SUBMISSION TO SENATE INQUIRY FOR FUNDING RESEARCH INTO CANCERS WITH LOW SURVIVAL RATES

Introduction

Definition
'Less common' cancers as those with an incidence of between 6 and 12 (inclusive) per 100,000 Australians per annum.[1]

'Rare cancers' are defined as those with an incidence of less than 6 per 100,000 Australians per annum – a total of 186 cancer types have been defined as rare.

In 2015 Rare Cancers Australia released its second "Just a little more time". The report was launched in Parliament House Canberra by the Assistant Health Minister, Ken Wyatt MP.

The report demonstrated that over the past 20 years, survival rates in many rare and less common (RLC) cancers have only improved marginally, if at all, while outcomes for common cancers have improved dramatically. It is no small coincidence that government research funding into rare cancers remains disappointingly and disproportionately low, as does the money we spend on treatments for these patients through the Pharmaceutical Benefits Scheme (PBS).[2]

There are inherent challenges in treating very small patient groups. These challenges have conspired to create an environment whereby these patients are completely excluded from the progress achieved for those with more common cancer variations. As a result of poor investment in research and treatment, patients with rare cancers are, almost without exception, those most likely to have the lowest survival rates.

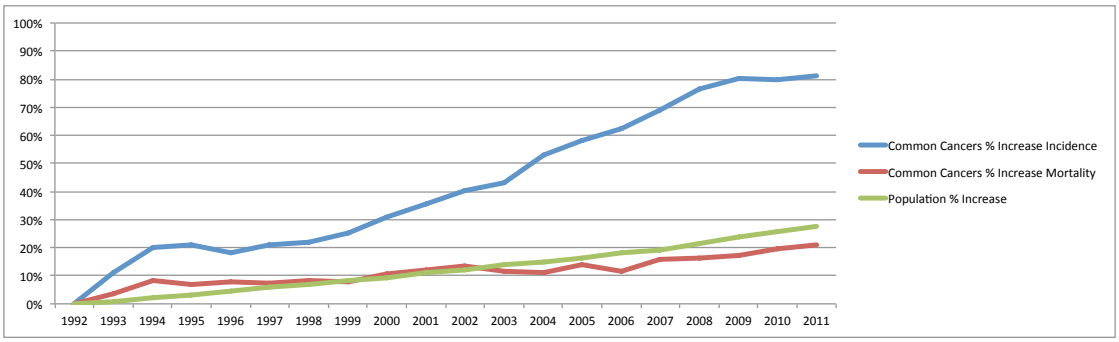
It is estimated that in 2014:

- **42,000 people** were diagnosed with an RLC cancer;
- **24,000 patients died** from an RLC cancer, accounting for half of all cancer deaths; and
- RLC cancers contributed to seven per cent of the total burden of disease in Australia.[3]

1 Gatta et al., Rare Cancers are not so rare: The rare cancer burden in Europe. European Journal of Cancer 47, 2493-2511 (2011).
2 Rare Cancers Australia 2014, Just a Little More Time: Rare Cancers Baseline Report
3 Rare Cancers Australia, Just a Little More Time: Rare Cancers Baseline Report 2013

The difference between common, RLC and rare cancers

Common Cancers

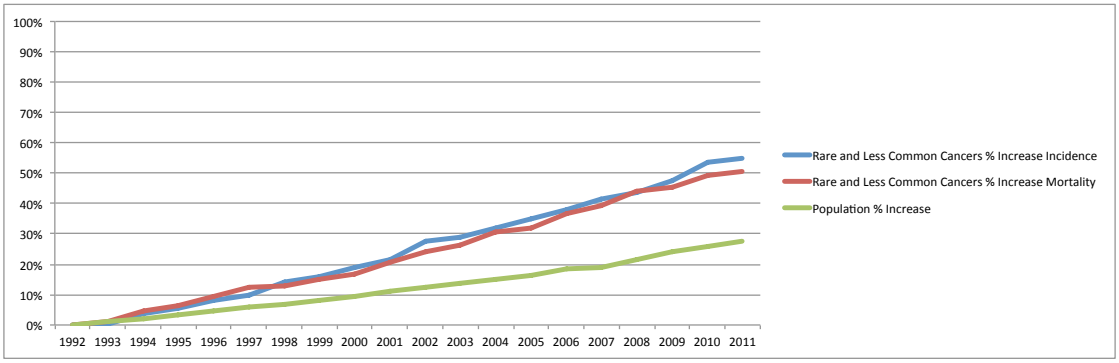


Graph 1: Incidence and mortality rates for common cancers compared to population change since 1992

