Maximising the clinical outcomes of medical research: the critical importance of supporting peer-review funded research in public hospitals

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1. Executive Summary

On a worldwide basis, Australian medical researchers make a very significant contribution to knowledge generation, particularly in the fields of cancer biology, neurobiology and diabetes - chronic diseases that are becoming more prevalent in the developed world, including Australia. Much of this fine work is carried out in Universities and independent Medical Research Institutes as there are significant disincentives to performing research in hospitals. More broadly, Australia's capacity to further develop the key findings made by its laboratory-based researchers is limited because of significant blocks to translating advances from the laboratory to the clinic. For similar reasons, predominantly the failure of the health system to support clinicians wishing to engage in research (due to lack of both infrastructure support and protected time) the capacity of clinical researchers to address clinical questions that could be addressed in collaboration with their laboratory –based colleagues is severely limited.

This submission argues that enabling hospital-based research and enhancing the role of hospital-based clinician/researchers will lead to more favourable outcomes for Australian patients, while allowing the newest and most important medical advances to be rolled out in accordance with local needs and with the greatest economic benefits for Australia.

In particular, it is argued that removing a small number of key obstructions to hospital-based research will enable Australian scientists whether based in the laboratory or the clinic to achieve these goals in a cost-effective manner. In brief, we argue that:

(i) holders of competitive, peer-review grants (especially those from NHMRC) that are employed in the public hospital sector should become eligible for funding to support indirect research costs associated with those grants;

(ii) qualified clinician/researchers employed in public hospitals should have a proportion of their time (at least 20% but in some specific and appropriately justified cases as much as 50%) 'protected', to allow them to take part in clinical trials and translational laboratory and health services research relevant

to the Australian health scene, and to train the next generations of clinician/researchers;

(iii) clinical research infrastructure such as biostatistics, human ethics and clinical trials support should be adequately funded to facilitate research translation. Otherwise, the risk is that many opportunities for maximising the potential health impacts of NHMRC funded grants as well as other grants will be lost.

2. Background

It is commonly acknowledged that Australia hits 'well above its weight' when it comes to measuring outcomes of medical research. Despite Australia having a small share of the world population and GDP, its researchers publish a significantly higher proportion of academic papers than counterparts in other nations, while its Universities turn out large numbers of highly qualified scientists and clinicians. Given the pre-eminence of Australian medical researchers and the fact that the public purse funds a great deal of laboratory-based research, it is reasonable to expect that the Australian health system should be a major beneficiary. For instance:

(i) it should be possible to fast track discoveries made in Australia so that they are rapidly available to Australian consumers;

(ii) there should be ample opportunity to add value to locally-developed intellectual property by carrying out pre-clinical and clinical studies locally;

(iii) the Australian taxpayer should benefit from evidence-based changes in clinical practice that can potentially produce costs savings; and

(iv) the 'virtuous cycle' of bench-to-bedside-to-bench research should be enhanced by co-locating laboratory and clinical research in the hospital sector and continual training of Australia's brightest emerging clinician/researchers.

These risks and opportunities presented in this scenario are all the more important, given:

(i) the ever-growing prevalence of chronic diseases such as cancer, diabetes and neuro-degenerative diseases in the Australian community;

(ii) the growing complexity and cost of new therapies, and therefore, the need for new preventive measures, health education and early screening programs;

(iii) the trend towards individualised therapy, based on the genetic profile of the patient (and, in the case of most cancer patients, their individual cancers). Individualised therapy, while appearing expensive, may offer opportunities for major cost-savings and reduction of patient morbidity, as molecular screening should identify only those patients likely to benefit from that specific therapy, saving unsuitable patients from unwanted side-effects and sparing the community the associated costs. Research into new models of health service delivery, responsive to changing morbidity profiles and therapeutic administration requirements are key to optimising efficiencies.

