



Royal Children's Hospital Campus Submission to McKeon Review

Introduction:

In this submission we focus on the important contributions that a Children's Hospital Campus like ours can make to Health and Medical Research.

Our Campus functions in the model of an Academic Health Science Centre with hospital, university and medical research institute staff all working together to create better health outcomes for children. We believe that using this model of building research teams involving staff from all three organizations and working on problems in an integrated way promotes faster and more effective translational outcomes leading to early intervention and prevention. Return on funding will be greatest if funding is tailored to encourage and support such collaborative research partnerships. We make the point that Australia has a comparative advantage in creating such research settings.

Our Campus supports mechanisms that will enhance multidisciplinary team building research. We oppose any changes to the Health and Medical Research sector that will divide areas of medical research and fail to leverage research success across all fields.

Firstly, we will respond to the four questions that the review Panel has posed. Secondly, we will describe our Campus and the three partner organizations and use case studies to demonstrate the team building approach to argue that an emphasis on multidisciplinary team building and translation of research is the cornerstone for effective health and medical research in Australia.

1) Why is it in Australia's interest to have a viable, internationally competitive health and medical research sector?

It is in Australia's interest to be globally competitive in health and medical research for demonstrated health, social and financial reasons.^{1,2,3} Australia is in a unique position to remain competitive for several reasons including:

- the interaction and integration of Medical Research Institutes and University Departments on Hospital Campuses and the opportunity this affords to bring together investigators in the basic sciences with clinical and public health researchers in working teams
- the flourishing Medical Research Institute sector via the "virtuous cycle" of Peter Wills, with effective medical research leading directly to better health through discovery and encouraging a higher standard of academic medicine which also improves general standards

¹ Extrapolated returns on investment in NHMRC medical research, Report from Deloitte Access Economics commissioned by Australian Society for Medical Research 2011

² The Economic Value of Australia's Investment in Health and Medical Research: Reinforcing the Evidence for Exceptional Returns. A report from Access Economics, commissioned by Research Australia, 2010

³ Exceptional Returns, the Value of Investing in Health R&D in Australia prepared for the Australian Society for Medical Research by Access Economics, 2008



of health care and hence health of children - both are particularly important in children as their health is an investment in the future health and wealth of the nation

- State and Federal Government health and welfare databases and the enormous potential for linkage of health information

2) How might health and medical research be best managed and funded in Australia?

Medical Research funding should remain tied to the Health portfolio and must be increased as the current plateau of funding for NHMRC will create a lag in research productivity in this sector. Funding sources can be broadened using opportunities to leverage funding with the private sector and both State and Federal Government. One international example of combined funding for research initiatives is in the UK where the Wellcome Trust and the National Health Service have both put funding behind large research efforts. This model of negotiation between two like-minded funding bodies is able to be responsive and flexible to new ideas and initiatives. Increasing our global links and forming more networks will also increase funding and productivity.

One of the most pressing issues for Health and Medical Research is the need for indirect costs to be tied to grant funding and be accessible to the organisation conducting the research. As well as indirect costs to medical research institutes, there are also substantial direct and indirect costs incurred by the hospitals. Hospitals currently have no direct financial support to meet these costs. Funding for hospitals must include support for the indirect costs of clinical and translational research activity – such as clinician time and integrated technology platforms which accommodate tracking research, tissue banking and clinical and outcome data collection. Without this funding it is difficult to ensure clinical research is of high quality and relevant to patient needs, and it is difficult for research to be fully translated into clinical practice.

3) What are the health and medical research strategic directions and priorities and how might we meet them?

A driving focus for funding of health and medical research in Australia must be early intervention and disease prevention and translation of research into clinical and public health practice. Currently only 2% of the health budget is spent on preventive services or health promotion.⁴ With this in mind, the importance of child health and research in children and adolescents being a high priority cannot be overstated. Childhood and youth are the periods during which prevention and early intervention programs are most effective.

Firstly, many diseases in adult life (eg cancer, heart disease, mental health disorders, obesity and diabetes) are increasingly being shown to have their origins during childhood. For example, 1 in 4 children aged 5–17 years were overweight or obese in 2007–08 with 3 in 5 adults either overweight or obese and Type 2 diabetes one of the top five conditions causing disease burden in 55–64 year

⁴ AIHW 2010. Australia's health 2010. Australia's health no. 12. Cat. no. AUS 122. Canberra: AIHW.



olds.⁴ Research into the genetics and environmental causes of obesity to enable the identification and prevention of risk factors in childhood can bring social, financial and health benefits to adults as well as children.