The successes we've seen over the past 20 years for common cancer patients are significant. While incidence rates have increased, as a result of increased surveillance and screening, mortality rates have decreased due to investment in research, and treatment. As a result, patients today diagnosed with a common cancer have a much higher chance of survival than they did in the early 1990s.

Despite the actual number of deaths for all cancers increasing, the mortality rate for **all cancers** fell by 20 per cent between 1982 and 2014.[4] While it is true that significant advances have been made for common cancers, data shows that this is not the case for RLC cancers.

Rare and Less Common Cancers



Graph 2: Incidence and mortality rates for rare and less common cancers compared to population change since 1992

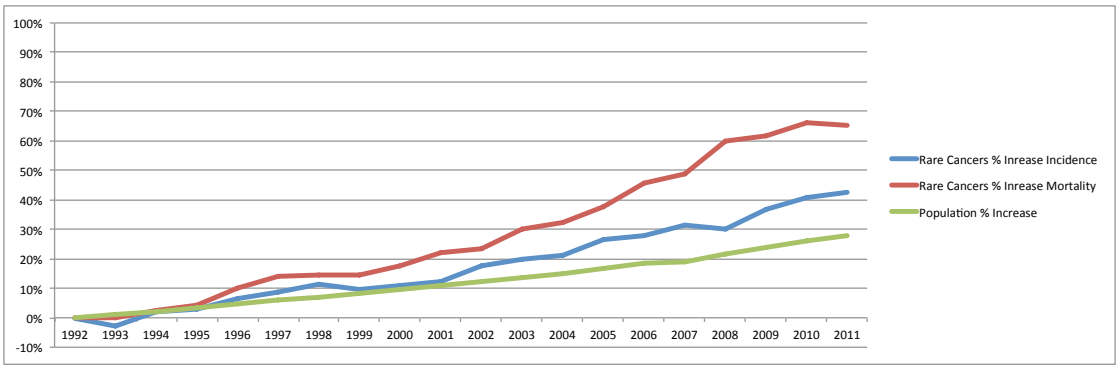
As distinct from common cancers, the percentage increase in incidence and mortality for RLC cancers occur at roughly the same rate, i.e. twice the rate of population increase. While we have seen increases in incidence for common cancers, we have also seen dramatic reductions in mortality due to early diagnosis and improved

4 Australian Institute of Health and Welfare 2014. Cancer in Australia: an overview 2014. Cancer series 90. Cat. No. CAN 88. Canberra: AIHW.

treatments, but this has not been the case for RLC cancers where research investment is poor and treatment availability limited.

The same effect is even more devastating in rare cancer diagnoses.

Rare Cancers



Graph 3: Incidence and mortality rates for rare and less common cancers compared to population change since 1992

