Children's Cancer Institute

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Children's Cancer Institute's submission to the Senate Inquiry "Equitable access to diagnosis and treatment for individuals with rare and less common cancers, including neuroendocrine cancers"

- **All paediatric cancers are rare cancers.**
- **Paediatric cancer is significantly underfunded compared to adult cancers.**
- **Every dollar of funding is invested in the whole life of a child.**
- **Equity and inclusion nationally are a challenge.**

Background

Childhood cancers are classified as rare diseases due to their low prevalence, and in addition have diverse and unique characteristics, leading to even rarer sub-types that require distinct treatments. Despite improved survival rates due to advances in medical research, cancer remains the primary cause of disease-related death among children in Australia. When a child dies, an average of 70 potential years of life are lost. Of those who do survive, two-thirds will have significant long-term side effects from the non-specific and highly toxic treatment they receive, including organ dysfunction, neurocognitive deficits, impaired fertility and secondary malignancies.

Children's Cancer Institute is Australia's sole independent medical research institute dedicated to understanding the causes, prevention, treatment, and cure of childhood cancer. Their goal is to save all children with cancer and alleviate their suffering. Over the past thirty years, Children's Cancer Institute has built a world-class research environment that merges laboratory-based science with clinical translation pathways.

Children's Cancer Institute, in collaboration with the Kids Cancer Centre at Sydney Children's Hospital Randwick, developed the national Zero Childhood Cancer Program (ZERO), the largest research initiative ever undertaken for childhood cancer in Australia, and one of the most advanced precision medicine programs globally. ZERO employs advanced precision medicine techniques, including comprehensive genomic testing like whole genome sequencing, whole transcriptome sequencing and methylation profiling, to identify genetic cancer drivers and recommend personalised treatment options. Through ZERO, over 1000 children with aggressive, high-risk, relapsed, or rare cancers have accessed this testing since 2017. Around 70% of these children received actionable treatment recommendations, benefiting from targeted therapies, improved diagnoses, and insights into genetic predispositions. Recently, the ZERO2 trial has been introduced, with plans to extend comprehensive precision medicine to all diagnosed childhood cancer cases by the end of this year (up to 1000 patients a year). While the initial ~1000 children have demonstrated clinical benefits,

showcasing improved outcomes for high-risk and hard-to-treat cancers, the ZERO2 trial aims to establish similar benefits for standard and medium risk childhood cancers. The ZERO and ZERO2 research trials operate in the research environment and are funded entirely through government and philanthropic research dollars.

Response to criteria

a. Barriers to screening and diagnosis, including the impact of factors such as:

i Geographic Location

All children with cancer must travel to a limited number of large children's cancer hospitals in major cities around Australia for treatment. Genomic testing is now being integrated as standard of care for the diagnosis of childhood cancer, however there is no single unified national testing approach for these children within the Australian health system. Most genomic tests are designed for adult cancers and not routinely available for childhood cancers. Individual centres have used ad hoc testing based on local development. This leads to unwarranted inequities to accessing genetic testing and genomically-guided paediatric oncology care across states and centres. On the other hand, the ZERO Program is significant as it affords equitable access to state-of-the-art genomic testing across every childhood cancer centre in Australia, and, since 2023, for every child diagnosed with cancer. However, as a research study, this platform only has funding for the next 2-3 years, meaning that there is potential for future inequitable access to genomic testing for children around Australia.

Recommendation: The ZERO platform should be adopted as a national paediatric precision medicine standard approach within the health system to ensure equity of access to comprehensive genomic testing for children with cancer around Australia.

ii. Cost

Paediatric cancers are highly heterogenous, and due to the small population size, it is not possible to achieve economies of scale. Genomic diagnostic testing for paediatric cancer is not served well by small tumour-specific gene panels (especially those developed for adult cancers which have different genetic drivers to paediatric cancers), and use of offshore large panel testing incurs out-of-pocket costs to families or hospitals. As a result, there are higher associated costs for both development and implementation of genomic diagnostic testing. In addition, inpatient testing at public hospitals is not eligible for MBS reimbursement. While almost every child with cancer has their diagnostic testing conducted as an inpatient in public hospitals, the testing is ineligible for MBS funding, leading to further out-of-pocket costs for families, public hospitals or paediatric oncology departments.

