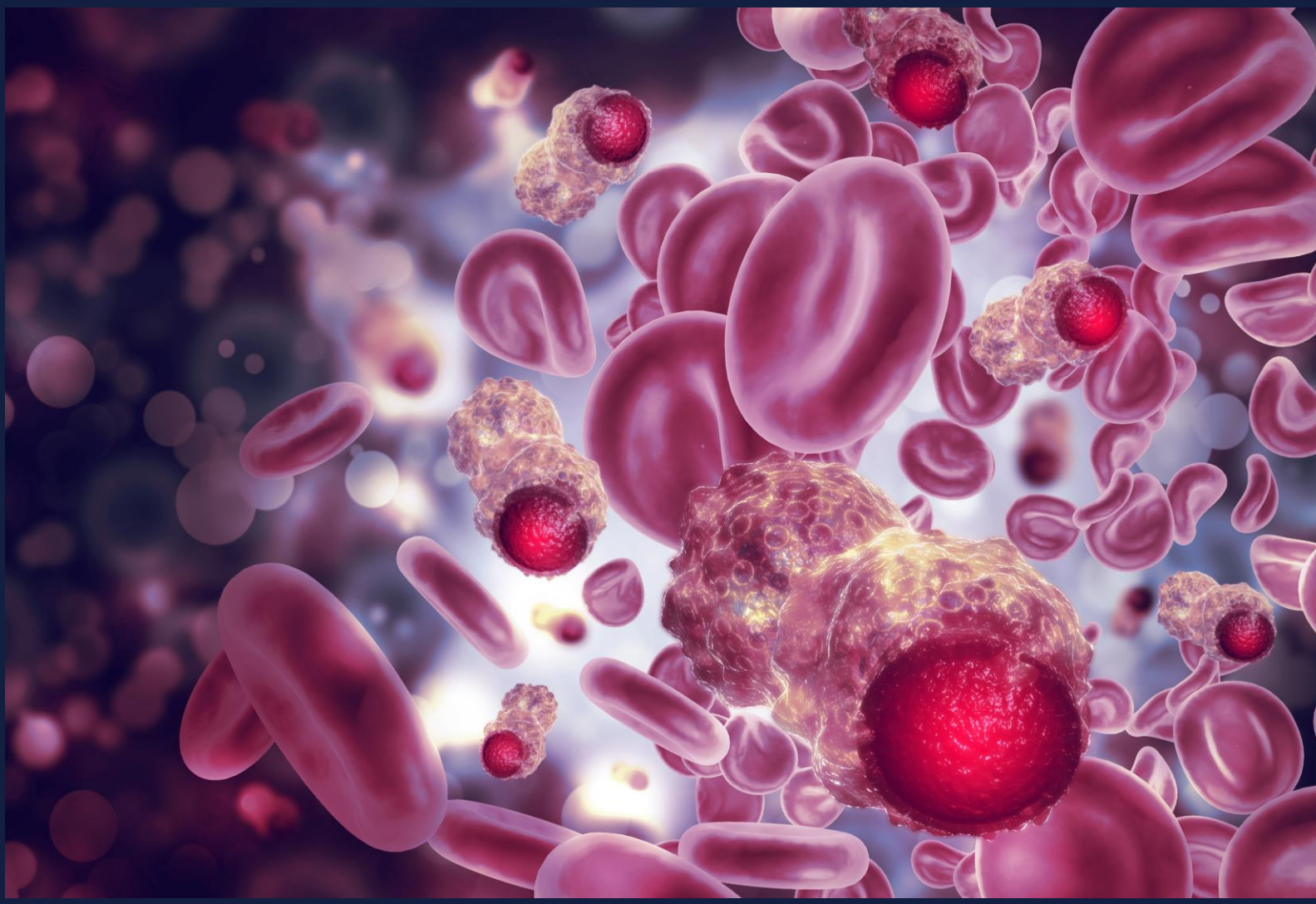
State of the Nation: Blood Cancer in Australia

Final Report to the Leukaemia Foundation

February 2019



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Foreword

Blood cancer is a complex set of diseases that can affect anyone at any stage of life.

Since the mid-1970s, the Leukaemia Foundation has led the way in representing the interests and supporting the needs of Australians living with a blood cancer. Our goal is zero lives lost to blood cancer by 2035.

This *State of the Nation: Blood Cancer in Australia* report sets out an ambitious agenda to help us save lives and to ensure that everyone with a blood cancer in Australia has access to the best possible information, treatments and care.

Advances in treatments and care over the past 40 years are transforming the way Australians live with a blood cancer; however, incidence rates are increasing and more and more Australians will be affected by these diseases if we don't act now.

This report into the state of blood cancer in Australia, calls for leadership and coordinated action to empower patients, ensure equity of access, accelerate research and to catalyse health systems reform to save the lives of our fellow Australians. It provides a person-centred blueprint for government, blood cancer clinicians, and researchers as well as the Australian community to work together in new, innovative, and meaningful ways to beat blood cancer.

As contributors to and users of the health system, we want to work in partnership with the whole blood cancer community so individuals living with blood cancer are at the centre of all strategic decision-making on their future.

The Leukaemia Foundation will act in partnership with governments and the entire blood cancer community to successfully implement. We will report on progress against each goal in an annual *State of the Nation: Blood Cancer Report*.

Friends and families of Australians living with a blood cancer have been the backbone of the Leukaemia Foundation since day one. As we embark on this ambitious agenda of zero lives lost to blood cancer, I encourage all members of the blood cancer community to rally around this important national objective and work with us to beat blood cancer and save lives.

Bill Petch
Chief Executive Officer
Leukaemia Foundation

Executive Summary

Blood cancer is among the most fatal and most costly conditions affecting Australians today, with survivors facing a long tail of late effects as a result of being exposed to cytotoxic therapies. The effect of a blood cancer extends for a lifetime, impacting adults and children alike, their families, and the wider community.

Each year an additional 15,000 Australians are newly diagnosed, and between 4,000 and 7,500 people will lose their lives as a result of their blood cancer, making blood cancer one of the biggest causes of cancer death. Moreover, State Cancer Registry data indicate that more than 110,000 Australians — young and old — are living with a blood cancer today.

Because blood cancers are traditionally reported by major sub-types, however, the incidence and prevalence of blood cancers in Australia are not well understood. Consequently, the significance of blood cancers as a priority for Australian communities is likely to be underestimated.

At the same time, new diagnoses of blood cancer are increasing. By 2035, the number of people expected to be diagnosed with blood cancer is projected to rise to more than 36,000 people per annum and the total number of deaths from blood cancer will approach more than 15,000 people per annum – more than the number of people diagnosed annually with blood cancer today.

The total lifetime financial costs of treating and caring for people who will be diagnosed with blood cancer between 2018 and 2035 is expected to be more than $82 billion in net present value terms. This cost rises to more than $542 billion in net present value terms for the total economic cost of blood cancer between 2018 and 2035 when burden of disease costs are added. More than 186,000 people are expected to lose their lives to blood cancer over that period, with more than 1.4 million years of potential life lost.

Through focused and strategic collaboration across the blood cancer community, however, the number of deaths from blood cancers can be substantially reduced and the quality of life of people living with blood cancer can be substantially improved — just by applying what is already known today.

By taking action to more consistently implement currently demonstrated best practice, using therapies that are *already available in Australia* today, it is estimated that the number of deaths could be reduced by 13 per cent. For example:

- *Addressing the metro-regional divide* — Implementing reforms to reduce variation in survival outcomes observed for people living in regional areas could reduce the number of deaths expected by five per cent compared to baseline projections, preventing the deaths of more than 9,300 people living in rural and regional areas that might have otherwise occurred and saving more than 200,000 years of life over the 2018 to 2035 period.

- *Ensuring consistent use of evidence based best practice nationally* — More consistent application of best practice treatment and care across all States and territories has the potential to reduce the number of deaths expected by a further

eight per cent, preventing an additional 13,400 deaths that might have otherwise occurred.

In total, more than 22,000 lives and 350,000 years of potential life could be saved over the 2018-2035 period just by doing *what is already proven to work and already funded in Australia* more consistently. Stakeholder consultations also indicated that the further adoption of novel therapies in use globally could have the potential to reduce the number of expected deaths by up to one third in total; the remainder will require new discovery. Additional work also needs to be done to understand the impact of blood cancer on indigenous and culturally and linguistically diverse people to ensure that no Australian community is left behind.

Combined with new approaches to evidence development to support access to therapies in use overseas, such as through the introduction of a Right to Trial Program and an International Blood Cancer Research Mission, it is estimated that deaths from blood cancer could be reduced by one-third in total today. Therefore, implementing currently available best practice could have the potential to double the number of lives saved.

Moreover, new thinking and approaches to international research collaboration offer the potential to accelerate further gains in survival.

Remarkable new advances in genomics, targeted therapies, immunotherapies, and other technologies are making the prospect of a cure more real every day. Since the completed mapping of the genome in 2003 and the identification of the Philadelphia chromosome, first discovered in 1959 and linked to treatments for chronic myeloid leukaemia in 2001, there has been a rapid progress in the understanding of blood cancers at a molecular level and the increasing development of novel therapies. Increasingly these therapies are changing the prognosis for many blood cancers from a poor survival outlook following a brutal cytotoxic chemotherapy regimen, to a chronic disorder that can be managed with targeted precision therapies with fewer off-target effects.

Even more exciting is the prospect of the next generation of major scientific advances in curative therapies, such as CAR-T, oncolytic viral therapies, CRISPR technologies, PARP inhibitors and preventative therapies, which hold the promise of a more limited treatment horizon, increased depth of disease response and fewer potential side-effects.

Reducing variation in services and ensuring timely access to these emerging therapies, however, requires new ways of thinking and policies to match.

Currently, people living with blood cancer face significant challenges in equitably accessing treatment and care. The barriers to consistent access to best practice begin from the moment a patient steps into a GP's office. Today, GPs see blood cancers less frequently than other diseases, and may sometimes be slow at times to recognise the blood cancer and refer a patient to the haematologist. New advances in diagnostic technologies may not be used, which can result in misdiagnosis and affects treatment planning. Patients are not empowered with information to engage with their doctors and navigate the complex care environment, which is complicated by multiple funders and poor private health insurance coverage of care. Written care plans are inconsistently and infrequently provided. Moreover, if a treatment is not publicly-subsidised through the Medical Benefits Scheme or Pharmaceutical Benefits Scheme it will be out of the reach of most Australians, and consequently probably not even discussed. Referrals to supportive care are also inconsistent, with blood cancer patients missing out on survival-improving and quality of life-enhancing interventions, such as cancer-friendly rehabilitation and psychosocial care.

At the same time, there are very significant opportunities to address these existing and emerging challenges. Empowering patients and their families from diagnosis to more effectively and meaningfully engage with their diagnosis, treatment plan and options for supportive care holds the potential to catalyse significant improvements in survival outcomes and patient wellness. The development of evidence-based clinical care guidelines, care pathways and quality indicators can support both patients and their clinicians to ensure the person is receiving the best care for them. To this end, more systematic genetic and genomic testing is essential to reducing errors and improving survival outcomes. New approaches to evidence development, such as a Right to Trial Program, could also be deployed to more systematically tackle barriers to evidence development and ensure more equitable, timely access to emerging therapies. A cancer-friendly rehabilitation program offers an evidence-based tool to reduce fatigue and improve survival outcomes, and more systematic screening for a range of supportive care, including psychosocial support, has been shown to also improve survival and quality of life.

