First global study on R&D funding flows for neglected diseases

Despite increased funding for research and development (R&D) for neglected diseases such as malaria, sleeping sickness and TB, donors still do not have a complete overview of what is currently being spent, which makes determining funding gaps extremely difficult. To address this, The George Institute has received a US$8.8 million grant from the Bill & Melinda Gates Foundation to review global investment into R&D for neglected diseases. For the first time, a team of international health experts will track global funding into the full range of product development for neglected diseases by surveying global public, private and philanthropic investments.

"Too many funders are forced to base substantial R&D investment decisions on out-of-date, unreliable information. They don’t know how much or where to invest, or how their investments sit in the context of overall funding flows and priorities," said Dr Mary Moran, Director of Health Policy at the Institute. "By providing an updated and in-depth overview, we hope to help donors around the world to avoid duplications and to determine where their investments are most needed," she added.

Although R&D funding to develop new tools to fight malaria, TB and HIV/AIDS has increased to over US$1.6 billion per year, funding for diseases of poverty does not match the disease burden or need. This major study will provide funders with evidence to help them better target their R&D funds.

Annually for a five-year period, The George Institute will survey and analyse public and private global funders, intermediaries and developers, collecting data through an online survey. The survey will examine all aspects of product research and development funding from basic research, through discovery and development, to post-registration activities that support product introduction. It will measure R&D investment into new drugs, vaccines, diagnostics, microbicides and other tools for tropical diseases such as malaria and sleeping sickness, as well as developing-country strains of global diseases such as pneumonia, meningitis and HIV/AIDS, which are often overlooked by product developers who typically prioritise industrialised country markets.

It is hoped that global mapping and better information will help governments, private research institutes and foundations to avoid duplication. The project maintains The George Institute’s focus on delivering quality public health outcomes. Given Dr Moran’s widely acknowledged work on neglected disease product pipelines and funding, the Health Policy Division of The George Institute is uniquely placed to deliver such an important and vital project.
A Message from the Principal Director

Many readers will be aware of early reports of the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial that were released by the US National Heart, Lung and Blood Institute (NHLBI) in February, suggesting that intensive glucose lowering treatment levels had increased the death rate among patients with diabetes recruited to the trial.

Due to this unexpected report, we felt it was in the public interest for us to ask the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation) Data Monitoring and Safety Committee to make a statement as to whether the available data from ADVANCE provide any support for the suggestion that intensive blood glucose lowering may increase mortality.

ADVANCE was designed to answer two questions in patients with type 2 diabetes: first, does intensive treatment to lower blood pressure improve outcome; and second, does intensive treatment to reduce blood glucose improve outcome. As in ACCORD, this intensive treatment program was designed to lower blood glucose to levels below those usually recommended by clinical guidelines.

At the time of the announcement by the NHLBI, patients participating in the ADVANCE study had completed their final visits, the study database was close to finalisation and we were expecting to have definitive results in the short-term.

The Data Monitoring and Safety Committee reviewed the data that were more than 99% complete, and the Chairman of the ADVANCE Data Monitoring and Safety Committee, Professor Rory Collins from the University of Oxford, provided the following statement: “The interim results from ADVANCE provide no confirmation of the adverse mortality trend reported from the ACCORD study.” He also noted that the ADVANCE interim results were based on more than twice as much data and similar levels of glucose control as in ACCORD. The members of the Data Monitoring and Safety Committee were the only members of the ADVANCE study team with access to the study results at this time.

Doctors and patients should feel reassured that the mortality trend reported by the ACCORD study has not been found in the interim results from ADVANCE. However, we need to await more definitive analyses and reports from both studies before drawing final conclusions.

We are pleased that the results of the blood glucose arm of ADVANCE will be presented at the American Diabetes Association Conference in San Francisco on Friday 6 June 2008. We look forward to disseminating these results in the following issue of George Research.

For more information about the ADVANCE study, visit www.thegeorgeinstitute.org or phone +61 2 9993 4500.

Professor Stephen MacMahon
The George Institute for International Health
Early and intensive lowering of high blood pressure has shown promising effects in stroke patients, according to early results of the INTERACT trial (the intensive blood pressure reduction in acute cerebral haemorrhage trial).

This was the first large-scale investigation into managing raised blood pressure after intracerebral haemorrhage (stroke), which demonstrated that rapid blood pressure lowering is well tolerated and appears to reduce the amount of bleeding in the brain, indicating that such treatment could reduce the risk of death and disability in stroke patients.