3. The current situation

3.1 Funding for research indirect costs

The current Federal arrangements actively discriminate against and impede research in the public hospital system. Largely for historical reasons, research must be carried out in the hospital sector by 'stealth' and with no infrastructure support; this is largely because NHMRC grants awarded to hospital-based chief investigators (CIs) are ineligible to access funding for research indirect costs through both the major Federal funding schemes: that operated by DIISR (which exclusively supports University-based research and research teaching) and the IRIIS scheme, which is funded through DHA and administered by NHMRC. Access to either scheme will typically provide the institution hosting the grant CI with between 20 and 30 cents for every dollar in direct research funding to support everything that encompasses mundane infrastructure such as utility costs, through to the operational support of expensive shared technology platforms (for instance, rapid throughout DNA sequencing). Without this additional funding, it is almost impossible even to attempt delivering on the aims of a funded grant application. Typically, a clinician/researcher wishing to engage with hospitals (or more precisely, with patients afflicted with their disease of interest, their surgical specimens and other critical samples!) bypasses this crippling problem by simultaneously holding an appointment at a University or Medical research Institute sited close to that hospital and having that institution submit and administer their grant.

Such arrangements are misleading, confusing and unnecessarily convoluted, adding additional layers of expensive bureaucracy. They diminish the capacity to perform high quality research that involves patients, and in turn, severely limit the benefits potentially accruing to both patients and the Australian taxpayer[1].

In some instances, even the convoluted administrative arrangements described above cannot enable high quality, peer-review grant-based research in the hospital sector. This is best illustrated by the situation at our own hospital, The Peter MacCallum Cancer Institute, in Melbourne. As a public hospital, Peter Mac is unusual in a number of ways; most notably, it is a specialist hospital that deals solely with cancer. In addition, Peter Mac has a research-led model of clinical care; our own research and the latest findings elsewhere dictate multi-disciplinary patient management. Operationally, Peter Mac is also unusual in that it houses a very large laboratory Research Division comprising around 350 wet and dry lab researchers and around 100 honours and post-graduate students. The Clinical Divisions also support approximately 100 EFT in clinical research effort. Around 100 staff members currently hold external grants and prestigious fellowships from

[1] The other remarkable consequence of this set of arrangements is that the same grant funded by NHMRC is treated in three completely different ways by the Federal government for the purposes of accessing funding for research indirect costs, depending on the type of institution that employs the grant holder. A university-based researcher can typically access 20-30 cents per dollar (cpd) through DIISR; A CI employed at an independent MRI is eligible for up to 20 cpd through the IRIIS/NHMRC scheme. Remarkably, if exactly-the-same grant is held by a CI employed by a hospital, no funding whatever is made available to cover the related indirect costs of research.

NHMRC, prestigious agencies such as Leukemia and Lymphoma Society, the Victorian Cancer Agency or Cancer Council Victoria, and through industry (for example, the Pfizer Fellowship Scheme). The annual operating budget for research at Peter Mac alone was $68M in 2010/11, with the majority sourced through competitive peer-review schemes, particularly those offered by NHMRC.

Despite these stellar achievements, research at hospital such as Peter Mac are largely hamstrung by the absence of funding for research-critical or even the most basic infrastructure, particularly that necessary for supporting successful peer-review grant funding from agencies such as NHMRC. That clinical research exists at all in hospitals is a testament to philanthropic giving, funding that ought more appropriately be applied to initiatives such as procurement of 'cutting-edge' equipment platforms to drive innovation rather than 'paying the electricity bill'.

Although adequately supporting such a large academic effort within a public hospital would pose a number of financial challenges, it would also have many benefits, particularly in the availability of the newest, evidence-based treatments for patients. This is because international Pharma companies need to partner with suitable hospitals to have their products tested in well-administered clinical trials, prior to applying for registration of those products. Investing in sophisticated health services research is an essential component of effective and efficient utilisation of new products.

Peter Mac is arguably unique Australia-wide in the scope of its research activity and the recently announced support by both Federal and State Governments (which will each contribute $426M) for the $1 billion Victorian Comprehensive Cancer Centre (VCCC) project acknowledges this. The new building will house the relocated Peter Mac, together with elements of The University of Melbourne and Melbourne Health; the broader joint venture will encompass collaborating nearby hospitals (Royal Women's, Royal Children's, Western, St Vincent's) and MRIs (Walter and Eliza Hall Institute, Murdoch Institute).

We argue that an opportunity will be lost if this generous and far-sighted gesture is not accompanied by operational funding of a scale that will enable world-class research at the new hospital.