Moreover, enhanced integration into international research offers the opportunity to accelerate progress towards a cure for all blood cancer sub-types. An International Blood Cancer Research Mission, organised around international collaboration in specific disease sub-types, has been shown through international research models to deliver breakthroughs that would not be possible through a more piecemeal and fragmented research approach, particularly in the context of an ever more precise definition of disease which will continue to see patient populations stratified to a greater and greater extent. Increasingly, the risk of market failure arising from muted commercial incentives will create a need for more clinician-led research, and attendant clinician- and patient-led submissions to government for funding.

Addressing these challenges and realising the benefits of emerging therapies is a demanding agenda, but through more consistent and equitable application of best practice and new discovery, it will be possible to reduce the number of deaths to zero over time.

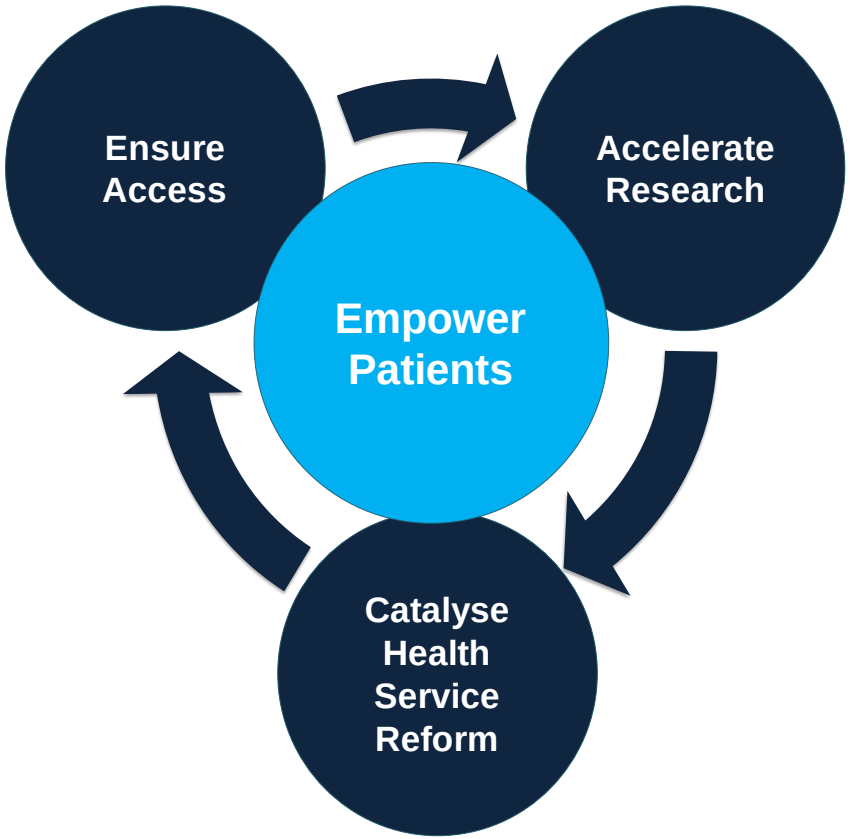
Building on its long-term Vision to Cure and Mission to Care, the Leukaemia Foundation has set a goal of zero lives lost to blood cancer by 2035. This includes:

- Zero preventable deaths by removing barriers to access and addressing inequality in survival outcomes
- Zero people living with blood cancer without access to information
- Zero people living with blood cancer without access to best practice treatment and care.

To reach these goals, the Leukaemia Foundation has developed a Zero by 2035 Strategy and wants leadership and coordinated effort in partnership with Governments and the wider blood cancer community, organised around four key priorities that together contribute towards the realisation of the vision for Zero by 2035. The four priorities are:

- Empower Patients
- Enable Access
- Accelerate Research for the Cure
- Catalyse Health Reform.

A comprehensive plan for the Zero by 2035 Strategy



Actions to Empower Patients

- Make blood cancer a notifiable disease
- Opt-out model for referrals to patient support organisations
- Create a one-stop shop for blood cancers
- Create a complex referral MBS item and referral support tools
- Support the development of Patient Reported Outcomes
- KPIs for written care plans

Actions to Accelerate Research

- Establish an International Blood Cancer Research Mission
- Develop a Real World Evidence Pilot for the MyHealthRecord
  - Including Patient Reported Outcomes

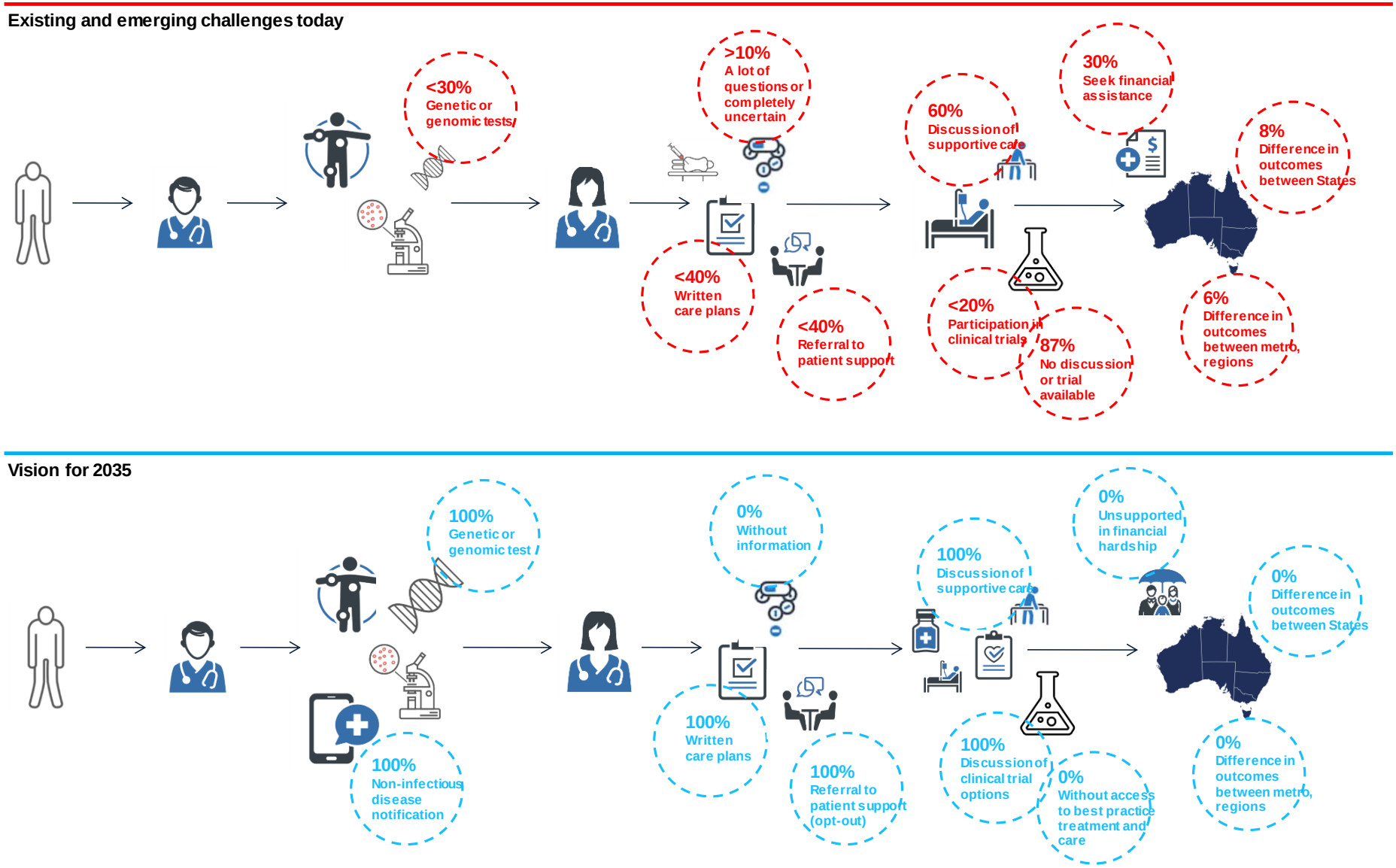
Actions to Ensure Access

- Make systematic genetic and genomic testing part of the standard of care
- Develop a Right to Trial Pilot Program
- Implement KPIs for clinical trial participation

Actions to Catalyse Health Service Reform

- Address care pathway and clinical guideline gaps
- Develop KPIs for sub-type specialist input to treatment plans
- Develop KPIs for supportive care screening and referrals
- Review of in-patient and out-patient funding arrangements
- Roll-out GP education and decision support tools
- Develop and roll-out a cancer-friendly rehabilitation program
- Support the expansion of community-based care
- Advocate for insurance reform
- Advocate for welfare support, including Centrelink payments reform
- Advocate for patient assisted travel scheme reform

Comparing Today and Tomorrow: A Vision to Cure and Mission to Care in 2035



The priorities are synergistic, and the implementation of progress against each of them will deliver outcomes that are greater than the sum of the individual parts.

In particular, the implementation of actions to improve Equity of Access are highly synergistic with actions to Accelerate Research for the Cure. Most significantly, the Right to Trial Program would provide a mechanism for the more systematic evaluation of off-label use and re-purposing of medicines. It could also reduce a current dependence on industry to conduct the research needed to advance potentially curative therapies. Combined with a Real World Evidence pilot and International Blood Cancer Research Mission, this could be used to develop robust control groups and better tackle the challenges of small patient populations — ultimately supporting more effective and systematic evidence development and progress towards a cure.

Importantly, realising the objectives of the Zero by 2035 Strategy will require the successful implementation of the actions against each priority, in partnership with people living with blood cancer, their families, clinicians, researchers, industry and governments at the State and Federal level.

Together, through coordinated and strategic action, the blood cancer community can reduce deaths from blood cancer and its impact on people living with blood cancer, their families and the Australian community.

Chapter 1

Understanding Blood Cancer: Nature and Numbers

Today, State Cancer Registry data indicate that more than 110,000 Australians of all ages are living with a blood cancer.

Each year an additional 15,000 new Australians are diagnosed, and between 4,000 and 7,500 people will lose their life as a result of their blood cancer, making blood cancer one of the biggest causes of cancer death.

At the same time, remarkable new advances in immunotherapies, genomics and other technologies are making the prospect of curing blood cancer more real every day. While our ageing population is contributing to the rising incidence of blood cancers, survival rates also have been steadily improving.

This chapter explains what blood cancer is, the major types of blood cancer that people can experience and the primary ways in which these cancers are treated today.

1.1 What is blood cancer?

Blood cancer, sometimes also referred to collectively as haematological cancers, haematological malignancies or haematological neoplasms, is a complex group of diseases linked by their origins in the bone marrow, where blood is produced.

Blood cancer arises from abnormalities in the blood cells that affect normal blood cell production and function.