“These results show that drug treatment to lower elevated blood pressure can be given quickly and safely to patients with intracranial haemorrhage,” according to Professor Craig Anderson, Director of the Neurological and Mental Health Division at The George Institute. Professor Anderson outlined results at the American Heart Association’s International Stroke Conference in New Orleans in March.

“Furthermore, this treatment appears to limit bleeding in the brain in this type of stroke, which may improve chances of recovery for patients.”

Intracerebral haemorrhage (ICH) is the most serious type of stroke that results from rupture of a blood vessel within the brain. This is often the result of high blood pressure and affects over one million people around the world each year. Over one third of patients die early after the onset of ICH and most survivors are left permanently disabled. The aims of the pilot study were to determine the feasibility and safety of rapid lowering of elevated blood pressure to more ‘normal’ levels after the onset of ICH, and also test whether the treatment reduces the amount of bleeding in the brain.

The results challenge current international guidelines for the management of blood pressure in stroke, which tend to indicate that high blood pressure is dangerous but are uncertain about either the level at which to commence or cease such treatment. Professor Anderson explained that currently there is wide variation in the use of blood pressure lowering as acute treatment for stroke around the world.

The INTERACT vanguard phase recruited 404 patients from 44 hospitals in Australia, China and South Korea from November 2005 to April 2007. Patients who presented within six hours of onset of ICH and with acutely elevated blood pressure were randomised to receive either a treatment strategy of rapid blood pressure lowering or the more conservative, American Heart Association guideline-based blood pressure lowering. Patients were assessed in terms of their response to treatment, degree of recovery and changes in brain scans.

“Despite the magnitude of the burden imposed by this disease, and the high cost to health services, there is no widely available treatment for the condition. However, early rapid blood pressure lowering shows considerable promise as a widely applicable, cost-effective therapy that can be readily incorporated into clinical practice,” noted Professor Anderson.

The hypothesis will be tested in a much larger main phase to INTERACT in some 2,000 patients with ICH, which will commence later this year. The study is funded by the National Health and Medical Research Council of Australia.
Chris Lawrence has received the 2008 Fulbright Indigenous Scholarship sponsored by the Australian Federal Department of Education, Employment and Workplace Relations. He is currently a Study Manager at The George Institute for International Health and completing a PhD in epidemiology at the University of Sydney. Through his Fulbright Scholarship, Chris will undertake research at the Brigham and Women’s Hospital in Boston, a teaching facility for Harvard’s Medical and Public Health Schools. He will also receive academic mentoring and supervision from within the School of Public Health at Harvard University.

“Diabetes is Australia’s fastest growing chronic disease and the seventh highest cause of death in Australia. Australia’s Indigenous population suffers the fourth highest rate of type 2 diabetes in the world, with Aboriginal and Torres Strait Islander people over 35 years among those at highest risk,” explains Chris.

“Scientists in the U.S. are world leaders in interventions designed to reduce the incidence of obesity and onset of type 2 diabetes amongst minority groups – African-American, Latino, Hispanic, and Vietnamese communities, as well as Native Americans, will be involved in my research project through the Brigham and Women’s Hospital.”

“To date, no Australian interventions designed to reduce the incidence of type 2 diabetes amongst minority groups have been published. Therefore there is limited scientific expertise in this area in Australia. In contrast, researchers in the U.S. have demonstrated excellent results in this area using flexible, culturally sensitive methods.”

Indigenous Australians experience epidemic levels of diabetes compared with other Australians, yet little research has been done into methods of reducing the incidence of this chronic health problem.


The Fulbright Program is the largest and one of the most prestigious educational scholarship programs in the world. It operates between the United States and over 150 countries worldwide. Established in Australia in 1949 through a binational treaty between the Australian and U.S. Governments, the program has supported over 5,000 scholarships.

The mission of the Australian-American Fulbright Commission is to promote mutual understanding through educational and cultural exchange between Australia and the United States. It does this primarily through the administration of Fulbright scholarships.

The Fulbright Indigenous Scholarship was established to support and recognise young Indigenous leaders’ commitment to achieving excellence, while seeking an international perspective and collaboration through their studies.
A clear, direct link between obesity and colorectal cancer, the second most common form of cancer in Australia with more than 12,000 new cases each year, has been shown in a new report, published in Cancer Epidemiology, Biomarkers and Prevention.

The report shows that obese individuals (Body Mass Index (BMI) ≥ 30 kg/m²) have a 20% greater risk of developing colorectal cancer compared with those of normal weight (BMI < 25 kg/m²). The analyses also indicated that obese men are at 30% greater risk of developing the cancer compared with obese women. Findings from the study also showed that carrying even a few excess kilos substantially increases the risk of colorectal cancer; for every 5kg weight gain the risk of developing the cancer increases by 7%.