Secondly, children with major medical problems that are left with lifelong disability are living well into adulthood and often generate enormous ongoing costs to the healthcare system. Maximising the potential of these children to participate as adults in our society makes good sense on every level. For example babies with congenital heart defects have been operated on for the past 40 years and are living well into their 20s and 30s. Maximising the procedure and follow up treatment will enable these children to live well into their adulthood and lead to less chronic illness and fewer heart transplants.

Finally, it is well known that early childhood is the most important developmental phase of life. The early years, including conception to birth, are critical for a person's overall development and wellbeing. Experiences within the family and community have an enormous impact on the ability to integrate into society and have a healthy lifestyle.

Given the information above, priorities for research must more appropriately embrace child health and development. In addition to this we recommend that consideration be made for the funding of large pieces of equipment, cohort studies and large clinical trials, eg. In the UK there have been large tranches of funding given for the UK Biobank (£100 million) and the UK Birth cohort (£28.5 million) jointly from the Wellcome Trust, the Medical Research Council and the National Health Service, which provide ongoing research resources and outcomes for that country for many years to come.

Other priorities are:

- Solving research workforce shortages by long term funding of all categories of fellowships (at least 5 years) and clearly delineating career structure and pathways
- Investigating positive ways to work with researchers in developing countries, particularly India and China
- More explicitly integrating health and medical research into the healthcare system

4) How can we optimise translation of health and medical research into better health and wellbeing?

- Promote a model of close integration between hospital and primary care providers with medical research institutes and universities using the Academic Health Science Centre model
- Improve clarity and accessibility of pathways for translation to clinical researchers by funding for Academic Health Science Centres, or by funding directed towards hospitals, and MRIs or University Departments specifically for translation



- Encourage engagement by hospitals and primary care providers by developing research and translational key performance indicators for hospitals and primary care providers
- Improve education and training for clinical and public health researchers in translation of research and the principles of health services research
- Improve the way we measure health outcomes in Australia and link these to research priorities in Academic Health Science Centres.

The Academic Health Science Centre model is well placed to be successful in Australia given the prominence of academic hospital campuses and the ability to focus research in the most appropriate settings, the capacity to build multidisciplinary teams of researchers and the potential for immediate translation of evidence into health outcomes

The Royal Children's Hospital Campus

This is a world-class children's hospital campus incorporating clinical care, research and teaching. It is a major contributor to the creation of knowledge for paediatric disease prevention and treatment, by educating health professionals and the community, and by applying the knowledge clinically and through appropriate population interventions.

The partner organizations:

The Royal Children's Hospital is the major specialist paediatric hospital in Victoria treating an average of around 35,000 inpatients per year and close to 230,000 outpatients and is the custodian of clinical care on the Campus. **The Murdoch Childrens Research Institute** is the largest child and adolescent medical research institute in Australia, with more than 1,400 staff and 60 large research teams and is the custodian of research on Campus. **The Department of Paediatrics** is a multi-disciplinary department within the Faculty of Medicine, Dentistry and Health Sciences at the University of Melbourne, with over 200 staff and research students and is the custodian for education on Campus. **The Royal Children's Hospital Foundation** is the fundraising arm of the hospital.

The campus approach:

Experience at the RCH Campus demonstrates that a model of joint leadership can facilitate effective integration and collaboration. The hospital, university department, research institute and fundraising arm each retain their own independent structure but work together through Campus Council to set strategic goals and develop Campus-wide initiatives. Campus Council comprises an independent Chair together with the CEOs and Board Chairs of each of the four entities. Each of the component entities is an equal partner and we stress that this is a key factor for effective governance. This governance structure has facilitated major progress in harmonising administration, aligning strategic research-clinical goals and developing relationship agreements to define the level



of support, collaboration and exchange of service. It has also been associated with an increased level of success in competitive grant funding and greater success in translation.

We are a hospital-university campus linked to medical research institutes with a strong international reputation and impact. We have critical mass (clinical cohorts, clinicians and researchers), strong research outputs (publications, peer-reviewed grant funding, translational outcomes and commercialisation), and are capable of leading Australia's translation of research into improved clinical outcomes. In **Appendix I**, we demonstrate the importance of building multidisciplinary teams to promote effective translation and health outcomes.

Conclusion:

We argue that translational research is most effective and patient care is most likely to be evidence based when there is a close, broad and functional integration between a hospitals, medical research institutes and universities. This partnership model should be promoted and seen as the preferred model, and such partnerships should be recognised in funding priorities.