Minimum Residual Disease (MRD) testing to measure early response to chemotherapy has been used to guide treatment decisions for children newly diagnosed with acute lymphoblastic leukaemia (ALL) and has been the established standard of care for children with ALL for more than 10 years. Since November 2022, MRD testing has been funded through the MBS, demonstrating a successful research translation story. thighlights the importance of strategic long-term support of the growth and translation of vital research into novel diagnostics to create the clinical utility evidence base.

The ZERO program currently provides comprehensive genomic testing for paediatric cancer patients through research and philanthropic funding, however it is important to note that funding for this program is only guaranteed until June 2025. Additionally, while ZERO remains a research program (i.e. testing is NATA accredited but reporting is not), it cannot access MBS funding mechanisms to support the costs associated with providing world-class essential tests to children with cancer.

Recommendation: A mechanism to access MBS funding for all laboratory diagnostics for children with cancer (regardless of whether inpatient or outpatient) needs to be considered. Additionally, appropriate public and/or private reimbursement pathways and continuous funding for new diagnostic and treatment approaches (including ZERO) are needed to ensure ongoing comprehensive genetic testing and reduced out-of-pocket expenses for families of children with cancer.

iii. Cultural and Language Barriers

Appropriate tools and resources to improve equity of access for culturally and linguistically diverse, and indigenous populations are vitally needed. There is very limited funding available for research and development of these resources. Currently, responsibility for development of such resources lies at the hospital/district level, as opposed to a national approach.

Recommendation: Provide funding at the Commonwealth level for research and development of appropriate tools and resources to improve equity of access for culturally and linguistically diverse, and indigenous populations, which is critical for addressing existing inequities.

iv. Type of Cancer

All paediatric cancer is rare, but within this group is a category of very rare cancers for which diagnosis and treatment are particularly challenging. A comprehensive genetic analysis of these ultra-rare tumours is the most time- and cost- efficient and effective way of ensuring these patients receive the correct diagnosis and treatment opportunities. The rare cancer cohort of the ZERO program enrolled >100 patients for whom standard pathology testing was unable to provide sufficient diagnostic or prognostic information. Of the patients enrolled in this rare cancer cohort of the ZERO program (including those with unknown diagnosis or prognosis), more than 75% received clinically meaningful results which had a strong impact on their diagnosis, treatment or prognosis.

Recommendation: The ZERO platform should be adopted as a national, comprehensive, standard testing approach for all children with rare cancers.

v. Availability of Treating Practitioners

Due to advances in research and technology, access to precision medicine is becoming increasingly feasible, with demonstrated improvements in diagnosis and outcomes for paediatric cancer patients. In line with these advances is a growing need for a precision oncology workforce and greater integration with clinical research. Training and education in the interpretation and application of precision medicine results is vital across the workforce to ensure equal standards of care and access to new medicines for children and adults with cancer.

There is currently a shortage of paediatric pathologists and specifically genetic pathologists - roles which are an important part of the diagnostic process. The growing number of children diagnosed with hereditary cancers in Australia through the ZERO Program are experiencing significant barriers to access to genetic services and long wait lists. Additionally, genetic counsellors, who are an integral part of the clinical care team, are not recognised as a profession (no Medicare item number for consultations), which puts added financial strain on clinical genetics services. There is also an urgent need for dual-trained paediatric clinical geneticists – there is currently only one in Australia. To date, this dual training, and the training of a small number of paediatric precision oncologists, has been funded by research grant and philanthropic funding. Similarly, small scale clinical precision medicine training is being funded by grants as part of the PrOSPeCT Program to help to address this workforce skills gap.