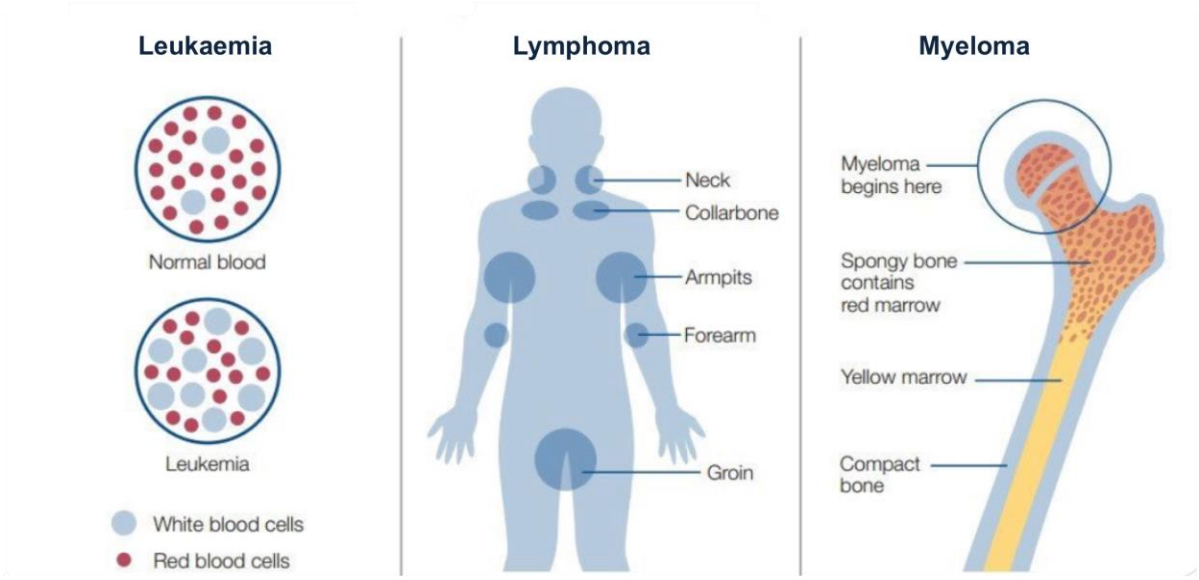
To understand why, it is important to know that every second of every day a person's body is replenishing its cells, including its blood cells, by making new ones and destroying old ones. If everything is working normally, a person's body makes the right number of each type of cell to keep that person healthy. To make blood cells, stem cells in the bone marrow mature and develop into one of three types of blood cells:

- Red blood cells, which carry oxygen through the body
- White blood cells, which fight infection as part of the body's immune system
- Platelets, which help the blood to clot.

If the DNA in the stem cells that tells the body how to make blood cells changes (or 'mutates'), these blood cells might start to develop abnormally, or fail to die when they should. These are the 'cancerous' cells that cause blood cancer. These abnormal blood cells prevent the blood from performing many of its usual functions, like fighting off infections, bringing oxygen to other tissues or helping to repair the body.

Blood cancer is generally sub-divided into three main diseases: leukaemia, lymphoma and myeloma, each with their own set of sub-types (Figure 1.1). There are also increasing diagnoses of other types of blood cancers (or disorders) that fall under the category of Myelodysplastic Syndrome and myeloproliferative neoplasms.

Figure 1.1: Blood cancer linked by origins in the bone marrow, where blood cells are produced



Source: The Mayo Clinic

Some forms of blood cancer are highly aggressive, requiring acute care in hospital, while others are slower growing and initially may be picked up by chance through a blood test for something else. Symptoms can include:

- Fatigue and vulnerability to infection, which is common to most blood cancers but is particularly severe in acute leukaemias
- Lumps, potentially in a variety of body sites, which are typical of lymphomas
- Bone fractures and kidney problems, which are characteristic of myeloma.

Understanding Leukaemia[1]

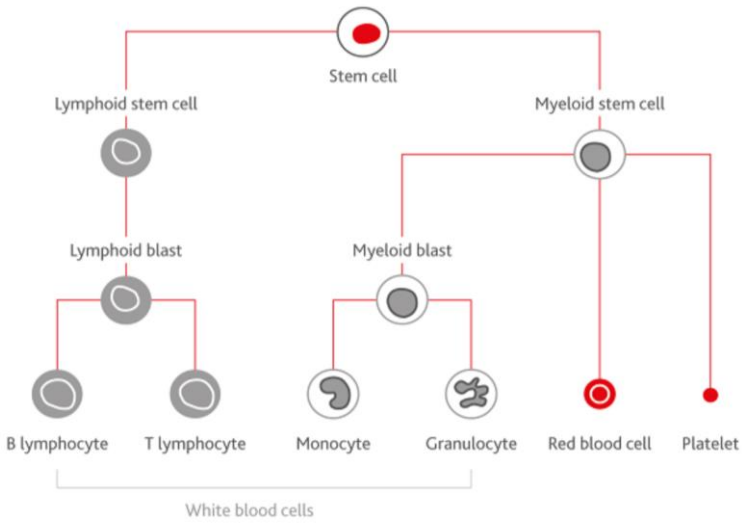
Leukemia is a type of cancer found in a person's blood and bone marrow. It is caused by the rapid production of abnormal white blood cells called leukocytes. The abnormal white blood cells are not able to fight infection, and they impair the ability of the bone marrow to produce red blood cells and platelets. This makes the person feel tired and vulnerable to infection.

[1] The disease descriptions in this section are derived from the Leukemia and Lymphoma Society (LLS) blood cancer summaries available at www.lls.org. For some disease sub-types, additional information developed from care pathway analysis in partnership with Australian blood cancer sub-type specialists consulted as part of this report has been added. See Appendix A for a detailed summary of the care pathway for major blood cancer sub-types.

There are several major sub-types of leukemia, based mainly on whether the leukemia is acute (fast growing) or chronic (slower growing), and whether it starts in myeloid cells or lymphoid cells:

- *Acute Myeloid Leukaemia* — Acute myeloid leukaeamia (AML) is a cancer of the bone marrow and the blood that progresses rapidly without treatment. AML affects the development of myeloid stem cells (Figure 1.2), which would normally mature into a number of different types of blood cells. As a result, these cells cannot carry out their normal functions. AML can be a difficult disease to treat, and researchers are studying new approaches to AML therapy in clinical trials. AML is currently treated with chemotherapy, drug therapy, blood transfusions and/or stem cell transplants.

Figure 1.2: How blood cells are made from stem cells in the bone marrow and develop into red blood cells, white blood cells and platelets



Source: Bloodwise UK

- *Acute Lymphoblastic Leukaemia* — Acute lymphoblastic leukemia (ALL) is a cancer of the bone marrow and blood that progresses rapidly without treatment. It does not have a clear cause. About 25 percent of adults and only about 3 percent of children who have ALL have a sub-type called “Ph-positive ALL”, which is also known as either “Ph+ or Philadelphia chromosome positive ALL”. Patients with this ALL sub-type have a chromosome alteration that results in a specific mutation of the BCR-ABL gene, which informs the treatment protocols for that person. The approach for treating each patient is based on an individual’s sub-type, risk factors and treatment goals. Generally, treatment can last between 18 months to three years. Depending on a person’s ALL sub-type, a range of treatment combinations is available including chemotherapy, drug therapy, blood transfusions and/or stem cell transplantation.

- *Chronic Lymphocytic Leukaemia* — Chronic lymphocytic leukemia (CLL) is a type of blood cancer that begins in the bone marrow and can progress either slowly or quickly depending on the form it takes. Current therapies do not offer patients a cure for CLL, but there are treatments that help manage the disease and clinical trials in development for novel approaches to the treatment of CLL that have shown significant improvements in potential survival outcomes. There is a range of treatment options and approaches depending on the person,

including watch and wait, chemotherapy, combination chemotherapy and drug therapy, radiation therapy and/or surgery.

- *Chronic Myeloid Leukaemia* — Chronic myeloid leukemia (CML) is a cancer of the bone marrow and blood that is usually diagnosed in its chronic phase when treatment is very effective for most patients. Most CML patients are treated with daily oral drug therapy. Since the introduction of tyrosine kinase inhibitor (TKI) drug therapy in 2001, CML has been transformed from a life-threatening disease to a manageable chronic condition for most patients. People are living longer with CML and experiencing fewer treatment side-effects. In some cases, patients have had a depth of response from their TKI that means they are able to participate in a stopping-treatment clinical trial.

Understanding Lymphomas[2]

Lymphoma is a type of blood cancer that affects the lymphatic system, which removes excess fluids from the body and produces immune cells. Lymphocytes are a different type of white blood cell that fights infection. Abnormal lymphocytes become lymphoma cells, which multiply and collect in a person's lymph nodes and other tissues. Over time, these cancerous cells impair a person's immune system.

There are several major sub-types of lymphoma, including Hodgkin Lymphoma which was first identified in 1832 and is one of the most well-known lymphomas in the community, even though it represents a small percentage of all lymphomas. Non-Hodgkin Lymphomas (NHL) are generally grouped, like leukaemia, into aggressive (or fast growing) lymphomas or 'indolent' (slower growing) lymphomas.

- *Hodgkin Lymphoma* — Hodgkin lymphoma is a cancer that affects the lymphatic system, which is part of the body's immune system, and is one of the most curable forms of cancer. Hodgkin lymphoma results from an injury to the DNA of a lymphocyte, a type of white blood cell. Treatment for Hodgkin lymphoma includes chemotherapy and/or radiation, depending on individual patient factors.

- *Aggressive Lymphomas*

  - *Diffuse Large B-Cell Lymphoma* — Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma. It grows rapidly in the lymph nodes and frequently involves the spleen, liver, bone marrow or other organs. Usually, DLBCL development starts in lymph nodes in the neck or abdomen and is characterised by masses of large B-cells. In addition, patients with DLBCL often experience symptoms such as fever, night sweats and loss of more than 10 percent of body weight over six months. For some patients, DLBCL may be the initial diagnosis. For other patients, an indolent (slow growing or 'low grade') lymphoma, such as small lymphocytic lymphoma (SLL) or follicular lymphoma (FL), transforms and becomes DLBCL.

[2] Based on Leukaemia and Lymphoma Society blood cancer summaries updated with information from care pathway analysis developed in partnership with Australian blood cancer sub-type specialists consulted as part of this report. See Appendix A for a detailed summary of the care pathway for major blood cancer sub-types.

- *Burkitt Lymphoma* — This aggressive B-cell subtype grows and spreads very quickly. It may involve the jaw, bones of the face, bowel, kidneys, ovaries, bone marrow, blood, central nervous system and other organs. Burkitt Lymphoma may spread to the brain and spinal cord, therefore, treatment to prevent central nervous system spread should be included in any treatment regimen. Doctors typically use highly aggressive chemotherapy to treat this NHL sub-type.
- *Central Nervous System Lymphoma* — There are two types of central nervous system (CNS) lymphoma: primary and secondary. Primary CNS lymphoma starts in the brain and/or the spinal cord. It is often a feature of AIDS-associated lymphoma, although it may be related to other lymphoma sub-types as well. Secondary CNS lymphoma starts in another area of the body and spreads to the brain and/or spinal cord. Patients with highly aggressive lymphomas are at a higher risk of CNS relapse. Thus, first-line treatment for these types of lymphoma may include chemotherapy given into the spinal fluid. Both primary and secondary CNS lymphomas are uncommon. Standard treatment may include chemotherapy, corticosteroid drugs and/or radiation therapy. Immunotherapy and high-dose chemotherapy with stem cell transplantation are also being studied in clinical trials.
- *Mantle Cell Lymphoma* — Mantle cell lymphoma (MCL) originates from a lymphocyte in the mantle zone of the lymph node. It begins in the lymph nodes and spreads to the spleen, blood, bone marrow and sometimes the esophagus, stomach and intestines. Some patients do not show signs or symptoms of the disease, so delaying treatment may be an option for them. Most patients need to start treatment after diagnosis.
- *Peripheral T-cell Lymphoma* — Peripheral T-cell lymphoma (PTCL) refers to a group of aggressive NHL sub-types that originate in mature T-cell lymphocytes. There are many sub-types, with the most common being:
    - Peripheral T-cell
    - Systemic anaplastic large cell lymphoma
    - Systemic anaplastic large cell lymphoma ALK-1 positive
    - Systemic anaplastic large cell lymphoma ALK-1 negative
    - Primary cutaneous anaplastic large cell lymphoma
    - Hepatosplenic T-cell lymphoma
    - Angioimmunoblastic T-cell lymphoma
    - Enteropathy-type intestinal T-cell lymphoma
    - Extranodal Natural Killer/T-cell Lymphoma.