In addition we argue that making child health and development a research priority is essential in order to obtain benefits for the health and wellbeing of future Australians through early intervention and prevention of disease.



APPENDIX I

Development and safety of rotavirus vaccines

Following the discovery of rotavirus as the cause of severe gastroenteritis by Professor Ruth Bishop, Dr Ian Holmes and colleagues at the Royal Children's Hospital in 1973, researchers from the Murdoch Childrens Research Institute, the University of Melbourne and the Royal Children's Hospital have worked on the development of a rotavirus vaccine. This oral vaccine is based on a unique human neonatal strain of rotavirus discovered in Melbourne. The goal is to protect infants from birth against disease and death due to rotavirus infection. Each year more than 500,000 children under 5 years of age die due to rotavirus gastroenteritis, mostly in developing countries. In Australia more than 10,000 children are hospitalised annually due to rotavirus infection. The vaccine is being developed with the support of the NHMRC, the New Zealand Health Research Council, the World Health Organisation and a key collaboration with a developing country vaccine manufacturer, BioFarma Indonesia. Phase II trials are underway for this low cost rotavirus vaccine that is safe and effective when delivered at birth. This work conducted by a large multidisciplinary team on our Campus has the potential to dramatically limit the current barriers to effective prevention of rotavirus disease and make a significant impact on child mortality worldwide.

Developmental haemostasis in children and interaction with anticoagulant drugs.

For many years there has been no knowledge of reference values of haemostasis in healthy children, hence up to 30% of children having haemostatic tests can be misdiagnosed. In addition these tests are used to monitor blood thinning drugs such as heparin. 15% of all inpatients in a tertiary Children's Hospital setting are treated with heparin. These children are at major risk of life-threatening sequelae e.g. thrombosis and/or stroke if under-medicated; or haemorrhage if over-medicated, and this risk increases if the monitoring tests are not accurate.

A multidisciplinary team of researchers from this Campus are focusing on two areas: 1) the characterisation of coagulation profiles in healthy children from birth to adulthood; 2) the characterization of children's response to anti-coagulation therapy and the changes that occur throughout development from birth to adulthood. This program has collected world first data defining reference ranges for numerous haemostatic tests in children. These data have been converted into clinical guidelines which are adhered to nationally and internationally. Also the production of Paediatric Haemostatic Reference Range cards has been translated into Chinese, Spanish and English.

Food Allergy

Childhood food allergy has become a major public health problem. Concern over the rapidly rising incidence of food allergy is magnified by the extremely rare but devastating consequences of sudden death in a healthy child. Our team has recently described that Australia has the highest prevalence



of IgE-mediated food allergy in the world, with a staggering 10% of infants demonstrating food allergy. Over the most recent ten year period there has been a five-fold increase in hospital admissions for life-threatening anaphylaxis. During this period, clinical referral for life-threatening peanut allergy of all ages has doubled in the UK, the US and Australia. These changes are most pronounced in children less than five years, suggesting a causal role for early life determinants.

Our HealthNuts study of 5300 infants is the world's first comprehensive population-based study of food allergy with objective measurement of true food allergy and will enable us to better understand the natural history of allergic disorders including food allergy, asthma, eczema and hayfever and the relationship of risk factors for development of these conditions in the first six years of life. The study has already had important implications for clinical guidelines and public health policy. Including changes to the Infant Feeding Advice guidelines from the Australian Society of Clinical Immunology and Allergy and both the European and the American Academy of Paediatrics.

Transforming diagnosis of mitochondrial disorders

Over the last 15 years, researchers on this campus have been leading contributors to improving the diagnosis of inherited mitochondrial energy generation disorders. The first major achievement was in defining the biochemical and genetic spectrum of Leigh disease, the most common paediatric presentation. Subsequently, they defined diagnostic criteria for mitochondrial disorders that have been adopted internationally, performed the largest epidemiological study of childhood-onset mitochondrial disease and improved diagnostic approaches by showing that frozen tissue biopsies could be assayed reliably using new enzyme assays. The major focus is on understanding the genetic basis of disease, and they have identified 10 novel "disease genes". Most recently, they have led the application of new genomic technologies to these disorders. Collaborative research internationally is revealing both the potential and the challenge of using NGS technology in clinical diagnosis, which is highly relevant to other complicated conditions such as developmental delay, epilepsy, deafness and heart disease. These advances have only been possible due to the integration of the clinical and laboratory research teams.