Recommendation: An in-depth analysis of the workforce skills gaps, including vital computational and curation scientists, and the development of formal, nationwide precision medicine education programs across the adult and childhood oncology health sector is necessary.

b. Barriers to accessing appropriate treatment

Over the last three decades, there has been a lack of industry-driven development of new therapeutics for paediatric oncology, primarily due to the small patient population and traditional drug development models reliant on economies of scale. The inconvenience, expense, and time associated with conducting paediatric clinical trials often lead pharmaceutical companies to delay consideration of such trials until after a drug's safety and effectiveness have been demonstrated in adults, leaving children with outdated therapies. Currently the median lag time from first-in-human to first-in-child trials of new targeted oncology agents that were ultimately approved by the regulatory bodies (such as FDA) is 6.5 years. Of those approved, children were included in only 5% of the initial applications.

Critically, the standard of care for paediatric cancers is enrolment on clinical trials due to the lack of approved medicines available. In the paediatric space this is particularly challenging as there is a lack of industry support to supply drugs and/or funding for paediatric trials, meaning trials are primarily funded by government or philanthropic sources. In Australia, there is a lot of variability in state government support of trial structure and funding is ad-hoc, with many centres relying on philanthropic donations to run their clinical trials programs.

International collaborations, like the ACCELERATE initiative, and new legislative frameworks (The Paediatric Regulation in EU, and the RACE for Children Act in the US) have emerged to address paediatric cancer drug access disparities. These legislations mandate pharma companies to consider and create development pathways for paediatric use where appropriate when developing new adult cancer drugs, as well as incentive schemes for extended market exclusivity and fast-track vouchers in the US. **However, in Australia, there are no legislative/regulatory provisions to encourage early access to novel drugs for paediatric cancer patients.** This absence of a supportive framework poses significant challenges. These include licensing drugs for diseases rather than molecular indications, lack of specific Pharmaceutical Benefits Scheme (PBS) criteria for paediatric cancers, significant lag times between approval and reimbursement for new drugs, heavy reliance on off-label drug use, and limited data collection on response to therapy through compassionate access.

Whilst there have been early developments in the shift towards a more molecular rather than disease indication emphasis in regulatory terms (for example, Larotrectinib targeting NTRK), this needs further momentum. In general, the majority of PBS funding is not genetically guided but based on histopathology, usually excluding childhood cancers. There are still a very limited number of drugs listed on the PBS that are genomically guided and these require co-dependent testing which must be undertaken in accredited labs to access the PBS funding.

The PrOSPeCT Initiative (led by Omico, of which Children's Cancer Institute is a foundational partner) aims to revolutionise the oncology clinical trials ecosystem in Australia. This initiative intends to attract pharma and biotech companies to our shores to undertake clinical trials, and therefore increase early access to new medicines for cancer patients and create new jobs. It is pleasing to see large-scale government investment in this important initiative.

Recommendation: To address the abovementioned barriers to accessing appropriate treatment, a national whole-of-system plan is recommended, involving broad stakeholder engagement and an international best-practice review to transform policy and improve the lives of Australians facing childhood, adolescent, and rare disease cancers. Additional areas to consider include specific criteria to ensure drug access for paediatric

cancer patients under the Pharmaceutical Benefits Scheme, international collaboration to share regulatory burdens, an increase in funding for clinical trials at each site in Australia for childhood cancer patients, and funding for children to travel interstate to access clinical trials.

c. The adequacy of support services after diagnosis

There are large gaps in workforce areas where new expertise is needed in the research sector to support technology advances, precision medicine and health systems research. For example, delivery of precision medicine requires a whole-of-system approach including a varied workforce of computational biologists, researchers, clinician scientists, health economists, implementation scientists and psychosocial researchers. There is also significant and growing demand for relatively recent specialisations, such as clinical geneticists, curation scientists and genetic counsellors. Many people with the rights skillset currently work outside the medical research sector. It is difficult to attract them to apply their skills to the challenge of children's cancer due to a lack of funding, security and growth opportunities. In addition, social workers, outreach nurses and other critical services are not federally funded, requiring funding to be found via charitable sources.