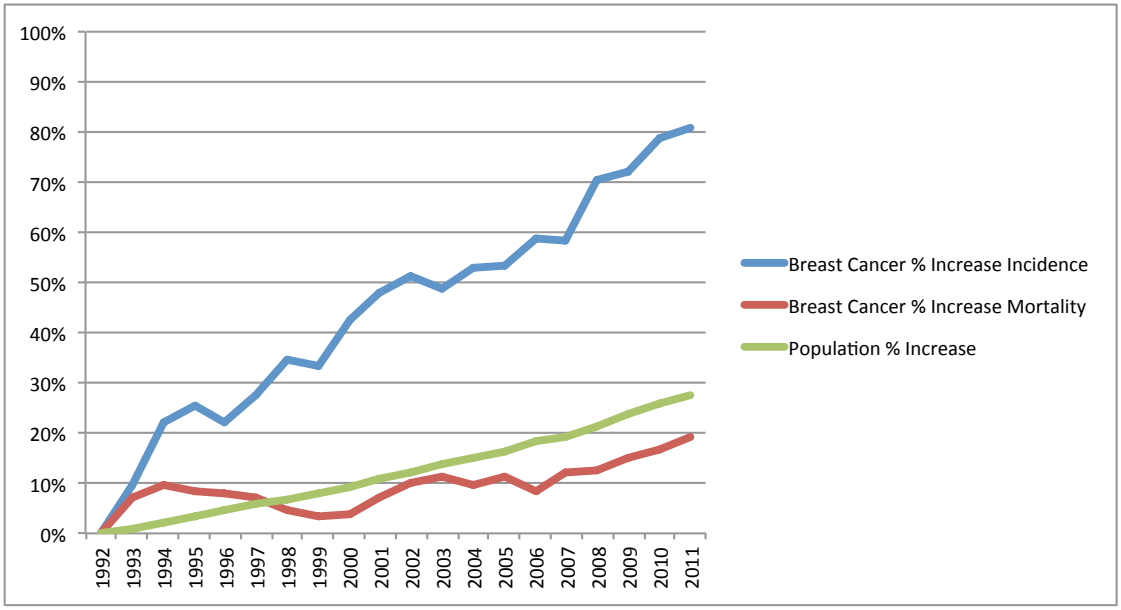
Australian patients diagnosed with a rare cancer face the greatest challenge of all; for rare cancer patients the increase in mortality rates far outstrip the rising incidence rates.

We need to recognise that a rare cancer diagnosis is often accompanied by a very poor prognosis and as our population ages Graph 3 provides a stark insight into the impact of these very neglected and undertreated cancers.

The following section shows the comparison between three cancers, and the impact that funding for research has had on improvements in survival.

Cancer Specific Example

Breast, Cervical and Ovarian Cancers



Graph 4: Incidence and mortality rates for breast cancer compared to population change since 1992

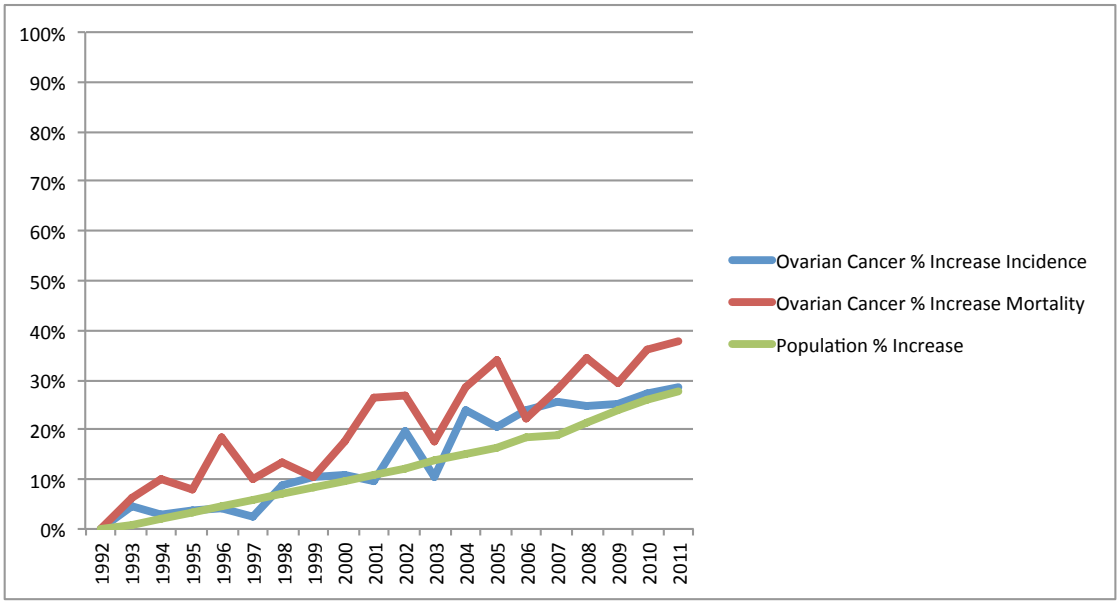
The AIHW estimates that in 2016 there will be 16,080 patients diagnosed with breast cancer; five-year relative survival at diagnosis for breast cancer patients is 89.6%. The age-standardised incidence rate for breast cancer is 116 per 100,000.[5]