  PTCL is commonly treated with the regimens used for diffuse large B-cell lymphoma (DLBCL).

  - *AIDS-associated Lymphoma* — AIDS-associated Lymphoma are the types of Non-Hodgkin lymphomas that are most often seen in people with Acquired Immune Deficiency Syndrome (AIDS). These are Diffuse Large B-cell Lymphoma (DLBCL), Burkitt lymphoma and CNS lymphoma. Treatment outcomes depend on how well the patient with AIDS responds to therapy and manages the effects of chemotherapy on blood counts. Because AIDS already leads to low blood cell counts, chemotherapy must be carefully considered to determine whether the chemotherapy's additional effects on blood levels can be managed. The number of people developing AIDS-associated NHL has decreased in the last several years because of improved treatment of HIV (the virus that can lead to AIDS).

- *Indolent Lymphomas*

  - *Cutaneous T-Cell Lymphoma* — Cutaneous T-cell lymphomas (CTCLs) are a group of NHLs that develop primarily in the skin and may grow to involve lymph nodes, blood and other organs. This type of lymphoma originates in a T-cell. Treatment can include topical therapies and drug therapies.

  - *Follicular Lymphoma* — Follicular lymphoma (FL) is the second most common subtype of NHL. Most follicular lymphoma cells have a specific chromosomal abnormality (a translocation between parts of chromosomes 14 and 18) that causes the production (overexpression) of the gene, BCL-2, which can make the cells resistant to therapy. FL is a very slow-growing disease. Some patients may not need treatment for several years, whereas others may have extensive lymph node or organ involvement and need treatment right away. In a small percentage of patients, FL may transform into a more aggressive disease.

  - *Lymphoplasmacytic lymphoma and Waldenström's macroglobulinemia* — Lymphoplasmacytic lymphoma and Waldenström's macroglobulinemia are both slow-growing types of lymphoma that originate in a B-lymphocyte precursor. Waldenström's macroglobulinemia is a type of lymphoplasmacytic lymphoma. In lymphoplasmacytic lymphoma, the lymph nodes are more involved than they are in WM. Both disorders show malignant lymphoplasmacytic cells in the marrow and spleen. Patients may experience increased blood viscosity (thickening of the blood), inadequate blood flow, and symptoms and signs of limited blood flow (e.g., headache, visual blurring, mental confusion). Treatments include watch and wait, chemotherapy, combination chemotherapy and drug therapies, and tyrosine kinase inhibitor drug therapies.

  - *Marginal Zone Lymphoma and Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma* — Marginal zone lymphoma can develop in either the lymph nodes (nodal) or outside the lymph nodes (extranodal). It begins in B lymphocytes in a part of the lymph tissue called the "marginal zone." The disease tends to remain localised. Treatment includes watch and wait, surgery, chemotherapy, and combination chemotherapy and drug therapy.

Understanding Myeloma[3]

Myeloma is a cancer of the plasma cells. Plasma cells are white blood cells that produce disease- and infection-fighting antibodies. Myeloma cells prevent the normal production of antibodies, leaving a person's immune system weakened and susceptible to infection. The multiplication of myeloma cells also interferes with the normal production and function of red and white blood cells. An abnormally high amount of these dysfunctional antibodies in the bloodstream can cause kidney damage. Additionally, the myeloma cells commonly produce substances that cause bone destruction, leading to bone pain and/or fractures. It is often called 'multiple myeloma', which is the most common sub-type, because the proliferation of myeloma cells can occur at more than one site in the body at once. Treatment includes chemotherapy and drug therapy, stem cell transplantation with high-dose chemotherapy, radiation therapy and/or blood transfusions.

Understanding Myelodysplastic Syndrome and Myeloproliferative Neoplasms[4]

Myelodysplastic syndrome (MDS) is a form of blood cancer with varying degrees of severity, treatment needs and life expectancy. MDS may be the primary diagnosis, or it may be related to another treatment. Primary MDS has no obvious cause. Treatment-related MDS has an obvious cause. In MDS the bone marrow produces underdeveloped (immature) cells that are abnormal in size, shape or appearance, which are called 'dysplastic' (abnormally formed) cells. There can be an accumulation of blast cells (immature bone marrow cells), which cannot yet perform the specific function of a mature cell. The bone marrow fails to produce enough healthy red blood cells, white blood cells or platelets, and as a result the number of healthy blood cells (red cells, white cells and platelets) is usually lower than normal. Treatment options include watch-and-wait, blood transfusions, iron chelation therapy, blood cell growth factors, infection management, drug therapy and/or allogeneic stem cell transplantation.

Myeloproliferative neoplasms (MPNs) are types of blood cancer that begin with an abnormal mutation (change) in a stem cell in the bone marrow. The change leads to an overproduction of any combination of white cells, red cells and platelets. There are three major MPN sub-types, including:

- Essential Thrombocythemia, which is a rare blood disease in which the bone marrow produces too many platelets
- Polycythemia Vera, which is a rare disorder where there are too many red blood cells are made in the bone marrow and, in many cases, the numbers of white blood cells and platelets are also elevated
- Myelofibrosis, which is a rare disorder in which abnormal blood cells and fibers build up in the bone marrow.

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[3] Based on Leukemia and Lymphoma Society (LLS) blood cancer summaries updated with information from care pathway analysis developed in partnership with Australian blood cancer sub-type specialists consulted as part of this report. See Appendix A for a detailed summary of the care pathway for major blood cancer sub-types.

[4] Senate Community Affairs References Committee, 2015, *Availability of new, innovative and specialist cancer drugs in Australia*, Commonwealth of Australia 2015, p 47 accessed at: https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs/Report

Treatment depends on the sub-type and fitness of the patient, and can include watch and wait, aspirin, drug therapy, allogenic stem cell transplant and/or therapeutic phlebotomy (venesection).

Understanding paediatric, adolescent and young adults with blood cancer

Critically, blood cancers are the most frequently diagnosed cancers and causes of cancer death among children. In particular, there is a high incidence (number of new cases diagnosed each year) of AML, ALL, Hodgkin and Non-Hodgkin lymphomas among children.

Developing children, adolescents and young adults are not the same as adults, and have different treatment needs and supportive care considerations. Cancer therapies, however, are developed for adults and therefore treatments must be trialled in children. Consequently, off-label prescribing is common in paediatric oncology. The Australian and New Zealand Children's Haematology and Oncology Group (ANZCHOG) reported that 68 per cent of chemotherapy agents were prescribed off-label and 80 per cent of new drug therapies were off-label.[5] For this reason, paediatric patients are generally receive treatment at capital city specialist centres and are enrolled in international clinical trials as a standard of care.

1.2 Blood Cancer is at the Forefront of Precision Medicine

There is an increasing understanding that cancer is not one disease, but many, influenced by genetic mutations that affect both disease development and treatment options.

Until recently, it has been almost impossible to target treatments to a person's unique genetic makeup, and historically cancer medicine, like other diseases, has been a 'one size fits all' approach aimed at the average. These older cancer treatments, such as intensive chemotherapy regimens, have often come with significant side-effects, including secondary cancers, heart problems, developmental delays (in children) and infections due to a weakened immune system, among others.

Precision medicine is now at the forefront of innovative cancer treatment, targeting specific changes in a patient's tumour DNA to treat the disease, while also taking into account of the genetic variations between people who have been influenced by environmental and lifestyle factors. These advances are transforming both the diagnosis and management of patients (Box 1.1).

[5] Senate Community Affairs References Committee, 2015, *Availability of new, innovative and specialist cancer drugs in Australia*, Commonwealth of Australia 2015, p 47 accessed at: https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs/Report

Box 1.1: What is precision medicine?

According to the National Institute for Health's Precision Medicine Initiative, precision medicine is:

> *An emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.*

A precision medicine paradigm enables doctors and researchers to predict more accurately which treatment and prevention strategies for a particular disease will work for different groups of people. This is in contrast to a 'one-size-fits-all' approach, in which disease treatment and prevention strategies are developed for the 'average person', with less consideration for the differences between individuals.

What does this mean in practice? It means that genomic and genetic data (information about your DNA) of both the person and the disease itself (yes, even tumours have DNA) combined with an understanding of environmental factors, such as the food you eat, or how much you exercise, or if you smoke, can be used to predict whether you will respond to a therapy or not. Environmental factors are important because they can influence how your genes express themselves.

As noted by the NIH, although the term "precision medicine" is relatively new, the concept has informed healthcare for some time. For example, a person who needs a blood transfusion is not given blood from a randomly selected person; instead, a donor's blood type is matched to the recipient to reduce the risk of complications.

What has changed in our lifetimes that has enabled this new precision medicine paradigm to emerge in a more meaningful way has been the mapping of the genome, which was completed in 2003. As this technology has advanced, the cost of genome testing has reduced, from more than US$95 million per genome in 2001 to just over a thousand dollars in 2017 (US$1,121 per genome test). In turn, its uptake has increased exponentially. As the uptake of these technologies accelerate, so does our understanding of disease and the potential to change the way we treat people.

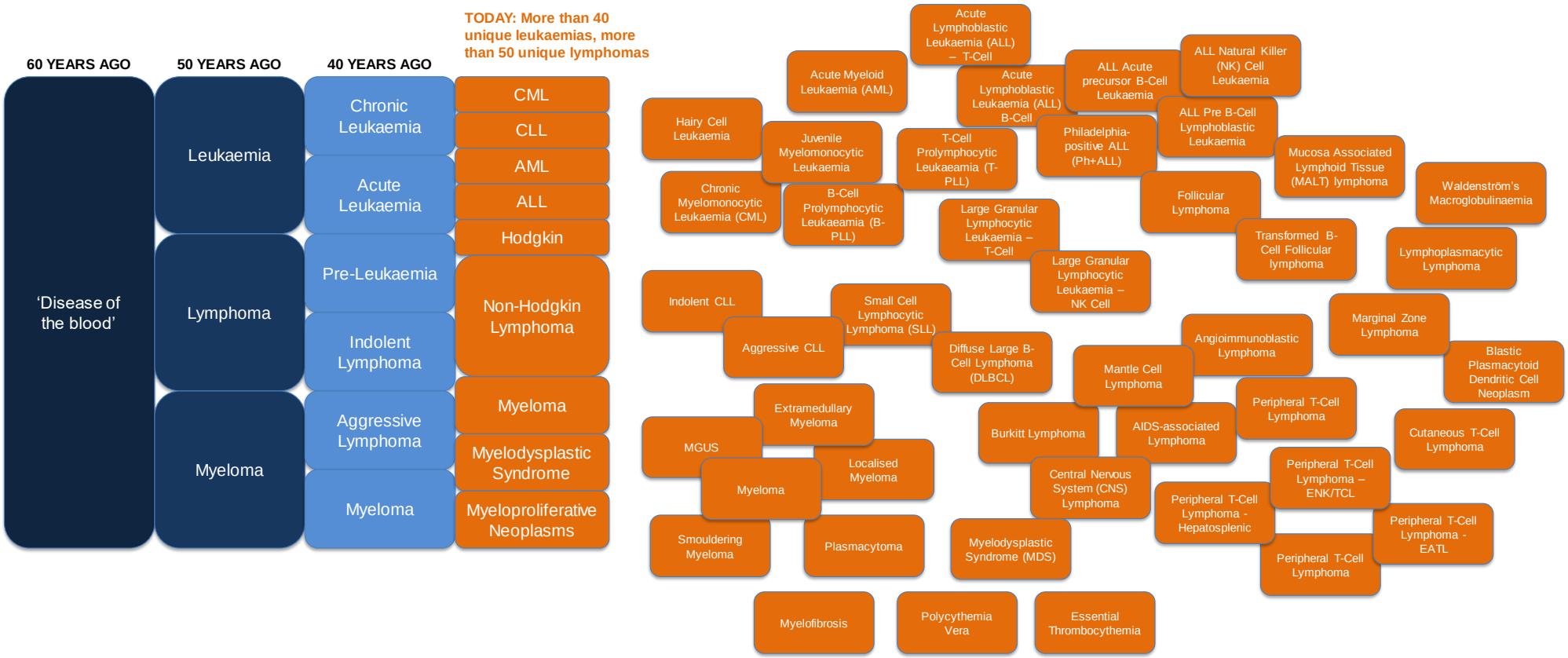
The potential benefits for precision medicine were acknowledged in 2018 with the launch of *The Future of Precision Medicine in Australia* by the Australian Council of Learned Academies: "Advances in precision medicine, and the technologies that support it, are poised to reshape health care".