Dr Rachel Huxley and co-authors in The George Institute’s Nutrition and Lifestyle team reviewed over 70,000 patients in an analysis that included studies all across the globe: “Approximately, one in twenty Australians will develop colorectal cancer in their lifetime and our data clearly indicate that the risk of developing the cancer can be substantially reduced by maintaining a healthy weight,” said Dr Huxley.

Both the World Cancer Research Fund and The George Institute report stress the increasing levels of obesity in both high income and developing countries. “Currently, around 300 million people across the world are obese. This figure is expected to rise up toward 700 million by 2015. Considering that obesity increases the threat of colorectal cancer by 20%, this means that 10,000 cases each year are due to severe excess weight. The number of cases of colorectal cancer alone, caused by obesity, is likely to rise to at least 25,000 by 2015,” added Dr Huxley.

Body Mass Index (BMI) is measured by dividing your body weight in kilograms by height in meters squared. An individual’s BMI is associated with their body fat and health risk, a high BMI is ≥30kg/m² and normal BMI is 25kg/m².

While 20% is a considerable risk, previous reviews have suggested that obesity may be associated with up to 30-60% greater risk of colorectal cancer. However Dr Huxley says, “This over-estimation is most likely due to the impact of publication bias in medical and scientific journals. Regardless, a 20% greater risk is still considerable and sends a clear message about watching what you eat and being more physically active.”

The new research findings draw parallel messages with the latest report from the World Cancer Research Fund Report, which provides further support regarding the link between obesity and cancer. Importantly, the primary recommendation of the report is; “Be as lean as possible within the normal range of body weight”, supported by a public health goal of ‘Median adult body mass index (BMI) to be between 21 and 23’. All eight recommendations made in the report were focused on healthy eating, drinking and physical activity, creating a sincere message of the relationship between diet and cancer risk. “Although the mechanisms that explain the link between excess weight and cancer remain to be elucidated, substantial evidence supports an important role for diet and physical activity,” added Dr Huxley.

Staff Profile

“During my 10 years as a veterinary practitioner I saw a great deal of chronic disease in pets caused by the lifestyle of the owner. I had always had an interest in international public health, and this triggered greater interest in chronic disease, such as diabetes and cardiovascular disease in developing countries. I decided to return to university to further pursue this interest,” says Vibeke.

During her Masters in International Public Health, Vibeke noticed the broad nature of work at The George Institute, and made a move to the Nutrition and Lifestyle team in 2007, joining the team as a research student. Currently, Vibeke is in Copenhagen following an invitation to study at the Research Unit for Dietary Studies at the Institute of Preventive Medicine, Copenhagen University Hospital.

“The opportunity to come to Copenhagen was very exciting,” says Vibeke. “I am here for a study visit of three months and am focused on research on perceptions of obesity in childhood and risk of disease and mortality in adulthood for women, analysing a Danish cohort of women. Some of the work will be presented at the European Association for Study of Obesity Congress in Geneva in May.”

At the George, Vibeke is working toward a PhD on chronic disease in women, with emphasis on differences in risk for cardiovascular disease between men and women.

Interested in lifestyle choices both at work and in her spare time, Vibeke loves triathlon training and competing. At work, she would like to investigate how public health measures will improve community lifestyle.

“At this stage, my goal is to obtain my PhD! In the long term, I would like to have an impact on prevention of chronic disease.”
Achieving global equity in treating kidney disease

Worldwide, approximately 1.4 million people, with severe (end-stage) kidney disease, rely on continuing dialysis or a kidney transplant to survive. High rates of kidney disease affect low-, middle- and high-income countries alike. However, in low- and middle-income countries, the costs and infrastructure involved in providing dialysis and transplant services mean that, for most sufferers, treatment options are seriously inadequate.

A number of strategies could make life-saving dialysis and transplantation available to many more people in need:

- development of locally appropriate transplantation and organ donor programs
- effectively coordinated use of public, non-governmental and private sources of funding
- service planning and cost containment
- use of generic drugs and local manufacture of dialysis consumables
- technical, educational and financial support from the international kidney disease and transplant community.

Associate Professor Alan Cass, Director of the Renal Division at The George Institute and Associate Professor of Renal Health, the University of Sydney explains, “A number of middle-income countries have shown that more equitable provision of dialysis and transplantation is possible. In Malaysia, dialysis services are provided through a mix of public hospitals, private, non-government and non-profit centres.