Breast cancer is the most common cancer in Australian women. Between 1992 and 1994, the incidence of breast cancer increased sharply from 98 new cases of breast cancer per 100,000 females to 114 per 100,000. This observed increase corresponded with the introduction of the national breast cancer screening program, known today as BreastScreen Australia, in 1991.[6]

Due to significant investments in research, diagnostics, and treatments we have been able to significantly reduce breast cancer mortality over the past 20 years.

5 Australian Institute of Health and Welfare 2014. Cancer in Australia: an overview 2014. Cancer series 90. Cat. No. CAN 88. Canberra: AIHW.

6 Australian Institute of Health and Welfare. Interpreting Cancer Data, accessed on 12th January 2016 http://www.aihw.gov.au/cancer/data/interpreting/



Graph 5: Incidence and mortality rates for ovarian cancer compared to population change since 1992

The AIHW estimates that in 2016 there will be 1480 patients diagnosed with ovarian cancer; five-year relative survival at diagnosis for ovarian cancer patients is 43%. The age-standardised incidence rate for ovarian cancer is 5.4 per 100,000. [7]

By comparison, despite being the sixth most common cause of cancer-related death in women in Australia, no screening programs are available for ovarian cancer and incidence continues to increase at the same rate as population increase. The AIHW estimates that in 2016 there will be 1,480 patients diagnosed with ovarian cancer; it is also estimated that there will be 1,040 ovarian cancer deaths in the same year.[8]

When ovarian cancer is detected at an early 'localised' stage, when the cancer is confined to the ovary, up to 93% of women are likely to survive more than five years. However, only about 15% of all cases are diagnosed at this stage,[9] and as a result the average five-year survival remains low at 43%.[10]

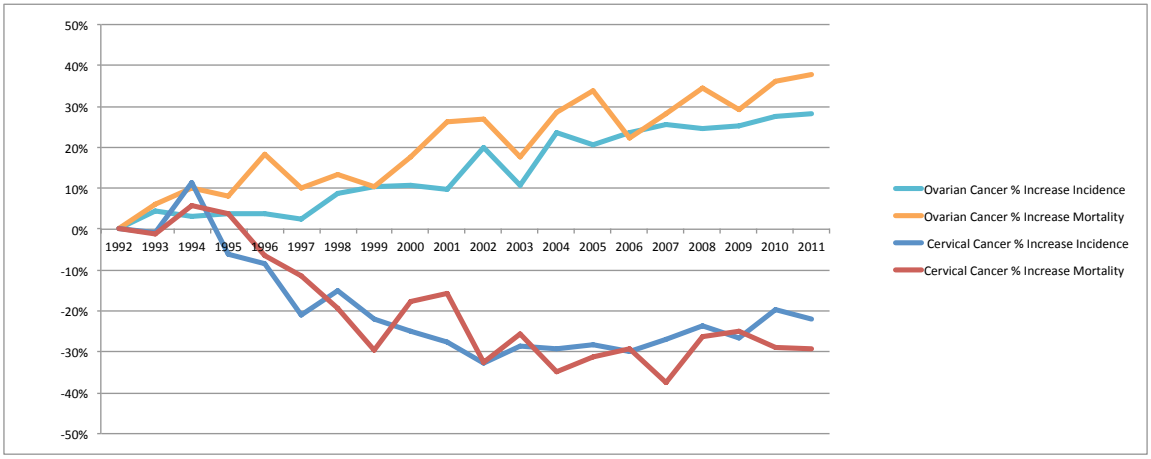
A further example of the impact of screening, and the introduction of preventative measures such as vaccination, is seen when comparing the outcomes incidence and mortality of cervical and ovarian cancers.