Critically, cancer medicine is at the forefront of precision medicine, and within cancer, blood cancer has lead the way: today there are more than 40 unique sub-types of leukaemia, more than 50 unique sub-types of lymphomas, and an increasing recognition of a range of Myelodysplastic Syndrome and myeloproliferative neoplasms.

Sources: NIH, 2018, *Precision Medicine Initiative*; Regalado, A., 2018, 'Look How Far Precision Medicine has Come, *MIT Technology Review,* October 23; Australian Council of Learned Academies, 2018, *The Future of Precision Medicine in Australia*, p 2.

Blood cancers have been at the forefront of precision medicine and continue to lead the way for other cancers in the characterisation of tumour cells using immunophentypic and molecular methods. Today there are more than 40 unique sub-types of leukaemia, more than 50 unique sub-types of lymphomas, and an increasing recognition of a range of myelodysplastic syndrome and myeloproliferative neoplasms (Figure 1.3).

Figure 1.3: The Evolution of Precision Medicine in Blood Cancer



Source: Insight Economics adaptation and expansion of M Aspinal, former president of Genzyme, presentation to the National Cancer Institute of SEER data based on Leukemia and Lymphoma Society (LLS) reporting of major blood cancer sub-types at www.lls.org.

The transition to precision medicine brings challenges as well as opportunities.

One of the primary challenges arising from an increasing understanding of the genetic basis for disease is the fragmentation of patient populations into ever smaller target markets. This can lead to delays in evidence development and funding for new therapies. Blood cancer patients have long understood this challenge, where medicines are not brought to market because the disease is 'rare' or 'less common'.

At the same time, building these advances into routine care has represented a demanding agenda for the health system. Often patients continue to be treated in a 'one size fits all' way, when there are now biomarkers of clinical importance that should be used to more accurately diagnose the disease and determine how a person should best be treated.

The advent of precision medicine requires new ways of thinking and policies to match. Importantly, however, getting policies right for blood cancer has the potential to deliver dividends across the health care system, as precision medicine transforms the diagnosis and treatment of other conditions. Reforms to our regulatory and health care systems have the potential to immediately improve outcomes for people living with blood cancer and their families, as well as having the potential to improve the foundations of our health system for other conditions.

1.3 Understanding the Incidence, Prevalence and Mortality of Blood Cancer

Blood cancers collectively represent one of the most common types of cancer in Australia today and one of the most common causes of cancer death among Australians, young and old.

Because blood cancers are traditionally reported by major sub-types, however, the incidence and prevalence of blood cancers are not well understood in Australia, and consequently the significance of blood cancers as a priority for governments and the health system is likely underestimated.

To support a more informed conversation about the challenges and opportunities for people living with blood cancer, projections of incidence, prevalence and mortality of blood cancer from 2018 to 2035 were developed, using data from the Australian Institute of Health and Welfare (AIHW) and State Cancer Registries. A technical appendix is presented in Appendix C, which outlines the key method and assumptions.

Understanding incidence – the new cases diagnosed each year

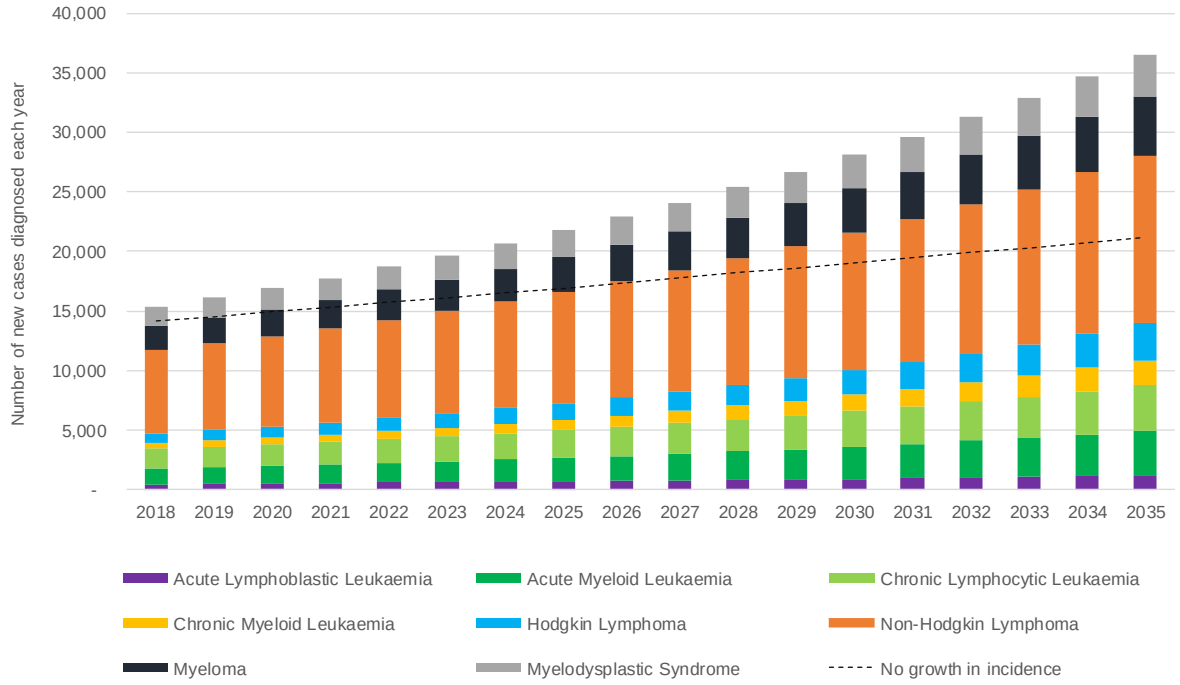
AIHW data indicate that blood cancers are among the most common types of cancer diagnosed each year, and that the incidence of blood cancer is increasing.

In 2018, it was estimated that just over 15,000 people would have been diagnosed (15,374 people) with blood cancer (Figure 1.4) based on AIHW data for AML, ALL, CML, CLL, Hodgkin lymphoma, Non-Hodgkin lymphoma, myeloma and myelodysplastic syndrome. Critically, data for MPN is not reported in the AIHW Australian Cancer Incidence and Mortality database; consequently, this may be a conservative estimate of blood cancer diagnoses each year nationally. Of this total, approximately 8,800 people (58 per cent) are expected to be male and just over 6,400 people (42 per cent) are expected to be female.

With approximately 15,000 people expected to be diagnosed in 2018, blood cancer is among the most commonly diagnosed cancer in Australia today, compared with expected incidence in 2018 of approximately 18,200 for breast cancer, 17,000 for colorectal cancer and 12,700 for lung cancer.

AIHW data also show the incidence of blood cancer is increasing. Over the past 20 years, the incidence of leukaemia, lymphoma and myeloma has increased by more than 80 per cent.[6] The incidence of blood cancers is increasing in part due to the ageing of the population, but also due to improved diagnosis methods and potentially other genetic and environmental factors that are not currently well understood.

Figure 1.4: Incidence of blood cancer in Australia by sub-type – 2018 to 2035



Source: Insight Economics projections to 2035 based on AIHW incidence data 2009-2014 by blood cancer sub-type, applied to ABS Series B population projections (mid case population projections). See Appendix C for technical assumptions.

Figure 1.4 shows expected growth in incidence by blood cancer sub-type based on the five-year average for the period 2009 to 2014, which likely represents a conservative projection given historic growth rates in blood cancer. There was a clear consensus among stakeholders that the incidence of blood cancers is continuing to increase. Nevertheless, the graph also shows a scenario for the growth in the number of new people diagnosed each year if there was no increase in incidence based on ABS Series B population projections (the dotted line).[7]

By 2035, the number of people expected to be diagnosed with blood cancer is projected to rise to more than 36,000 people per annum. If there is no increase in incidence rates from 2014 then total incidence would be expected to increase to just over 21,000 people

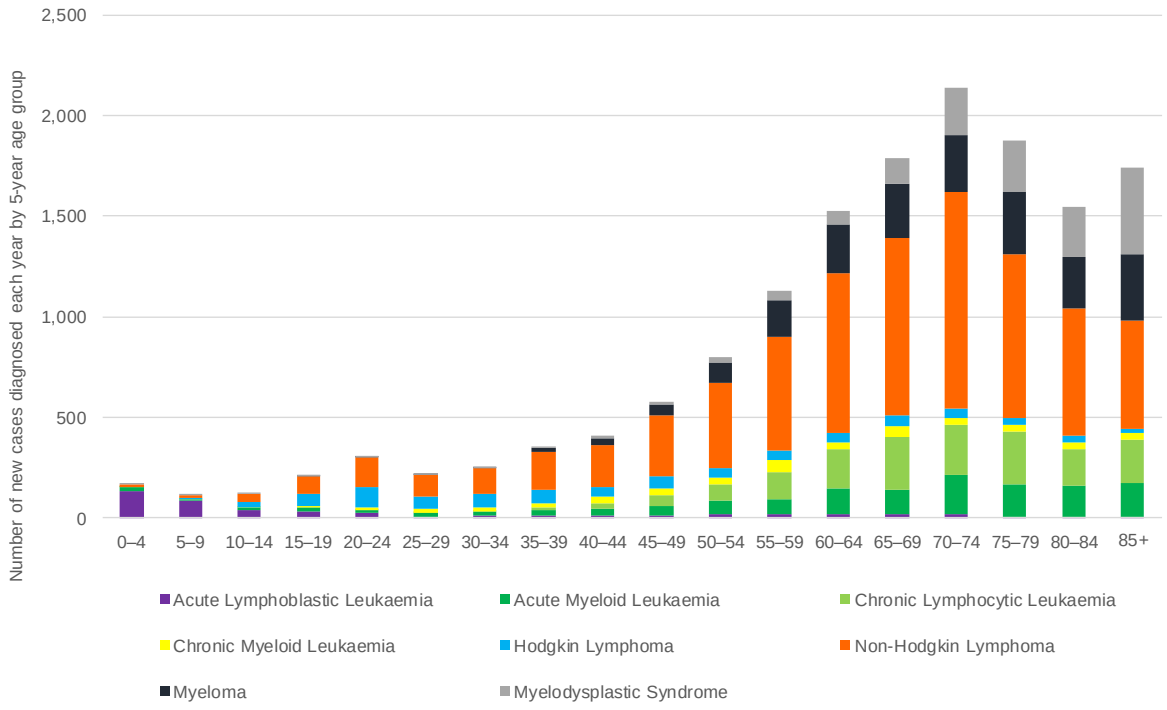
[6] AIHW data, reported by the Australasian Leukaemia & Lymphoma Group, 2018, *The ALLG Story*
[7] Appendix C provides a technical discussion of the projection methodology.

by 2035 as a consequence of Australia's increasing and ageing population, based on ABS Series B projections.