Recommendation: Federal funding for support services including psychosocial research, social workers and outreach nurses should be considered. For effective delivery of data-driven precision medicine results to treating oncologists, funding is required for new workforce positions such as curation and computer scientists. Further, a consideration for extending the support services to regional areas, to enable post-diagnosis support and genomically guided care at the regional level is needed

d. The adequacy of Commonwealth funding for research into rare, less common and neuroendocrine cancer

Childhood cancer differs significantly from cancer in adults due to differences in causes, growth patterns, spread, and treatment response. Tailored research and treatment approaches are necessary. However, childhood cancer research receives only 4% of government funding allocated to adult cancer research. It heavily relies on philanthropy, charities, and hospital budgets, impacting funding availability for projects and discouraging potential clinicians and researchers. As a result, progress is slower than adult oncology, with children suffering the consequences.

While recent federal funding for Australian paediatric cancer programs is promising, funding is needed across the entire research pipeline. Many adults and children lack targeted treatments despite known molecular targets. Utilising available data for new drug discovery and development requires funding, including for challenging high-risk projects that struggle to find philanthropic support.

Traditionally, there has been little pharma interest in supporting or funding clinical trials or research for children with cancer. However, regulatory changes, the international success of the ZERO Program, and initiatives such as PrOSPeCT aiming to attract more pharma to Australia, are expected to increase the paediatric oncology interest and could open joint commonwealth and industry opportunities to fund research and trials in this space.

Efficient collaboration between adult and paediatric cancer fields is essential to avoid duplication of research efforts, particularly as cancer classification becomes more molecularly oriented. This is especially critical for adolescents and young adults who often lack proper medical attention. Despite potential benefits in technology, data sharing, and expertise exchange, the disconnect between adult and paediatric oncology fields hinders progress in cancer research spanning age groups and cancer types.

Finally, systems research is very underfunded, including areas such as health implementation, socioeconomics, culturally and linguistically diverse cancer population and health systems research. This is a fundamental barrier to translating and embedding new research into the health system.

Recommendations:

Increase funding dedicated to childhood cancer research: Australia's research investment in paediatric cancer needs to be bolstered. The Australian Government should conduct a review of the balance of research investment across the entire pipeline of paediatric cancer research to bolster research translation and ensure continuous support from bench to bedside. Furthermore, the review should include clinical translation pathways and a deeper understanding of this devastating disease, which will bring us closer to a cure for every child.

Workforce: The Government should explore alternative grant opportunities for those with health, industry and commercial backgrounds to re-enter the medical research workforce and build capacity to support future-facing research projects. These options would ensure there is a workforce capable of effective delivery of the 10-year Australian Cancer Plan.

New Funding Areas: Direct research investment (and research/industry partnership incentive schemes) specifically aimed at supporting new drug development for children would be highly impactful in addressing the lack of drugs available specifically to treat childhood cancers. This would provide opportunities for researcher development with industry, de-risk research partnerships for industry and increase and accelerate research translation opportunities. . Additionally, more funding for health systems research to ensure a pathway to translating research into clinical care is key.

Adult and paediatric collaboration: A full review of sector-specific funding schemes followed by tailored funding aimed at cross-field collaboration would be highly beneficial to improve cancer research and control for all Australians, irrespective of age.

e. Any other related matters

Life Insurance - Despite the benefits genetic testing may provide with respect to diagnosis, treatment, and understanding of cancer predisposition, there is a perceived risk by the public that genetic testing results may impact their ability to access personal risk-rated insurance. This perceived risk causes some patients to refuse genetic testing. Since June 2019, the Financial Services Council (FSC) introduced a Moratorium of Genetic Tests in Life Insurance, which is set to run until June 2024.

Recommendation: There is a legislative opportunity for the Australian Government to legislate a moratorium instead of leaving it self-regulated by the FSC, alleviating the anxiety in the community around genetic testing and therefore ensuring patients access the right testing and support services at the right time for their disease.

Yours faithfully

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