Recommendations from Section 3.1

1. ***The holders (CIs) of peer-reviewed NHMRC and similar peer-review grants should, in their own right, be eligible for funding of research indirect costs on a basis similar to their colleagues employed at MRIs and in Universities.***

2. ***The mechanism for assessing and distributing indirect research cost funding should be centralised under a single agency. The simplest and most appropriate mechanism would be to distribute a quantum of funding for research indirect costs to the institution employing the CI on the successful grant, irrespective of whether the CI is employed at an MRI, a University or by a public hospital.***

3. ***Funding for indirect costs should be allocated contemporaneously with the grant funds, not several years later as occurs now.***

3.2 Protected time for clinician/researchers and supporting clinical trials infrastructure.

Co-locating high-quality laboratory-based and hospital based clinical research 'makes good sense'. It ensures that each discipline benefits from the expertise of the other, a synergy which would undoubtedly fast-track novel approaches to addressing many unresolved clinical issues. These sorts of collaborations are not that frequent in the Australian health sector but have often been limited by funding silos in which it's been argued that research budgets should not pay for health care and health budgets should not fund research. In fact, the reality is that many advances in health care will only occur by research embedded in the health sector and both funding streams must be linked in order to ensure that the revolution of molecular insights into tumour biology are translated into patient benefits.

Given the nature of these rapid advances, the role of clinician researchers who are trained in laboratory research, clinical medicine and complex patient care becomes paramount. Increasingly however, the lack of support for clinical research in the hospital sector, the lack of support for young clinicians to interrupt their careers (apart from a select few) to devote time to fundamental science and ultimately the lack of the positions in which dual-trained researchers can practice appropriately, means that these critical members of the research and clinical workforce sector are a dying breed.

Addressing this critical short-coming requires action in two directions:

(i) We need to provide opportunities for clinicians to conduct research via providing protected time away from the clinic and their ever increasing administrative responsibilities. We need to provide additional opportunities for young clinicians to take time out of their clinical career pathways to spend time in the laboratory or the clinical sciences in order to understand how to address clinically important questions. At a minimum, established clinicians need the opportunity to select careers in which they have 20% of their time protected for research, although in some specific instances there needs to be career opportunities for this to reach 50% protected time.

(ii) In creating such a model, it is imperative it be accompanied by support for clinical research platforms that underpin hospital based clinical and translational research – the need for biostatistical and database support, clinical trials nurses, the need for the creation of carefully clinically annotated tumour banks (which not only refers to tumour biopsies but germ line DNA, plasma DNA, circulating tumour cells, normal plasma), access to molecular and functional imaging, funding for molecular pathology. Using cancer as a relevant example, the latter is particularly critical given that the development of targeted therapies now involves full genetic sequencing of a tumour in order to attract major pharma and the emerging biotech sector. Major pharmaceutical companies are actively seeking

out centres whose patient tumor profiles are already known, given the time otherwise required to identify the most tractable molecular targets.

Recommendations from Section 3.2

1. ***Establishment of clinical research fellowships based on a formula that relates number of funded positions to the underlying research program. Funding would be in proportion to the budget for peer-review funded research at that hospital.***

2. ***Establishment of a model of protected research time for appropriately trained clinician/researchers funded as a small percentage of the overall health budget of the hospital and paid for by the relevant State government***

3. ***Support for key clinical research platforms (biostatistical and database support, clinical trials nurses, clinically annotated tumour banks, molecular and functional imaging and molecular pathology) modelled as a percentage of the overall research budget and paid from additional State/Federal funds.***

4. ***A requirement that institutions streamline research governance and ethics review in order to expedite the conduct of research and reduce associated costs.***

4. Conclusion

We submit that a number of significant, but potentially reversible structural impediments are currently limiting the tangible health and associated financial benefits arising from Australia's investment in laboratory-based medical research. The solution involves (i) encouraging new links between the excellent researchers in MRI's and Universities with clinicians in hospitals; (ii) removing financial disincentives to hospital-based laboratory and translational research, particularly addressing the availability of funding for research indirect costs on competitive grants; (iii) building enabling infrastructure for clinical research; and (iv) freeing up sufficient clinician time to allow a discourse with their laboratory colleagues, to jointly develop ideas and test the most promising in the clinic. Finally, we submit that Australia's investment in basic research has been spectacularly successful in fostering bright ideas and academic achievement, but the yield in useful clinical and/or financial outcomes can be markedly improved with relatively modest targeted investments that address these issues.