It is worthwhile noting that stakeholder consultations indicated that the incidence of blood cancers may also be under-reported. The potential risk arises from the use of a bone marrow biopsy to automatically confirm diagnosis for some sub-types and trigger a report to the State Cancer Registry. A survey of people living with blood cancer indicated that approximately one in five people had not had a bone marrow biopsy to confirm a diagnosis. Not all sub-types require a bone marrow biopsy; CML can now be confirmed through a blood test, for example. Clinicians can also report a diagnosis as well, though it was unclear how often that would occur in practice. In addition, MDS and MPN, which are coded to the International Classification of Diseases (ICD-10)[8] codes D45–D46, D47.1 and D47.3–D47.5, were not considered cancer at the time the ICD-10 was first published and were not routinely registered by all Australian cancer registries. The Australian Cancer Database contains all cases of these cancers which have been registered since 1982 but the collection is not considered complete until 2003 onwards, and only D46 is included in the Australian Cancer Incidence and Mortality books.[9]

Moreover, blood cancers affect Australians of all ages, from children to adolescents and young adults, to working adults with families and ageing Australians. Figure 1.5 shows the distribution by age at time of diagnosis for the 2018 cohort based on AIHW data.

Figure 1.5: Age profile of people newly diagnosed with blood cancer by sub-type – 2018



Source: Insight Economics projections to 2035 based on AIHW incidence data 2009-2014 by blood cancer sub-type, based on ABS Series B population projections (mid case population projections). See Appendix C for technical assumptions.

[8] ICD-10 refers to the 10th edition of the International Classification of Diseases maintained by the World Health Organisation.
[9] Australian Institute of Health and Welfare (AIHW) 2017 Australian Cancer Incidence and Mortality (ACIM) books: Myelodysplastic Syndrome Canberra: AIHW. <http://www.aihw.gov.au/acim-books>.

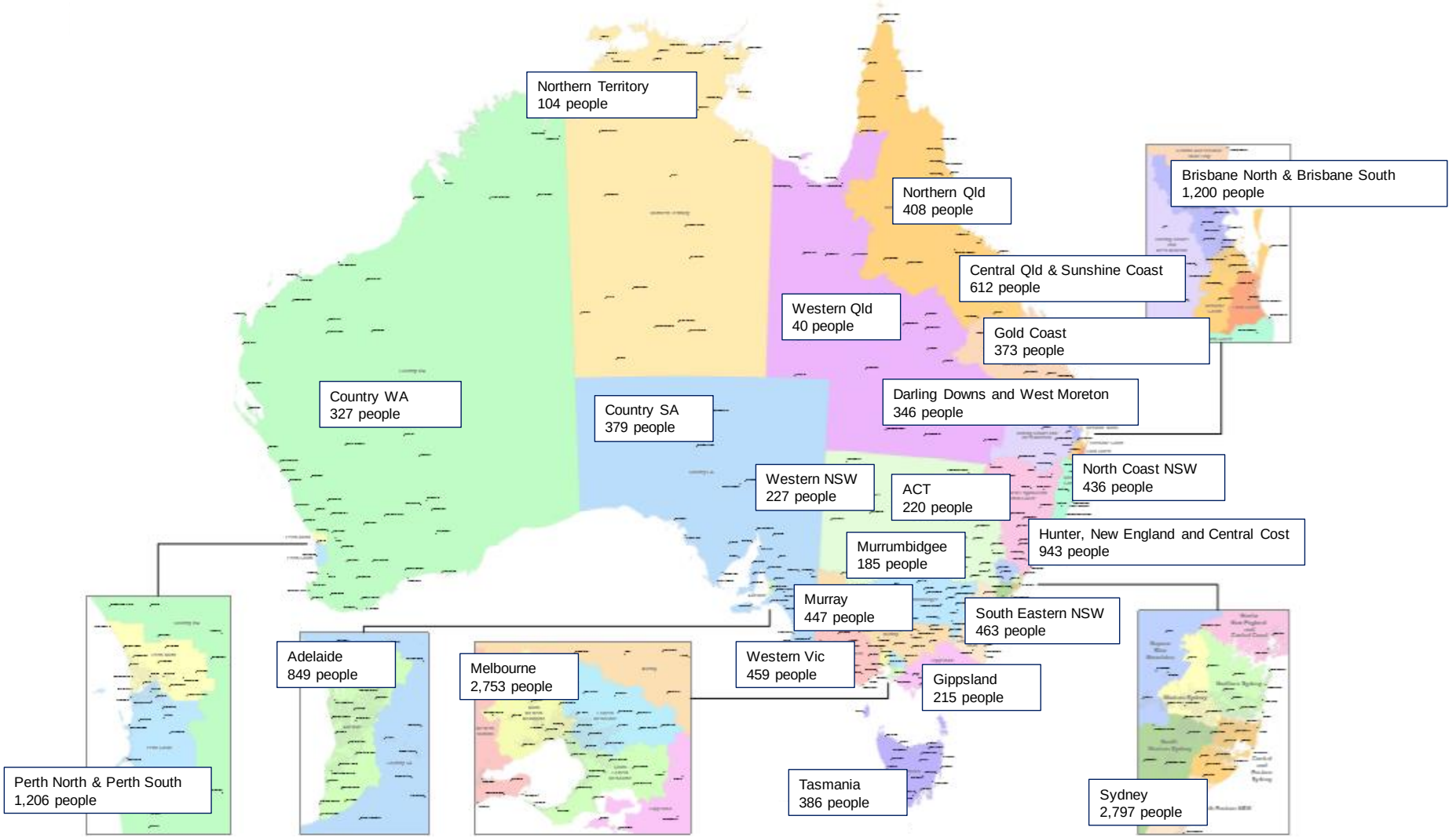
As shown in Figure 1.5:

- Approximately 400 children are currently diagnosed with blood cancer each year. The major sub-types for children include ALL, AML, Non-Hodgkin lymphoma and Hodgkin lymphoma.
- Just over 500 adolescents and young adults (persons aged 15-25 years old) are expected to be diagnosed with the same mix of sub-types as the paediatric cohort.
- More than 5,200 adults between the ages of 25 and 65 will be diagnosed, and approximately half of these diagnoses will be for some form of Non-Hodgkin lymphoma.

The balance of people diagnosed in 2018 (more than 9,000 Australians) are expected to be aged over 65 years old, and the mix of blood cancer sub-types shifts towards an increasing incidence of myeloma, CLL, MDS and Non-Hodgkin lymphoma.

Geographically, approximately 59 per cent of people diagnosed with blood cancer in 2018 will be living in a metropolitan area and 41 per cent will be living in a regional area (Figure 1.6).

Figure 1.6: Geographic distribution of blood cancers by Primary Health Network (PHNs)



Source: Australian Government map of Primary Health Networks, Insight Economics modelling 2018 incidence

Understanding prevalence – the people living with blood cancer

Prevalence refers not just to the number of new people diagnosed each year, but also all the people who were diagnosed at some point and are still living following diagnosis and treatment. Prevalence is the sum of people who have been newly diagnosed plus all of the survivors who were diagnosed, 1-, 5-, 10-, 15-, 20- or even 25 years ago.

Prevalence is important from a government perspective because it informs health service planning. Following active treatment, people living with blood cancer are likely to require further health services to manage co-morbidities and side-effects of treatment. Blood cancer survivors are more likely to have heart problems, secondary cancers, infections and other diseases as a result of the treatment for their cancer, even though many may be functionally cured from their blood cancer.

Prevalence is less well-measured than incidence and not widely reported. Victoria and Queensland State Cancer Registries produces the most comprehensive prevalence statistics by sub-type and by year. Both Victorian and Queensland data indicate that the number of people living with blood cancer could be more than 110,000 people nationally:

- Victoria's 2017 prevalence data suggests approximately 30,000 people are living with blood cancer in Victoria, out of its population of 6.4 million (which represents 26 per cent of Australia's population).
- Similarly, Queensland data indicate that across all blood cancers more than 22,000 people are living with blood cancer (based on 25-year prevalence totals) out of their population of 4.5 million people (which represents 18 per cent of Australia's population).

Extrapolating these results nationally produces an estimate of between 115,000 people and 122,000 people living with blood cancer, based on Victorian and Queensland data, respectively.

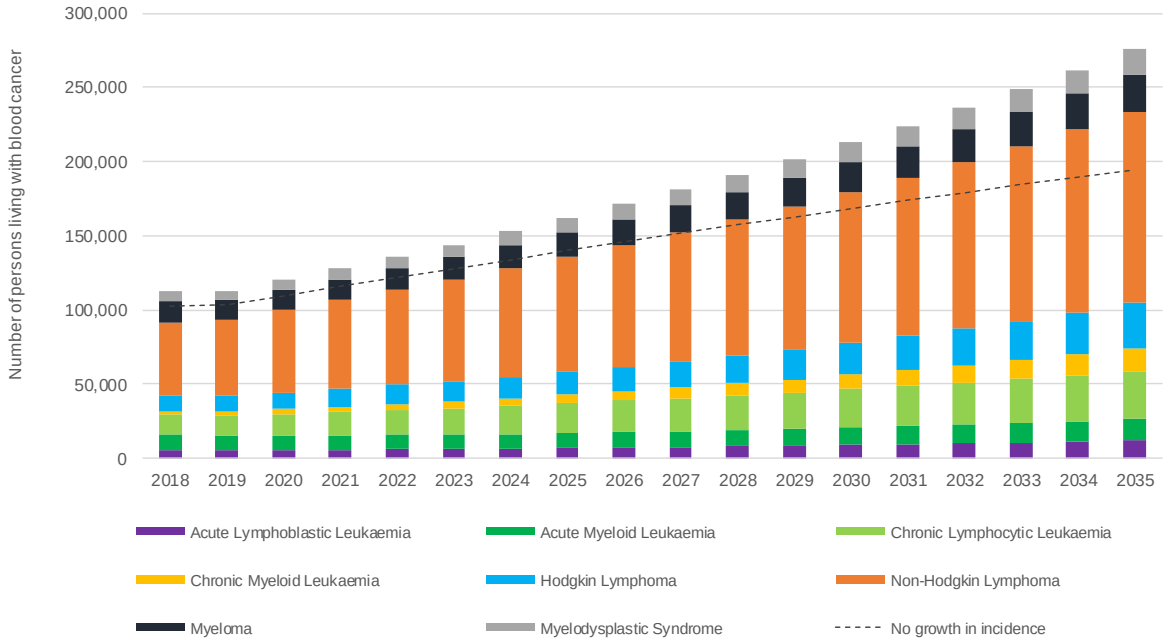
This means that for every person diagnosed with blood cancer in a year, there are likely to be 10 more living with blood cancers as survivors or people living with a chronic disease. This number is increasing as treatments improve and survival rates increase.

To understand the impact of the prevalence of blood cancer to 2035, the number of people living with blood cancer today was projected to 2035 based on age-based survival curves by State and sub-type and long-term conditional survival rates by sub-type available from the AIHW. Combined, the model projects the number of people living with blood cancer to increase from around 112,000 persons in 2018 to more than 275,000 persons by 2035 (Figure 1.7).

To the extent that treatments and care for people diagnosed and living with blood cancer improve, the number of people living with blood cancer could increase above these projections.

Conversely, if the incidence rate of blood cancers holds steady at 2014 rates, the total number of people living with blood cancer would be expected to increase to approximately 195,000 people.