7 Australian Institute of Health and Welfare 2014. Cancer in Australia: an overview 2014. Cancer series 90. Cat. No. CAN 88. Canberra: AIHW.

8 Australian Institute of Health and Welfare 2014. Cancer in Australia: an overview 2014. Cancer series 90. Cat. No. CAN 88. Canberra: AIHW.

9 World Ovarian CancerDay. 5 Facts Everyone Should Know about Ovarian Cancer, accessed on 12th January 2016 http://ovariancancerday.org/about-ovarian/5-facts-everyone-should-know-about-ovarian-cancer/

10 Australian Institute of Health and Welfare 2014. Cancer in Australia: an overview 2014. Cancer series 90. Cat. No. CAN 88. Canberra: AIHW.



Graph 6: The difference between screening and prevention has on cancer incidence and mortality for cervical and ovarian cancers

The AIHW estimates that in 2016 there will be 905 patients diagnosed with cervical cancer; five year relative survival at diagnosis is 71.9%. The age-standardised incidence rate for cervical cancer is 3.5 per 100,000.[11]

Unlike ovarian cancer, there have been major advances in cervical cancer in the past 20 years. The current National Cervical Screening Program was introduced in 1991, and in 2007 the Government introduced the free National Human Papillomavirus Virus (HPV) Vaccination Program, using Gardasil, for school girls (boys were included in 2013). As of 1 May 2017 the National Cervical Screening Program (Pap test) will be replaced by an improved primary HPV test.

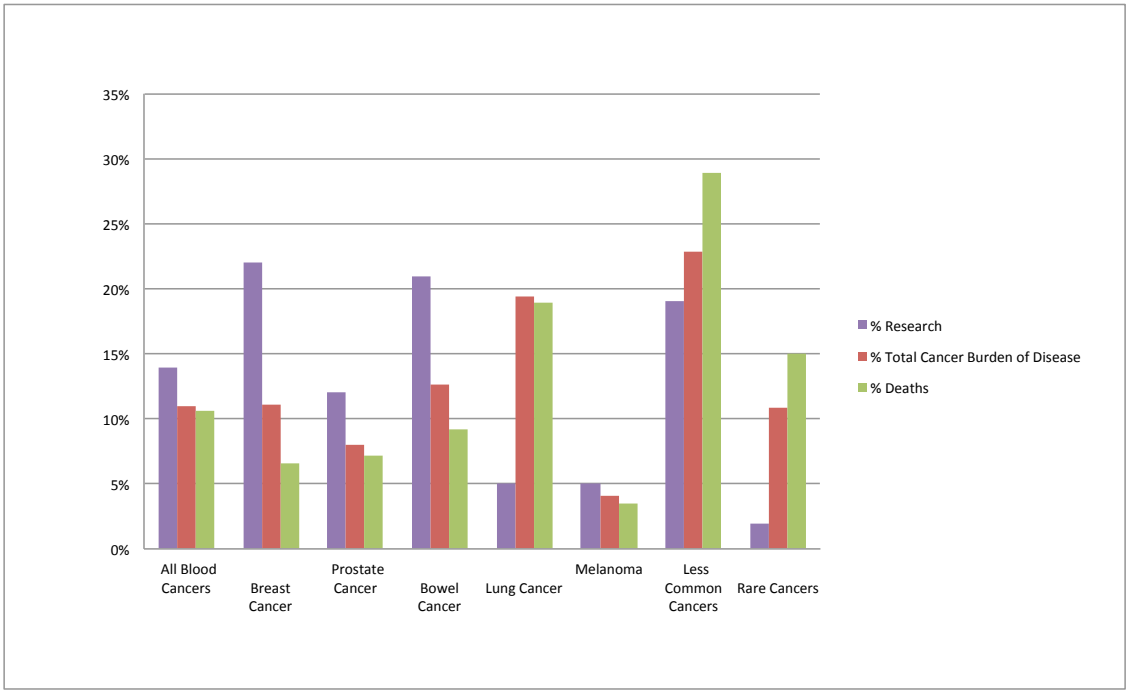
Both breast cancer and cervical cancer offer great hope for what is achievable in cancer prevention and treatment and, in different ways, can be seen as the 'gold standard' in terms of what is possible for improving outcomes for Australian cancer patients through investment in research. The demonstrable effect of preventative interventions, early diagnostic tests and improved access to treatment on the incidence and mortality of breast and cervical cancers is unfortunately not yet replicable across all cancers.

