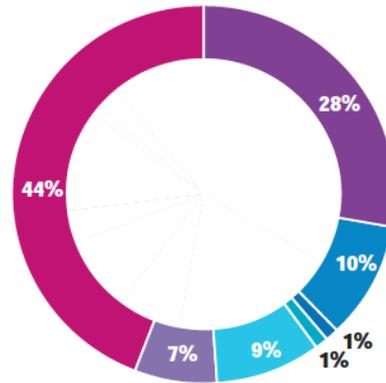
A decade of

DISCOVERY · INNOVATION · IMPACT

# People and funding

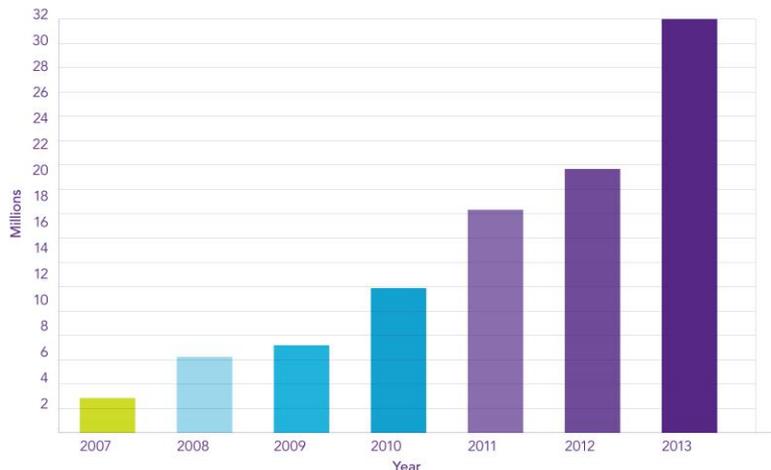
## Our funding sources 2011-12

- Peer review **28%**
- Infrastructure grants **10%**
- Donations received **1%**
- Other government **1%**
- Other **9%**
- Contract research **7%**
- George Clinical **44%**