Figure 1.7: The number of people living with a blood cancer (prevalence) – 2018 to 2035



Source: Insight Economics projections to 2035 based on AIHW incidence data 2009-2014 by blood cancer sub-type, based on ABS Series B population projections (mid case population projections). See Appendix C for technical assumptions.

It is important to reflect on what these figures mean in real life for people living with blood cancers. Due to the harsh nature of older cancer therapies (cytotoxic chemotherapies, which literally means 'cell killing chemical therapies' that would kill the cancer cells but also kill other, healthy cells), these survivors are living with the 'side-effects' or late effects of their treatment. As noted above these late effects include cardiovascular problems, a weakened immune system, developmental delays, anemia and other health risks (Box 1.2). For these people, the challenge is not just about survival, but about *living well*, and managing these side-effects in a way that leads to a higher quality of life.

Box 1.2: What does it mean to be a blood cancer survivor? Understanding side-effects and late effects

Current treatments for blood cancer can result in a number of side-effects or 'off-target effects' for patients as a result of treatment. Side-effects from treatment can be both physical and emotional and vary depending on the sub-type, disease progression, and the treatment administered.

Some side-effects go away quickly; others can take weeks, months or even years to improve. Some may be permanent. In addition, some people experience late side-effects. These are problems that develop months or years after treatment finishes and may result from scarring to parts of the body or damage to internal organs.

Common side-effects of blood cancer treatments include:

- *Feeling very tired (fatigue)* — Fatigue is different from tiredness, as it doesn't always go away with rest or sleep. Many people say that fatigue has a big impact on their quality of life in the first year after treatment. Many survivors worry that fatigue is a sign that the cancer has come back or that it never really went away. This is usually not true. Most people find that their energy returns six to 12 months after finishing treatment. However, some people lack energy for years after treatment and their energy levels may never fully recover.
- *Pain* — Pain can have a big impact on a person's life and prevent them from doing the things they want to do. Chemotherapy and surgery may damage nerves and cause pain and numbness in certain areas of a person's body.
- *Numbness or tingling in feet or hands (peripheral neuropathy)* — Tingling or numbness in the hands or feet (peripheral neuropathy) is a common side-effect of chemotherapy. It may last for a few months after treatment finishes or it may be permanent.Peripheral neuropathy can be painful, annoying and frustrating. It may make it difficult for a person to return to normal hobbies and activities. There is no proven treatment to repair nerve damage.

- *Heart problems* — Some types of chemotherapy and drug therapy for blood cancers may damage the heart muscle and lead to an increased risk of heart problems after treatment. Risk factors include certain types of drugs, radiation therapy combined with chemotherapy, being a younger age during the treatment, diabetes, high blood pressure (hypertension), obesity, and smoking.
- *Sleeping difficulties* — Difficulty sleeping is common among people who have had cancer. Sleep can be affected by symptoms related to cancer treatment, such as pain, breathlessness, anxiety or depression.
- *Persistent swelling (lymphoedema)* — Lymphoedema is swelling that occurs in the soft tissues under the skin due to a build-up of lymph fluid. If lymph nodes have been removed during surgery or damaged by infection, injury, or radiation therapy, the lymph fluid may not drain properly. Swelling usually occurs in an arm or leg, but it can also affect other areas of the body. Lymphoedema requires lifelong self-care and management.
- *Forgetfulness or memory problems ('chemo brain' or 'cancer brain')* — Many cancer survivors say they have difficulty concentrating, focusing and remembering things. This is called cancer-related cognitive impairment. Other terms used to describe this include 'chemo brain' and 'cancer fog'.
- *Fertility problems* — Some cancer treatments can cause temporary or permanent infertility (inability to have a child). Although chemotherapy and radiation therapy can reduce fertility, after treatment some women may be able to become pregnant and some men may be able to father a child. Other people take steps to preserve their fertility before treatment starts by storing eggs, sperm or embryos. Due to the rapid progression of some types of blood cancers it is not always easy to preserve fertility all patients. If a patient is told their infertility is permanent, they may feel a great sense of loss and grief, even if their family is complete. They may feel angry, sad or anxious that the cancer and its treatment caused these changes to their body or affected plans for the future.
- *Other physical and psychosocial problems* — In addition to these major challenges, patients experience a wide range of other side-effects and late effects including depression, anxiety, bladder problems, mouth or teeth problems, bone density loss (osteoporosis), joint pain, problems with eating or drinking, changes in body image, e.g. hair loss, weight loss or gain, changes in sexuality and sexual function, and menopausal symptoms for women, among other effects.

Treatments that have the potential to minimise these effects can support patients to live longer, and to live well.

Sources: Cancer Council Victoria, 2018, *Coping with Side Effects*, April, accessed at: https://www.cancervic.org.au/living-with-cancer/life-after-treatment/treatment-side-effects.

Prevalence projections also encourage Governments to consider policies and investments that increase the availability of more targeted treatments or therapies which spare these harsh treatments and lead to health system efficiencies compared to what would have otherwise occurred, and more importantly, helping people to live happier, healthier lives.

Understanding mortality – the people who have died from blood cancer

Blood cancers are also among the most common causes of cancer death.

It used to be that a diagnosis of blood cancer would indicate death within one to five years. But advances in treatment are substantially improving the survival outcomes for patients, transforming blood cancers into a chronic disease for several sub-types.

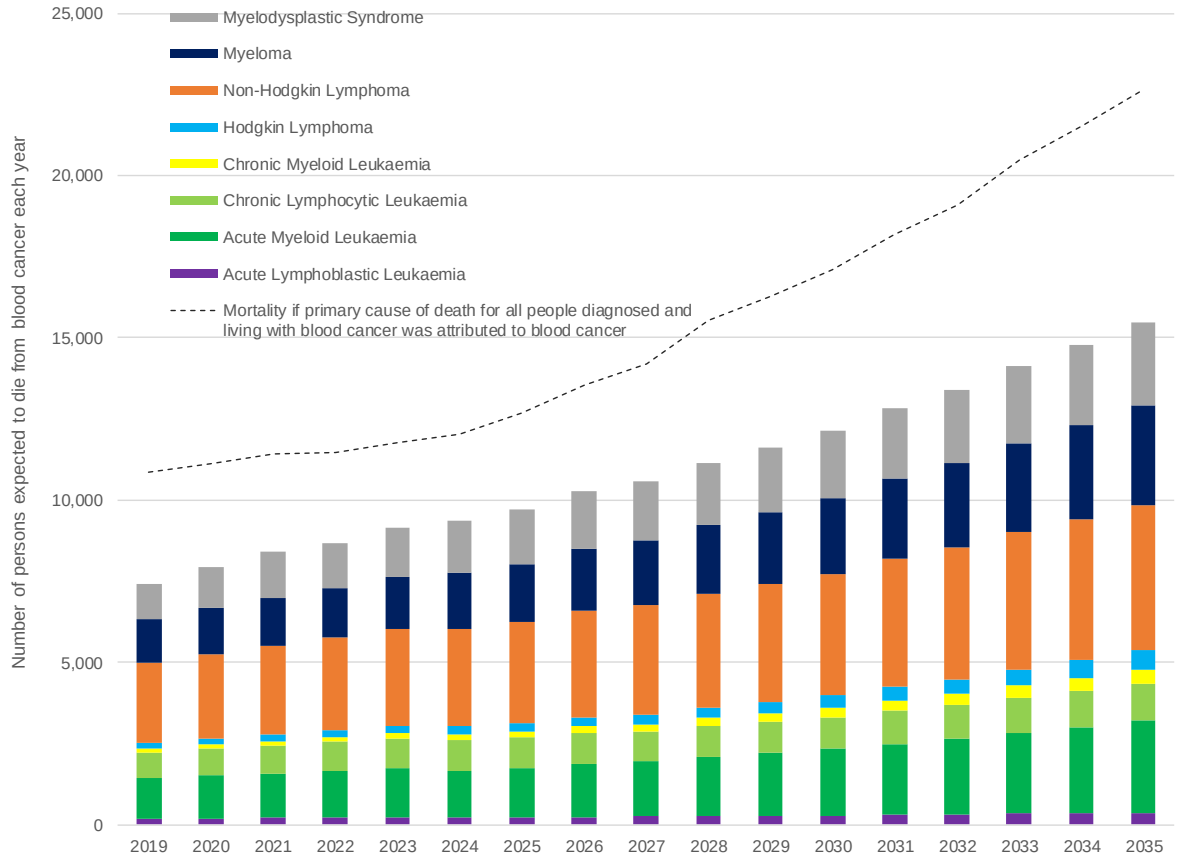
As more and more treatments improve the survivorship of blood cancer, however, the attribution of death may over time become less clear. Stakeholders noted that many deaths may be attributed to the 'off-target' or side-effects of treatment, such death from cardiovascular disease or infection, but these are in fact the secondary effects of the treatments for the blood cancer.

To evaluate mortality rates for each cohort in the model, age-based survival curves were developed incorporating custom data requests from State Cancer Registries and long run conditional survival outcomes by sub-type reported by the AIHW.

As shown in Figure 1.8, if the primary cause of death for all people diagnosed and living with blood cancer was wholly attributed to blood cancer, the total number of deaths from blood cancer would exceed 10,000 persons per year.

Controlling for the attribution of death for long term survivors (living with blood cancer for six or more years) based on conditional survival rates by sub-type, however, indicates that mortality from blood cancer is closer to 7,400 people per annum. This is a higher estimate than ABS underlying cause of death statistics, which reported 4,300 deaths from blood cancers where blood cancer was identified to be the primary cause in 2017. The difference is likely attributable to people living with blood cancer being classified as having died from a co-morbidity or off-target effect rather than the blood cancer.

Figure 1.8: Deaths from blood cancer (mortality) – 2018 to 2035



Source: Insight Economics projections to 2035 based on AIHW incidence data 2009-2014 by blood cancer sub-type, based on ABS Series B population projections (mid case population projections). See Appendix C for technical assumptions.

By 2035, the total number of deaths with blood cancer as the likely primary cause is expected to approach 15,500 people per annum – more than the number of people diagnosed with blood cancer today.

In total, between 2108-2035, more than 186,000 people are expected to die from blood cancer based on current incidence, prevalence and survival data by sub-type by State.

Chapter 2

The Call to Action: the Costs of Blood Cancer to the Community

Of all cancers, blood cancer is among the most fatal and most costly conditions affecting Australians today, with survivors facing a long tail of late effects as a result of being exposed to cytotoxic therapies. The effect of a blood cancer extends for a lifetime, impacting adults and children, their families, and the wider community.

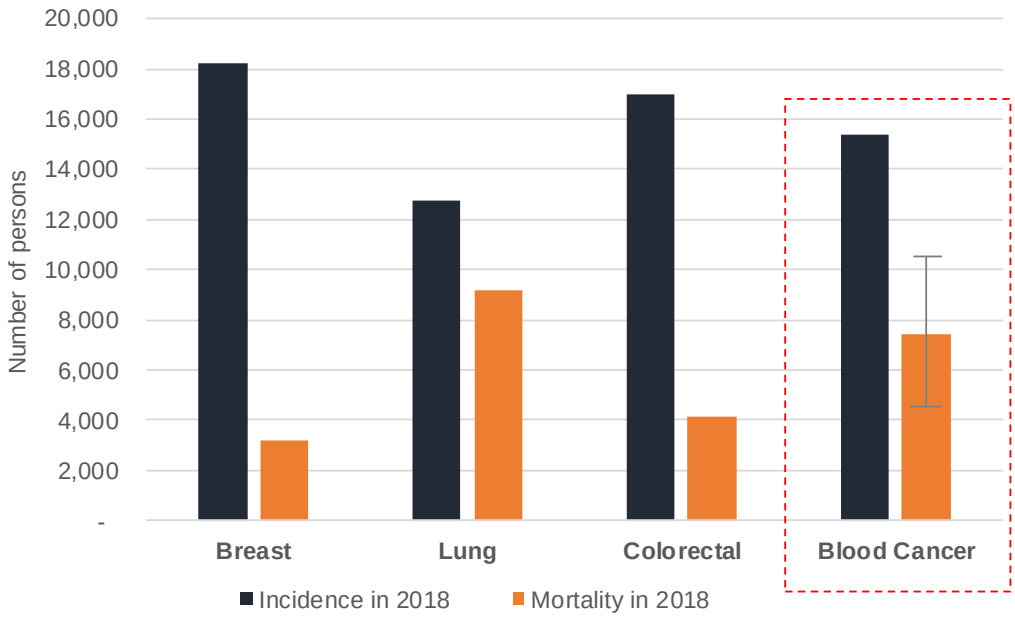
This chapter explores the financial, economic and social costs of blood cancers, based on expected incidence (new diagnoses), prevalence (people living with blood cancer) and mortality (deaths from blood cancer) between 2018 and 2035.