11 Australian Institute of Health and Welfare 2014. Cancer in Australia: an overview 2014. Cancer series 90. Cat. No. CAN 88. Canberra: AIHW.

Funding Cancer Research

Australia is a leader in cancer research. The 2015 Audit of Cancer Research in Australia reported that between 2006 and 2011, the Australian Government (including the NHMRC) provided $1.03bn (or 58% of $1.77bn total funding) for cancer research. Of the $350m spent annually on cancer research only a negligible 2% of that goes to solid rare tumours.[12]

The Audit report noted that while breast cancer, colorectal cancer, haematological cancers and genitourinary cancers received the highest levels of funding in Australia, the proportional funding to research in many cancers was low compared to incidence, mortality and burden of disease on the Australian population. Those cancers included lung, lymphoma, pancreas, oesophagus, kidney, stomach, bladder, myeloma and cancer of unknown primary.[13]



Graph 6: Percentage cancer research expenditure (per annum) versus percentage burden of disease and deaths

While the Audit report showed a slight increase in research funding for less common cancers, it demonstrated a continuing strong focus on common cancers within the Australian Research Community. Indeed it even recommended that '*Research funding investment in Australia could be prioritised for cancers which have a high impact*

12 Cancer Australia, 2015. Cancer Research in Australia: an overview of funding initiatives to support cancer research capacity in Australia 2006 to 2011.

13 Cancer Australia, 2015. Cancer Research in Australia: an overview of funding initiatives to support cancer research capacity in Australia 2006 to 2011.

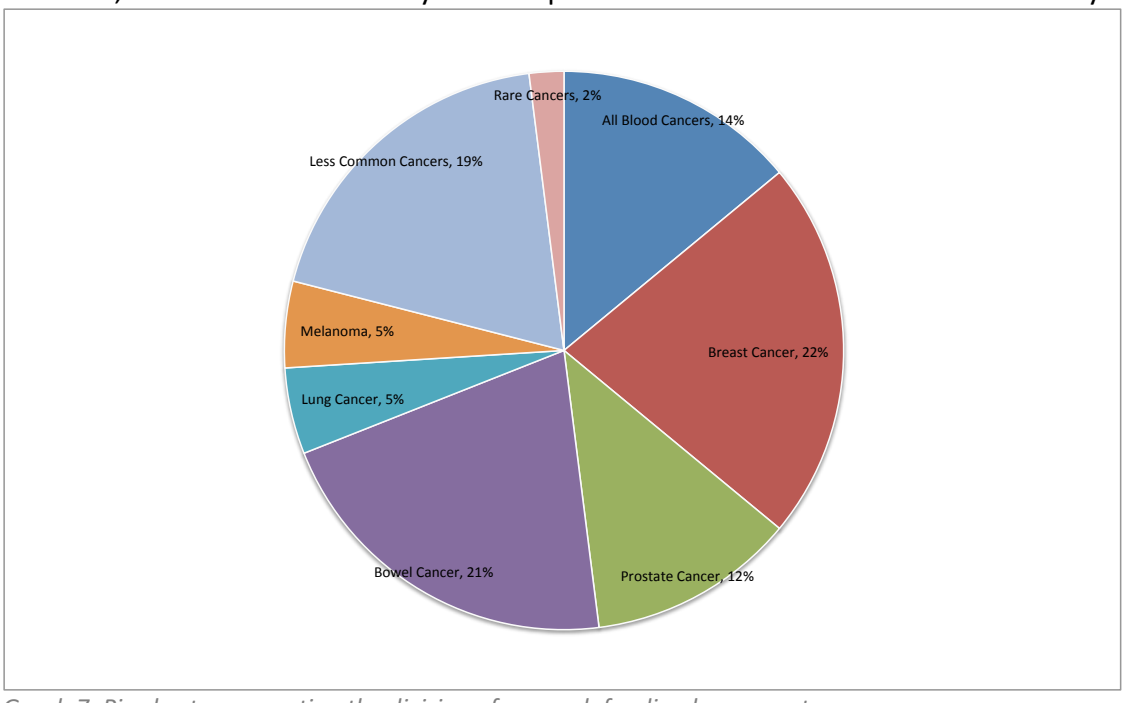
(incidence and mortality) and burden of disease – disability-adjusted life years (DALYs)'.[14]