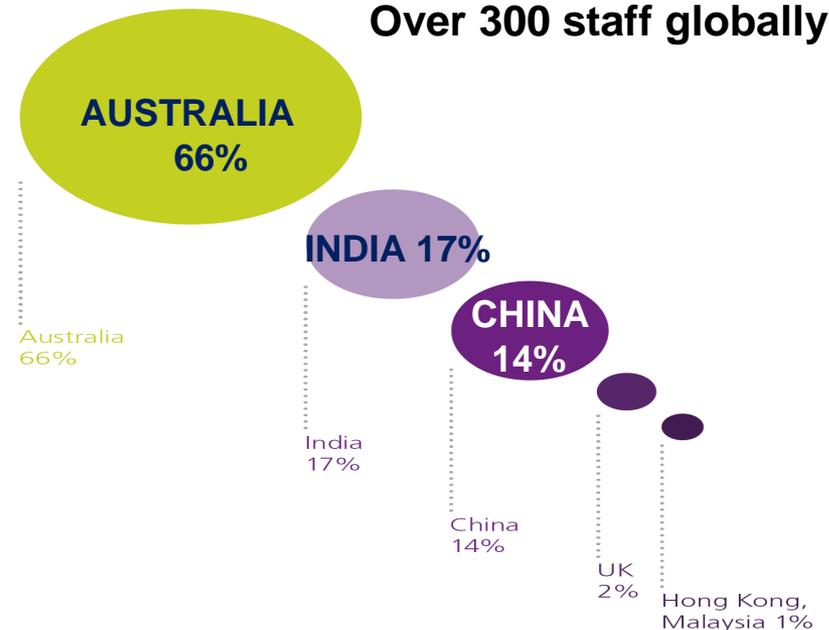


**RANKED 1<sup>st</sup> in 2011  
and top 10 in 2012  
SCIMAGO**

## Peer Reviewed funding awarded



**Over 300 staff globally**



# Example 1

**An Investigator Initiated study of a common problem, with affordable treatment, and wide applicability**

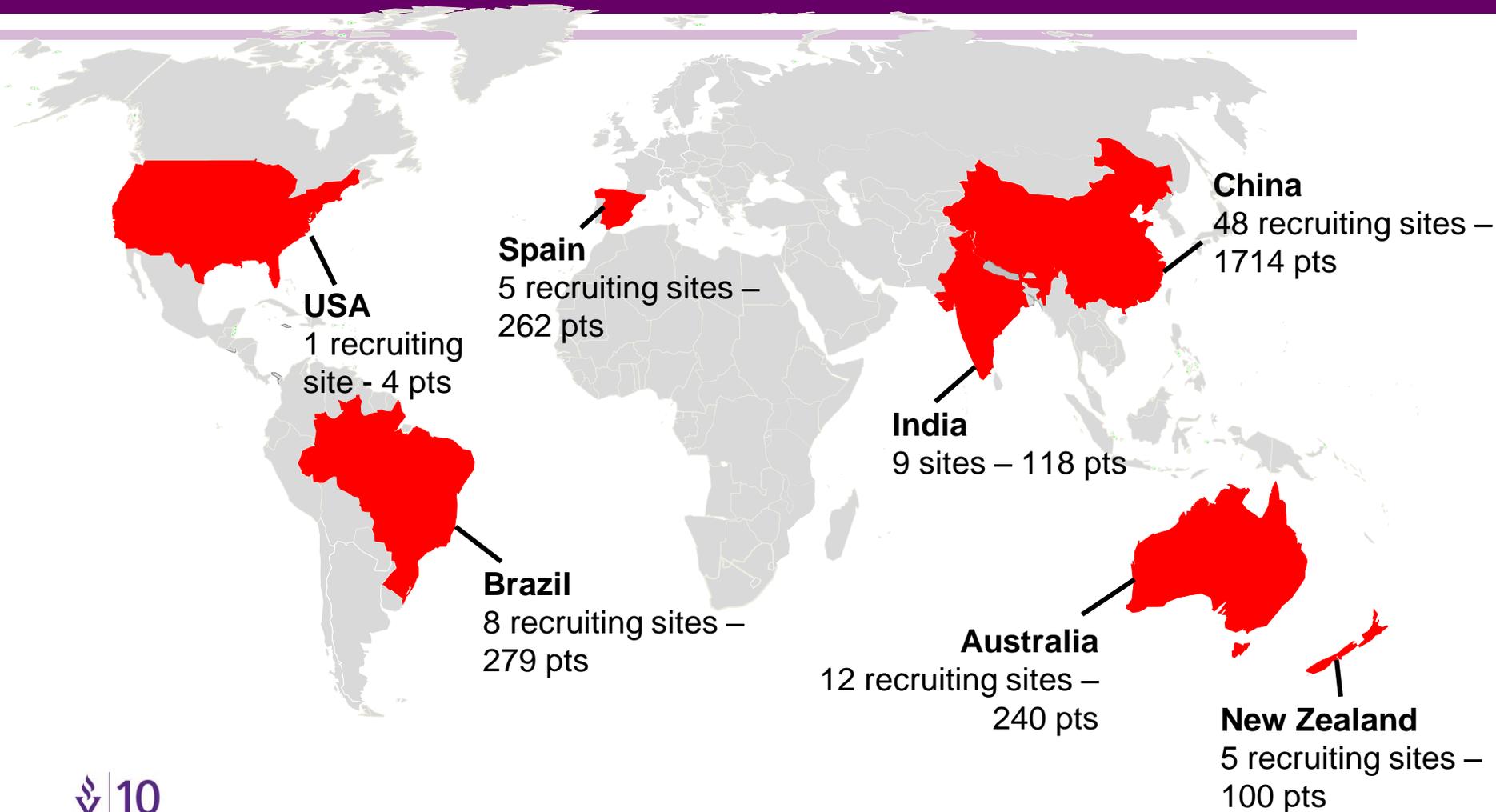


*A decade of*

DISCOVERY · INNOVATION · IMPACT

# INTERACT2 : Participating Countries

Final Global Recruitment = 2717 patients



ORIGINAL ARTICLE

# Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D., Candice Delcourt, M.D., Richard Lindley, M.D., Thompson Robinson, M.D., Pablo Lavados, M.D., M.P.H., Bruce Neal, M.D., Ph.D., Jun Hata, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Mark Parsons, M.D., Ph.D., Yuechun Li, M.D., Jinchao Wang, M.D., Stephane Heritier, Ph.D., Qiang Li, B.Sc., Mark Woodward, Ph.D., R. John Simes, M.D., Ph.D., Stephen M. Davis, M.D., and John Chalmers, M.D., Ph.D., for the INTERACT2 Investigators\*

Name	Date	Duration (months)	Centres	Sponsor	Patients	Recruitment rate/month	Recruitment rate / centre
INTERACT2	2008-12	47	144	NHMRC	2839	60	20

N Engl J Med 2013.

DOI: 10.1056/NEJMoa1214609

Copyright © 2013 Massachusetts Medical Society.

# INTERACT2 - results

- **Early intensive BP lowering:**
  - ❖ debunked longstanding neurological dogma over risk of treatment-induced ischaemic stroke
  - ❖ resolved longstanding uncertainty over the management of elevated BP in ICH
  - ❖ defined the first proven medical therapy for the management of ICH
- **Treatment is low cost, simple to implement, and widely applicable across the world**



### Guidelines for the Management of Spontaneous Intracerebral Hemorrhage. A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Lewis B. Morgenstern, J. Claude Hemphill, III, Craig Anderson, Kyra Becker, Joseph P. Broderick, E. Sander Connolly, Jr, Steven M. Greenberg, James N. Huang, R. L. Sacco, M. D. Macdonald, Steven R. Messé, Pamela H. Mitchell, Magdy Selim, Rafael J. Tamargo, and on behalf of the American Heart Association Stroke Council and Council on Cardiovascular Nursing

*Stroke* published online Jul 22, 2010;