In Costa Rica, transplantation, which is the most cost-effective form of treatment, is a high priority in resource allocation.”

Ms Sarah White, Research Fellow in the Renal Division and PhD student, Central Clinical School, the University of Sydney says approximately 80% of the world’s dialysis and transplant patients live in Europe, Japan or North America. “In India, by contrast, at least 90% of people with end-stage kidney disease die without any treatment.”

“Low- and middle-income countries have limited capacity to fund treatment. In China, dialysis costs around US$7,500 per patient per year, and in India US$5,000. This poses major challenges for affected individuals or for their governments. Budget constraints and lack of trained personnel mean that therapies are rationed and, in most cases, a user-pays system is relied upon.”

Diabetes is now the leading cause of end-stage kidney disease in many countries. The global epidemic of type 2 diabetes, coupled with an ageing population, will increase the prevalence of end-stage kidney disease, particularly in developing regions.

“The actual global burden of end-stage kidney disease is hidden behind statistics which reflect only the number of people treated, not those who die without having received treatment. This is particularly true for low-income countries,” said Associate Professor Cass.

“To achieve greater equity in access to dialysis and transplantation for people in low- and middle-income countries, education, policy development and ongoing support from international professional bodies, government and non-government organisations are essential. Prevention, ideally an integrated approach to heart disease, stroke, diabetes and kidney disease, must also be a key objective,” he said.

The full report, How can we achieve global equity in provision of renal replacement therapy? by the The George Institute, in collaboration with the Central and Western Clinical Schools of the University of Sydney, was published in the March edition of The Bulletin of the World Health Organization.

Events

Health Economics Seminars

MODELLING THE COST-EFFECTIVENESS OF A TELEPHONE AND PRINT INTERVENTION TO IMPROVE DIET & EXERCISE - METHODS AND PRELIMINARY FINDINGS

Associate Professor Nick Graves
Health Economist
Queensland University of Technology

Date: 20 May 2008
Time: 4-5 pm
Location: The George Institute Level 10, KGV Building Royal Prince Alfred Hospital Missenden Rd, Camperdown

MABEL (MEDICINE IN AUSTRALIA: BALANCING EMPLOYMENT AND LIFE). METHODS AND PILOT RESULTS FROM THE AUSTRALIAN LONGITUDINAL SURVEY OF DOCTORS

Professor Tony Scott
Professorial Fellow
Melbourne Institute of Applied Economic and Social Research, The University of Melbourne

Date: 17 June 2008
Time: 4-5pm
Location: The George Institute Level 10, KGV Building Royal Prince Alfred Hospital Missenden Rd, Camperdown

This joint health economics seminar series is the result of a collaboration between the School of Public Health, the University of Sydney, The George Institute for International Health and the National Drug and Alcohol Research Centre, the University of NSW.

Information on the health economics seminar program is available on the following website: www.health.usyd.edu.au or by calling Nafisa Alam on 02 9036 9262.

If you would like information on future seminars and events send your details to info@george.org.au.
Results from the largest cardiovascular study in high-risk patients, has shown that combination treatment with commonly used blood-pressure lowering drugs, ARBs (angiotensin receptor blocker) and ACE-inhibitors (angiotensin-coverting enzyme inhibitor), does not provide extra protective benefit for patients at high-risk heart disease, stroke, and heart failure. In fact, the treatment increases the risks of dizziness, blackouts and kidney problems.

The landmark study compared the effectiveness of two types of anti-hypertensive drug treatments: the ACE-inhibitor ramipril, and the ARB, telmisartan. The study had two aims: to determine whether telmisartan was equivalent to ramipril, and that the combined treatment was superior to ramipril alone, in the prevention of cardiovascular death, myocardial infarction, stroke, or hospitalisation for heart failure in people at high-risk of cardiovascular disease on the basis of being aged over 55 years and having a history of heart attack, angina, stroke, peripheral vascular disease, or diabetes with complications.

“Separately, ACE inhibitors and ARBs have shown benefits and to effectively lower blood pressure. The combination of ARBs and ACE-inhibitors was therefore thought to provide extra benefit over using the therapies individually. However, this study has shown that this is not the case, with no extra benefits of combining ACE-inhibitors with ARBs in people with cardiovascular disease. This has been further underlined by apparent side-effects such as increased dizziness and blackouts from lower blood pressure, and an increase in kidney problems, including the need for dialysis,” said global co-chair of the study, Professor Craig Anderson from The George Institute.