The impact of this neglect of rare cancer research is significant in a number of ways. The first and most obvious being that if "you don't look you don't find" meaning that without focussed research we are unlikely to find and evaluate worthwhile treatments.

Equally important however, is that without research we do not build up centres of knowledge and clinical excellence that are critical to providing the best possible standard of care for patients with specific rare cancers. **The establishment of properly funded centres for rare cancer research is now an urgent priority.**

In the 2014 Budget the Government announced that it would create a Medical Research Future Fund (MRFF), to deliver additional Commonwealth funding for medical research and innovation into the future. In August 2015 the Bill to pass the MRFF into law was passed.

This new source of research funding presents an ideal opportunity for Government to take affirmative action and specifically target areas of neglect such as rare cancer research, which remains woefully low compared to combined incidence and mortality.



Graph 7: Pie chart representing the division of research funding by cancer type

14 Cancer Australia, 2015. Cancer Research in Australia: an overview of funding initiatives to support cancer research capacity in Australia 2006 to 2011.

Anecdotal information from researchers suggest that while there may have been some changes in these ratios with more funding going to less common cancers such as pancreatic and cancer of unknown primary, there is still a dearth of funding provided to the vast majority of RLC cancers.

The impact of research funding

When we look across the spectrum of cancers it is clear that a correlation exists between research spend, burden of disease and mortality.

While Australian research is only a small part of all global cancer research, with the possible exception of melanoma, there is no reason to believe our overall focus on common cancers would not be replicated throughout the global research community.

Lack of research into RLC cancers has two direct impacts; the first and most obvious is that without research, there is no likelihood of improved treatments and potentially cures, the second and perhaps less obvious, is that without research we will not develop the knowledge to design screening tests or early diagnosis mechanisms.

Early diagnosis is highly significant in improving patient survival and our experience, as seen with many of our patients, is that many Australians with RLC cancers had their outcomes compromised by late diagnosis.

Given the neglect of rare and less common cancer research when compared to burden of disease and mortality we must take action to encourage the research community to increase activity related to these cancers.

Research has shown that increasing the allocation of resources to research and funding treatments through the PBS positively impacts survival of cancer patients. The lack of focus on RLC cancers manifests in poor survival outcomes and consequently much higher mortality.

Addressing the discrepancies for RLC cancers compared with common cancers needs to occur at the highest level, and we need the Australian Government to take action. We need to improve outcomes for rare and less common cancer patients and to do so we must review existing mechanisms and improve research, diagnostics and access to medicines for RLC cancers.

Without similar mechanisms created for tackling common cancers, i.e. those specifically designed to address the prevention, diagnosis, and treatment, we cannot hope to have an impact on mortality or on improving patient outcomes for RLC patients in the future.

Improving Research Funding for Rare Cancers

Despite the Cancer Australia Audit of research funding demonstrating that total funding for rare and less common cancers has increased in recent years, the total funding required to close the gap between funding and the burden of disease and mortality caused by RLC cancers compared to common cancers remains significant.

Clinical trials into effectiveness of novel, targeted therapies, in small patient populations, require collaborative trial development and research which crosses traditional boundaries of trials currently being undertaken in Australia, and the evidentiary requirements for regulators must also be made to be more flexible for rare and super rare cancers.

The Australian Government, through the NHMRC, and other Departments is the largest funder of cancer research in this country, and this funding is set to increase through the MRFF.