DOI: 10.1161/STR.0b013e3181e6511b

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

Copyright © 2010 American Heart Association. All rights reserved. Print ISSN: 0039-2499. Online

ISSN: 1524-4628

#### Recommendations

1. Until ongoing clinical trials of BP intervention for ICH are completed, physicians must manage BP on the basis of the present incomplete efficacy evidence. Current suggested recommendations for target BP in various situations are listed in Table 6 and may be considered (*Class IIb; Level of Evidence: C*). (Unchanged from the previous guideline)
2. In patients presenting with a systolic BP of 150 to 220 mm Hg, acute lowering of systolic BP to 140 mm Hg is probably safe (*Class IIa; Level of Evidence: B*). (New recommendation)

Revision of guidelines around the world

# Benefit in INTERACT 2 vs Other Acute Stroke Interventions

Intervention	Net Benefit per Thousand
TPA under 3h	290
IA Pro-UK	208
Coiling in SAH	169
TPA 3-4.5h	136
BP lowering for ICH	81
Clinician worthwhile	50
Socioeconomic model worthwhile	20

--Samsa et al, Am Heart J 1998;136:703-13

--Saver, Stroke 2007;38:3055-3062

--Saver et al, Stroke 2009;40:2433-7

# Media around the results

- **Results presented at the European Stroke Conference in London 29 May 13**
- **Simultaneous NEJM publication**

	<b>Australia</b>	<b>International</b>	<b>Worldwide</b>
Media clips generated across print, TV, online and radio	353	343	693
Estimated audience reach	13,416,327 people	18,629,312 people	32,045,639 people
Social media - twitter			80,058



A decade of

DISCOVERY · INNOVATION · IMPACT

# Lower blood pressure link to stroke recovery

**Kate Hagan**  
Health Reporter

Rapidly lowering the blood pressure of patients who have had the most serious type of stroke reduces their risk of long-term disability, a major study has shown.