A total of 25,620 patients were recruited from 41 countries across the world to take part in the randomised controlled trial and followed up for over four years, providing an exceptional amount of data.

According to Professor Craig Anderson (right) the combined use of ACE-inhibitors and ARBs are not recommended among patients with cardiovascular disease.

According to Professor Garry Jennings from the Baker Heart Research Institute and Australian national leader of the study, “The study has established the benefits of an ARB as a suitable alternative to an ACE-inhibitor for the prevention of cardiovascular events, but there is no additional advantage from combining ARBs and ACE-inhibitors. Such combination treatment cannot be recommended as part of routine care in the management of high-risk patients with cardiovascular disease or diabetes.”

Cardiovascular disease is a major global healthcare problem accounting for 40-50% of all deaths in industrialised countries and about 25% in other countries. Cardiovascular disease, which includes heart attack, stroke, congestive heart failure and sudden death, causes major health problems and much distress for many people, families and health care systems around the world. Research has shown that several different types of drugs used for the treatment of high blood pressure can prevent cardiovascular disease, but there is uncertainty over the ability of one type of drug to be more effective than another or, if a combination of two different types of drugs, is more effective at reducing risk of cardiovascular events.

The risk of coronary heart disease is significantly reduced by commonly used drugs that lower blood pressure, including ACE-inhibitors and ARBs. Both have shown to improve health by preventing cardiovascular complications in high-risk patients, while ACE-inhibitors may cause an irritable cough in about 10% of patients. According to authors, ARBs are now readily available and allow effective lowering of blood pressure without the side effects associated with ACE-inhibitors.

The results will provide important recommendations about the options for treatment in patients with cardiovascular disease. The benefits of ARBs are being evaluated in additional placebo-controlled trials that are expected to be known later in 2008.

The findings were announced at the American Congress of Cardiology in April, by Australian researchers from the Baker Heart Research Institute and The George Institute, which coincided with publication in the New England Journal of Medicine.
Building on the Institute’s firm foundation in musculoskeletal research, staff and students from the Centre for Evidence-based Physiotherapy, previously based within the Faculty of Health Sciences at the University of Sydney, joined The George Institute in April 2008 forming a new Musculoskeletal Division.

This new, larger team now brings together the Institute’s work in osteoarthritis with the University of Sydney’s expertise in physiotherapy. The Musculoskeletal Division research, which will be lead by Professor Chris Maher, will address four principal themes: ageing, osteoarthritis, back pain and contracture.

“Our interest is in developing simple, cost-effective treatments, and improving service delivery for the most common and costly musculoskeletal health conditions,” says Professor Maher. “We also have a strong focus on improving the health and function of older adults.”

The Musculoskeletal Division research priorities include:
- understanding the mechanisms and treatment of contracture
- developing a better understanding of causes and source of low back pain
- evaluating new models of service provision for musculoskeletal conditions that aim to reduce cost, complexity, waiting times
- implementation of evidence-based exercise programs to enhance functioning in older people and those with physical disability
- rigorous evaluation of intervention strategies for common and costly musculoskeletal health conditions.

Utilising a multidisciplinary approach to research, staff will work with national and international collaborators to improve musculoskeletal health and health services. The division will also continue to host the Centre for Evidence-based Physiotherapy, which aims to foster clinical practice that is informed by the best evidence.

The team of around 30 experts also brings a considerable track record in grant successes and widely acknowledged publications to the table. Their approach to research is consistent with that undertaken across The George Institute, and their focus on musculoskeletal conditions will undoubtedly strengthen the previous musculoskeletal activities undertaken at the Institute.

Falls prevention research shows innovation is required

Falls are a serious problem for older adults, many of whom have been shown to experience a fall in hospital, resulting in injury and increased length of stay. There is little evidence that shows how best to prevent falls in hospitals.

Dr Cathie Sherrington of the new Musculoskeletal Division at The George Institute recently contributed to the largest falls prevention intervention trial to date, which was carried out among 4,000 patients in aged care and rehabilitation wards in 12 Sydney hospitals.

The intervention included a risk assessment of falls, staff and patient education, drug review, modified bedside and ward environments, an exercise program and alarms for selected patients.

After three months, no effect on falls was found. The length of stay (average of seven days) was shorter than in previous studies which have found such interventions to be effective. According to Dr Sherrington, more innovative approaches are required to prevent falls in short-stay wards.

The paper, Cluster randomised trial of a targeted multifactorial intervention to prevent falls among older people in hospital, was published in the British Medical Journal in April 2008.