Given the significant role that the Government has to play in funding this important work, RCA calls on the Government to take the lead through affirmative action to direct funding to specifically target areas of neglect such as rare cancer research.

Examples of Rare Cancer Research

The Molecular Screening and Therapeutics (MoST) study is Australia's first precision medicine trial focused on the rare cancer population. It is a joint initiative of the Garvan Institute and the NHMRC Clinical Trials Centre, and is funded by the NSW government.

The goal of the MoST is to offer 1,000 patients with advanced cancer a state-of-the-art genomic profile, and then match the outputs to multiple therapeutic options in the form of a basket of signal-seeking trials. Where cognate therapeutic options don't exist within MoST, patients and their clinicians are reffered to appropriate external trials, or are provided suggestions for compassionate access programs.

After 5 years in planning, the MoST opened for recruitment at the Kinghorn Cancer Centre at SVH in October 2016, with the first therapeutic modules coming on line in November 2016. RCA wwas important in advocating for expediting the process of opening the trial at SVH.

Over 70 subjects have been recruited in the first 4 months of the study, the overwhelming majority of which comprise subjects with advanced rare cancers. Subjects have come from all parts of Australia, and even from New Zealand.

To date, approximately 35 subjects have had results returned, and of these 8 subjects have been offered treatment on one of the two therapeutic modules currently

available (palbociclib, and durvalumab/tremelimumab immunotherapy). This is a pleasing result, and confirms that the study is addressing a substantial population with unmet need.

Garvan Insitute and NHMRC Clinical Trials Centre have plans to open another 3 modules (vismodegib for tumors with mutations in PTCH1; olaparib and durvalumab immunotherapy for patients with BRCA-type mutations; and eribulin for vascular cancers). They are also seeing a number of mutations in genes such as HER2, for which there are good therapies available. They would dearly like to open additional modules over the next 24 months to increase the range of options available.

Excerpt from Professor David Thomas of the Garvan Insitute emphasising the importance of this research

> 'For example, at this week's molecular tumor board, we had a patient with metastatic salivary adenocarcinoma with HER2 amplification, who can currently only access the drug by paying for it (part subsidy from Roche). I estimate that the cost to this individual for a year's treatment will be ~$50,000, most of which will be either out-of-pocket, or sourced from philanthropy (thanks for [RCA's] help in this case). Roche are willing to support new modules, including Herceptin.
>
> An impending limitation in opening more therapeutic options is funding. The trial has core funding for the NHMRC CTC for 5 years, with an intention to apply for further core funding. We have funding for the correlative science at Garvan. However the site costs of enrolling patients is $5000/case, meaning that every new module costs about $80,000.
>
> In addition, we want to franchise the MoST to VCCC, and then to other national centres who treat large populations with rare cancers. This is because it is undesirable for patients with advanced disease to travel to NSW from as far as WA to get access to these treatments. In the next 12 months, as the program consolidates its operations, it will be ready to commence opening at non-NSW centres.'

Conclusion

Only by improving our investments in rare cancer research will we ever be able to deliver improvements to patients and reduce mortality rates for these otherwise neglected patients.

The simple cost of doing nothing to improve outcomes for RLC cancers is too high and the challenge therefore, is to find a mechanism whereby research:

- Funding is increased and specifically directed to encourage and drive research into RLC cancers and rare molecular sub-types;

- That focuses on “re-purposing” existing drugs for rare cancers is actively funded – e.g MOST Trial (as above);
- Partnerships are created with the pharmaceutical industry so that they provide drugs in return for clinical trial data - that is, getting researchers to partner with industry in advance of requests for funding; and
- Rare cancers patients can receive equitable and fair access to medicines that have reasonable and proven safety and efficacy for those diseases, specifically by developing a simplified pathway for repurposed drugs to achieve TGA and PBS listing based on the results.

Rare cancers represent a major diagnostic as well as therapeutic challenge and they represent a major source of discrimination among patients. It is time we took the action necessary so that we can give these Australian patients the resources, support and treatment they need and most importantly provide them all with “just a little more time”.