The study, led by Australian researchers, involved more than 2800 patients who had haemorrhagic strokes - in which a blood vessel in the brain bursts.

tended to have worse outcomes. If they attended hospitals within six hours of a haemorrhagic stroke they received either standard care, or drugs to lower their blood pressure.

Drugs were given intravenously to take rapid effect as part of the study, published in the *New England Journal of Medicine*.

Researchers found that patients who received the treatment had improved outcomes after three



Tina Robinson had a

# NEW HOPE FOR STROKE RECOVERY

A landmark study released on May 30, titled *Intensive Blood Pressure Reduction in Acute*

said the study challenges previous thought about blood pressure lowering in intracerebral haemorrhage.

"The study findings will

option to date has been risky brain surgery, so this research is a very welcome advance," Professor Neal said.

## Neurology update

NEUROLOGY UPDATE NEWSLETTER

### Latest news



Australian trial a game-changer in ICH

A major Australian trial is being hailed as a game-changer in the treatment of acute brain haemorrhage.



# New treatment for stroke boosts chances of recovery

**Helen Hawkes**



Australian-led study confirms that lowering blood pressure gives better outcomes for stroke victims

older and men are also more likely to have a stroke.

Now a new treatment for stroke is set to increase the chances of recovery.

A landmark Australian-led study, by The George Institute of Global Health, found that intensive blood pressure lowering in patients with intracerebral haemorrhage (spontaneous bleeding within the brain), reduced the risk of major disability and improved

guidelines for stroke management worldwide.

"By lowering blood pressure, we can slow bleeding in the brain, reduce damage and enhance recovery," Professor Neal said.

"The only treatment option to date has been risky brain surgery, so this research is a very welcome advance."

In Australia, the number of people living with disability as a result of



**TASCS**



Theophylline and Steroids  
in COPD Study

---

**Example 2**  
**About to commence...**  
**Theophylline and Steroids in COPD**



*A decade of*

DISCOVERY · INNOVATION · IMPACT

# The 10 most common causes of death in 2008

Deaths attributed to	Worldwide (milions)	WHO European Region (millions)
Ischaemic heart disease	7.3 (12.8%)	2.40 (24.7%)
Cerebrovascular disease	6.2 (10.8%)	1.40 (14.0%)
Lower respiratory infections	3.5 (6.1%)	0.23 (2.3%)
<b>COPD</b>	<b>3.3 (5.8%)</b>	<b>0.25 (2.5%)</b>
Diarrhoeal diseases	2.5 (4.3%)	0.03 (0.3%)
HIV/AIDS	1.8 (3.1%)	0.08 (0.8%)
Trachea/bronchus/lung cancer	1.4 (2.4%)	0.38 (3.9%)
Tuberculosis	1.3 (2.4%)	0.08 (0.8%)
Diabetes mellitus	1.3 (2.2%)	0.17 (1.7%)
Road traffic accidents	1.2 (2.1%)	0.12 (1.2%)

**LUNG DISEASE TOTAL GLOBAL MORTALITY 9.5 MILLION ( 16.7%)**

Source: World Health Organization (WHO) World Health Statistics 2011

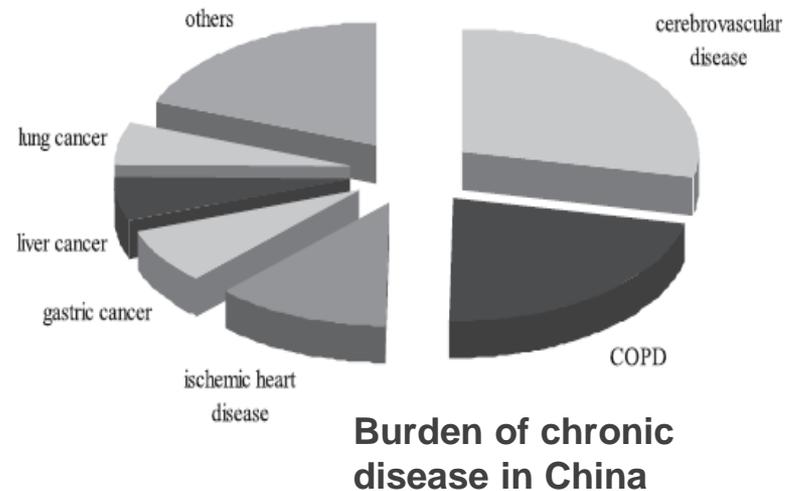


### East Asia



# Respiratory Health in China

- Total population 1.334 billion
- Ageing population (36% elderly by 2020)
- Rural population
  - 2009 53%
  - 2015 50%
  - 2035 30%
- **Tuberculosis** – world's 2<sup>nd</sup> largest burden after India, kills 160,000 people each year  
27% drug resistance
- **Asthma** probably under-estimated: prevalence 5%

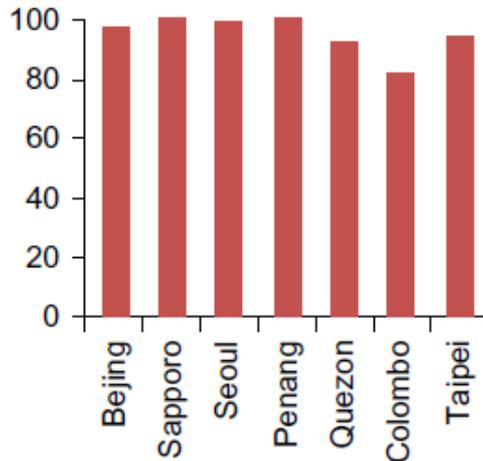


# COPD in Asia...more than smoking

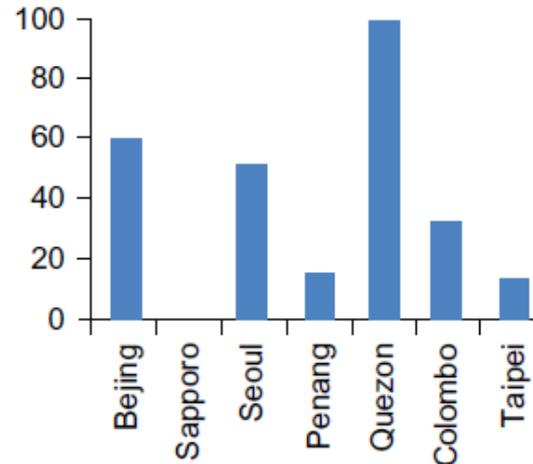
Int J COPD 2013;8 31-39



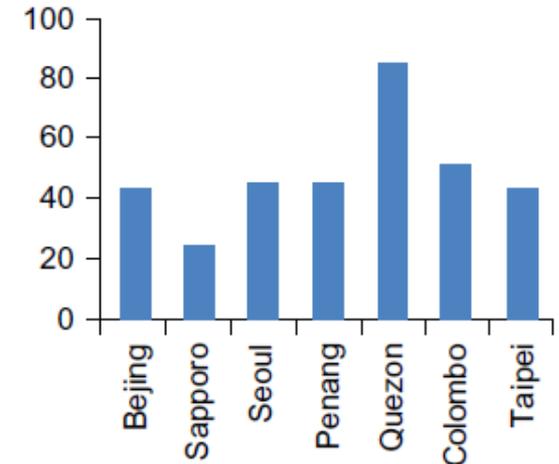
Cigarette smoker (%)



Subjects exposed to biomass fuel (%)



Subjects exposed to dusty job (%)

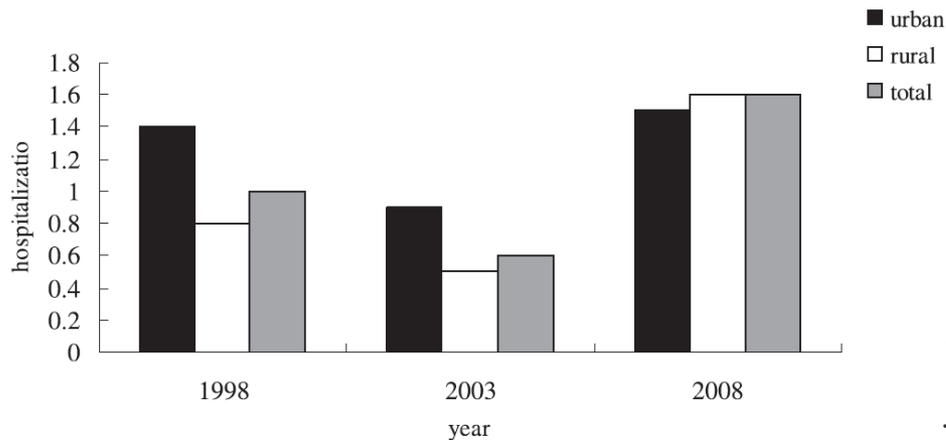


A decade of  
DISCOVERY · INNOVATION · IMPACT

922 COPD patients from pulmonology clinics in 7 cities in Asia  
Beijing, Colombo, Penang, Quezon City, Sapporo, Seoul, Taipei

# COPD in China : The Burden and Importance of Proper Management

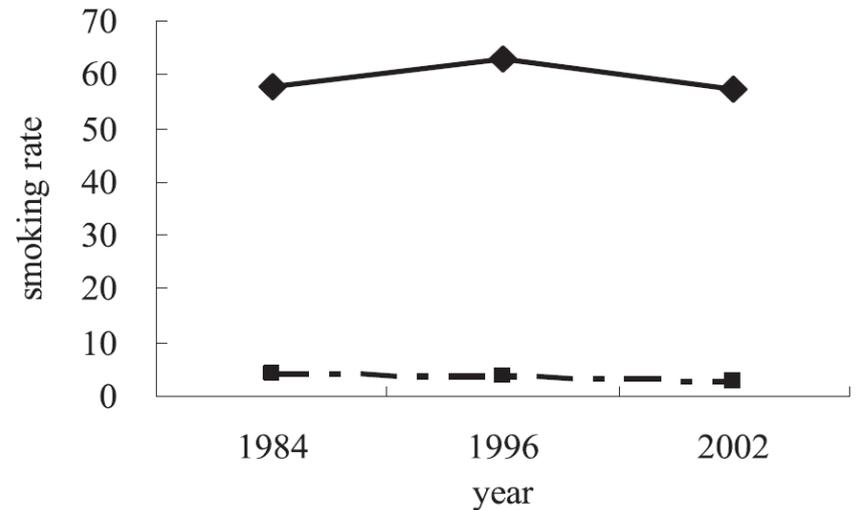
Fang X, Wang X, Bai C. Chest 2011;139;120



Hospitalization rate for COPD 1998, 2003, and 2008 in China. The decline of hospitalization in 2003 could be attributable to the outbreak of SARS

## COPD Prevalence rates in China

- Males 12.4%
- Females 5.1%



Smoking rate trend for women and men 1982 and 2002



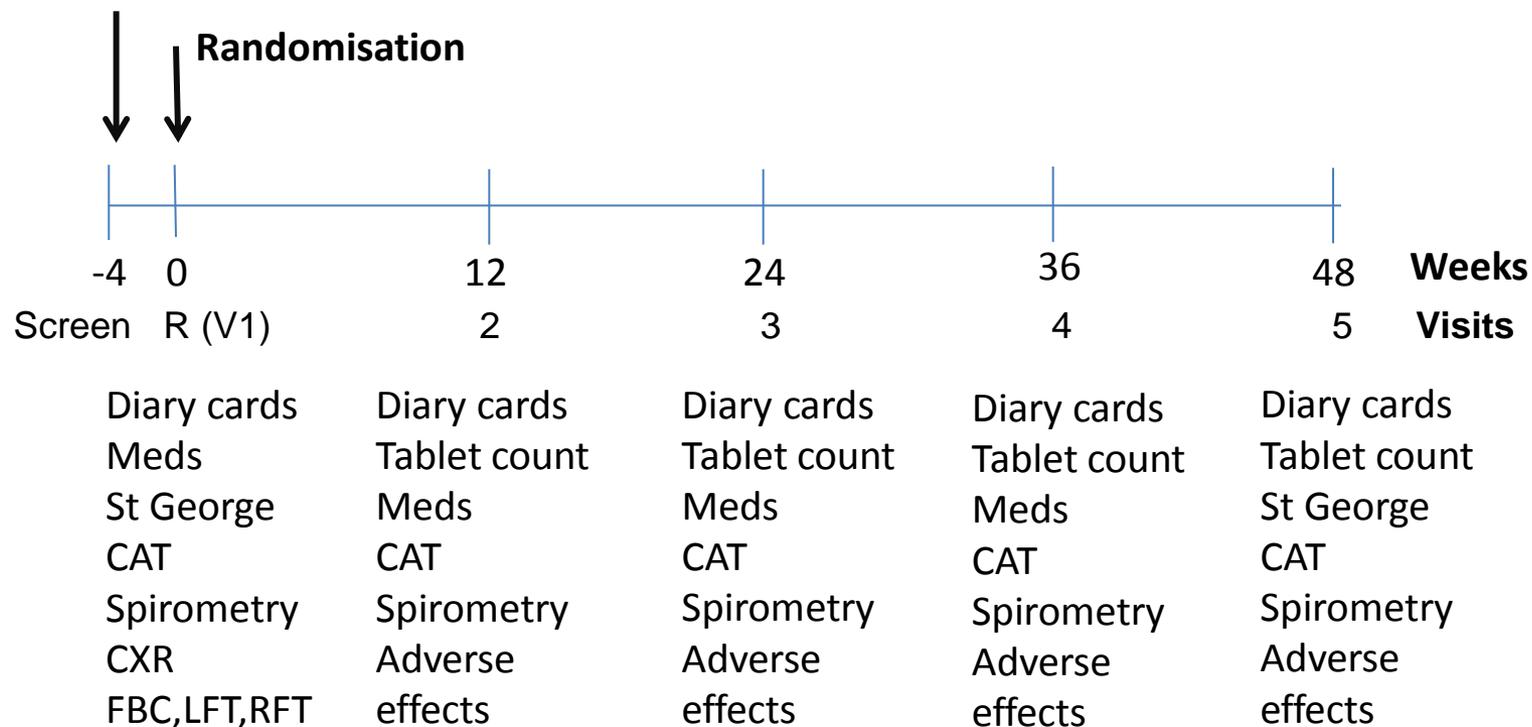
# COPD comprehensive treatment

Fang X, Wang X, Bai C. Chest 2011;139;120

- Smoking cessation
- Pharmacologic treatment
- LVRS / transplantation
- **COPD costs of treatment**
  - Health care costs ~10% of total societal costs
  - Hospitalisation ~ 63% of health care costs
  - Health care costs - drugs ~ 20% health care costs
  - Drugs are expensive – global pricing policy, inhalers

# TASCS STUDY DESIGN

Withdrawal ICS,  
theophylline



Plasma theophylline at 12, 48 weeks in 100 random subjects  
 Plasma cortisol at 50 weeks in 100 random subjects.



# Building networks

## ■ **Justification**

- ✓ High burden of disease
- ✓ Need for affordable, applicable interventions
- ✓ Must be achievable in urban and rural settings

## ■ **Investigator initiated Study**

- ✓ Asking a mechanisms question
- ✓ Develop skills and capacity
  - ✓ GC project management and implementation
  - ✓ Investigators and research staff
- ✓ Develop investigator networks for future trials
- ✓ Challenges current treatment recommendations

# Where's Wally?



OR....in the wider population,  
Where is the person who was eligible for  
the study?



# Ensuring inclusiveness

Respiratory Medicine (2007) 101, 1313–1320

Respiratory Medicine (2007) 101, 1313–1320



ELSEVIER

Travers et al

respiratoryMEDICINE

External validity of randomized controlled trials in COPD

- Postal survey (Wellington NZ) to 3500 randomly selected residents aged 25–75; invited to complete a detailed respiratory questionnaire & RFTs
- Assessed against the eligibility criteria of 18 major RCTs cited in the Global Initiative for COPD guidelines
- 749 subjects completed full survey, 117 had COPD
- A median of 5% (range 0–20%) of subjects met inclusion criteria for the major RCTs
- Of 55 subjects with COPD receiving treatment, 0–9% (median 5%) met inclusion criteria for the major RCTs
- Major COPD RCTs on which treatment guidelines are based may have limited external validity
- **Over 90% of the COPD subjects in the community who were taking medication, did so on the basis of RCTs for which they would not have been eligible**



A decade of

DISCOVERY · INNOVATION · IMPACT



ELSEVIER

Travers J. et al

respiratoryMEDICINE

## External validity of randomized controlled trials in COPD

Table 4 Selectivity of eligibility criteria.

Criterion	Percentage of WRS subjects with COPD excluded by criterion (%)
Doctor's diagnosis compatible with COPD	86
No atopy*	57
FEV <sub>1</sub> ≥ 50% and < 80% of predicted	57
At least 10 pack-years cigarette exposure	55
No asthma diagnosis	42
Bronchodilator reversibility < 15%	29
Age at least 40 years	9

WRS: Wellington respiratory survey.

COPD: chronic obstructive pulmonary disease.

FEV<sub>1</sub>: forced expiratory volume in 1 s.

\*Positive skin prick test to a common allergen.

# TASCS has Broad Eligibility Criteria

- Patients will be eligible for inclusion if they
  - Are current or former smokers (> 10 pack years)
  - 40-80 years of age
  - Have a clinical diagnosis of COPD
  - Have a post-bronchodilator FEV1/FVC < 70% and FEV1 < 70% predicted
- Patients are ineligible if
  - Coexistent illness precluding participation
  - Inability to complete QoL questionnaire
  - Concomitant major illness that would interfere with visits & F/U
  - Evidence of chronic liver disease or random blood glucose level > 8 mmol/L
  - High chance of non-adherence to protocol

# TASCS Challenges

- Recruitment!!!
  - More than 2,400 eligible subjects recruited in 12 months
  - 2,400 completed eligible subjects in next 12 months
  - Minimising withdrawals
- High quality spirometry to ATS standards
- Consistency over all 50 centres
- High quality data entry
- Patient engagement & commitment to
  - Medication adherence
  - Diary card recording
  - Study visits

# Outcome and significance

- COPD is a major and growing global health problem
- The cost of currently recommended treatment is high
- The proposed clinical trial is based on a large and growing body of *in vitro* data, supplemented by a number of published preliminary clinical studies
- The study treatment is affordable and accessible in all parts of the world
- The study will be published in a high profile journal
- The impact of a positive trial outcome has the potential to revolutionise the treatment of COPD not only in developing countries but will also spill over into other markets.

# Research and Health Improvement Academic-Public-Private partnerships

## Opportunities for academic involvement

- Expands views and expertise, identify more options
- Potential to generate and progress novel strategies further
- Academic leverage can deliver efficiencies
- Under-developed in Australia : 3.5% of Australian businesses co-operate with universities compared with 31 % in UK

## Challenges to academic involvement

- Research institutions have varied reputations and abilities
- IP, confidentiality, sharing profits and profile
- May require a longer timeframe than is customary in business
- Additional complexities for structure and reporting



A decade of

DISCOVERY · INNOVATION · IMPACT

# Research and Health Improvement

## Asking the hard questions

- Good Clinical Research thrives on effective academic and commercial partnerships for funding, effective and ethical trial conduct, applicability and incorporation of findings into practice to improve health outcomes
- Challenge is to
  - Ask the right research question
  - Design the right study to answer it in the right population
  - Engage the right investigators and partners
  - Develop and sustain cross-sector collaborative research, flow of ideas, financial support and benefit
  - Translate it into practice





# THE GEORGE INSTITUTE for Global Health



Sydney, AUSTRALIA | Beijing, CHINA | Hyderabad, INDIA | Oxford, UK



*Affiliated with the University of Sydney*