2.1 Blood Cancer is a Bigger Issue Than is Understood

When combined, blood cancers are among the most frequently diagnosed cancers in the Australian community, and the most significant cause of non-preventable cancer death.

Compared to AIHW projections for incidence and mortality of breast, lung and colorectal cancers in its *Cancer in Australia 2017* report, it is possible to see that blood cancers are among the most common types of cancer (Figure 2.1).

Figure 2.1: Blood cancer incidence and mortality compared to the 'big three' cancers

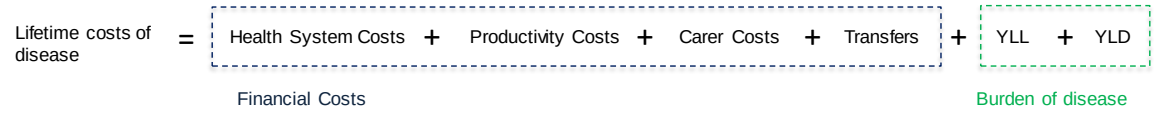


Sources: Breast, lung and colorectal cancer data taken from AIHW Cancer in Australia 2017, blood cancer incidence and mortality based on AIHW incidence rates applied to ABS Series B population projections and age-based survival curves from custom data requests from State Cancer Registries. The lower bound shown in the figure shows the number of deaths where blood cancer identified as the primary cause of death in ABS cause of death statistics in 2016 (ABS Cat No 3303.0 Table 1.1). The upper bound reflects the mortality rate if the death of every person currently living with a blood cancer was attributed in some way to blood cancer.

2.2 Economic Costs of Disease: Conceptual Frameworks

Cancer is one of nine National Health Priority Areas and accounts for 19 per cent of the total disease related burden, making it the highest disease-related burden on society.

Figure 2.2: Understanding the costs of disease – financial costs and burden of disease costs



The economic cost of blood cancer is therefore determined by valuing the direct financial costs of a disease to a patient, their carers and the healthcare system, and adding these to the health and economic costs arising from the burden of disease, where the burden of disease is comprised of years of potential life lost (YLL) and years lived with a disability (YLD). This is shown in Figure 2.2.

There have been several studies that have estimated the lifetime costs of cancers, including blood cancers, which have consistently found that the costs of blood cancer to the community are among the highest of all cancers. Often, however, because the cancers are reported at the sub-type level their total cost and burden is underestimated.

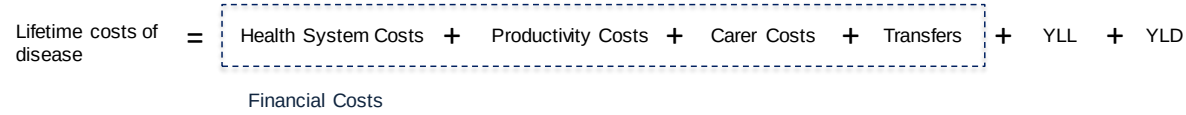
The following sections consider the direct financial costs (Section 2.3) and the burden of disease costs (Section 2.4) in turn, and then combine these cost dimensions together to estimate the total costs of blood cancer (Section 2.5).

2.3 The Direct Financial Costs of Blood Cancers from 2018 to 2035

Blood cancer is among the most costly cancers to treat in Australia today.

The high financial costs of blood cancers, which are comprised of health system costs, impacts on productivity and carers as well as the impacts of dead weight loss from taxation and transfers, are due to the use of treatments that involve long term hospitalisation including high dose chemotherapies, stem cell transplants and blood transfusions, as well as the costs of drug therapies and other services (Figure 2.3). Other costs of blood cancer include, particularly for younger populations, an increased productivity impact on carers and loss of work.

Figure 2.3: Focus on direct financial costs



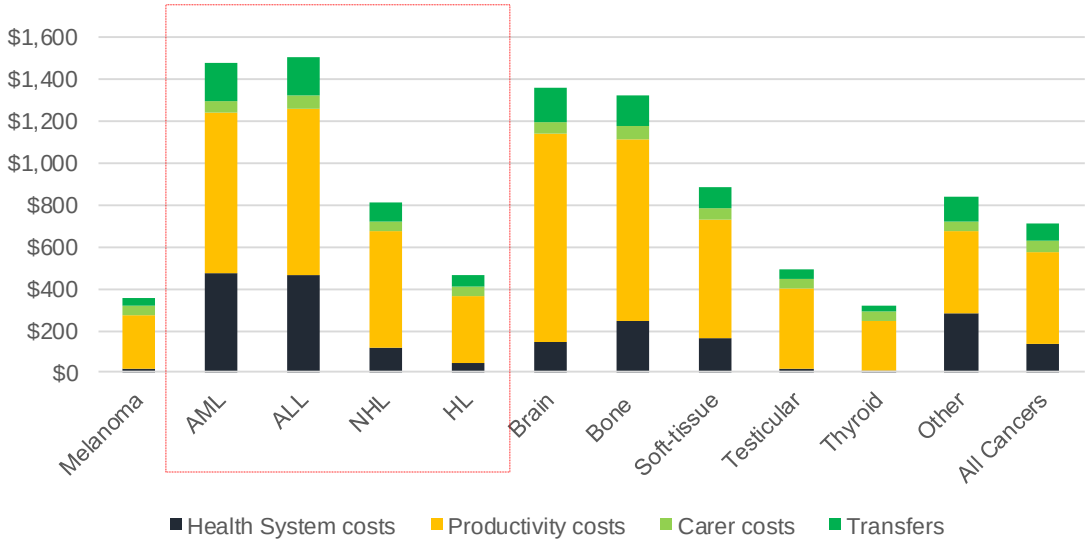
Literature and data estimating the direct financial costs

The direct financial costs of blood cancers have been estimated in several studies. For example, in 2018, CanTeen published a study of the economic costs of cancer for adolescents and young adults (AYA) aged 15-24, which included an estimate of the lifetime financial costs of cancer for the AYA cohort for AML, ALL, Hodgkin and Non-Hodgkin lymphomas.

The CanTeen study shows that *excluding the burden of disease costs* the total lifetime financial costs per person diagnosed in $2018 for AML, ALL, NHL and Hodgkin lymphoma were $1.5 million, $1.5 million, $807,000, and $460,000, respectively

(Figure 2.4). These were the costs of treatment and other financial costs before considering the impact to the person of years of life lost and years lived with a disability.

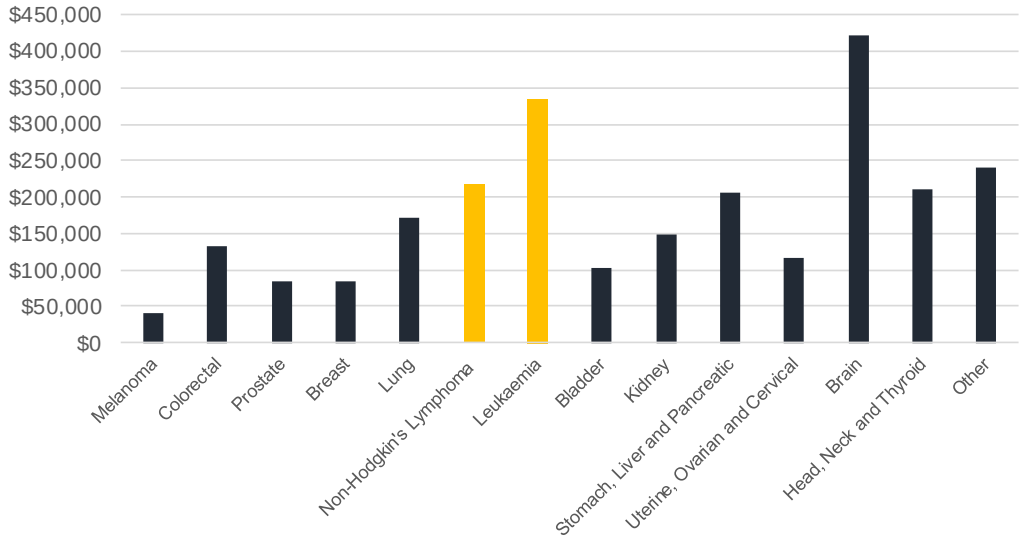
Figure 2.4: Direct financial costs per person for AYA cancers ($2018, '000s)



Source: CanTeen, 2018, *Economic Costs of Cancer in Adolescents and Young Adults* prepared by Deloitte Access Economics 2016 costs inflated to $2018 for consistency, p55.

Similarly, an older study (2005) was completed for the Cancer Council NSW that also estimated the lifetime costs for leukaemia and Non-Hodgkin lymphoma. This study, which included both children and adults, found the expected lifetime financial costs for leukaemia and Non-Hodgkin lymphoma to be among the highest cost cancers to treat following Brain Cancer (Figure 2.5). The direct financial costs for leukaemia were estimated to be $334,000 per person for leukaemia (inflated to $2018) and the direct financial costs for Non-Hodgkin lymphoma were estimated to be $216,000 per person (in $2018).

Figure 2.5: Direct financial costs per person all age groups ($2018)



Source: Access Economics, 2005, *Cost of Cancer in NSW*, report to the Cancer Council of Australia.

More recently, the Sax Institute also published analysis of the health system costs including hospital costs, MBS item costs and PBS costs for people aged 45 years and older that were

diagnosed with cancer between 2006 and 2010. These people were followed to 2014. The study found that blood cancer patients have a high cost of treatment per person compared with other cancers, however, did not clearly provide an indication of the number of years blood cancer patients in the sample lived – that is, it was unclear how many years of the 'continuing phase' costs were identified in the study. In its final analysis of total costs, it appeared the analysis only counted the costs of people who were still alive in 2013, so it was difficult to draw complete conclusions around the health system costs per person for blood cancer. Table 2.1 provides a summary of the estimated hospital, MBS and PBS costs for leukaemia and NHL patients based on the phases of treatment.

Table 2.1: Direct financial costs per person all age groups ($2018)

Cancer type	Initial phase - mean cost	Continuing phase costs per year	Terminal phase
Prostate	$19,224	$1,717	$44,968
Breast	$40,242	$4,442	$42,638
Colorectal	$48,597	$6,622	$65,439
Melanoma	$5,931	$1,290	$46,343
Lung	$32,390	$7,169	$47,882
NHL	$45,071	$6,868	$71,940
Head & Neck	$36,269	-	$73,037
Leukaemia	$39,941	$16,638	$70,067
Kidney	$34,819	$8,180	$60,387
Pancreas	$41,345	$15,846	$47,655
Other	$35,377	$7,875	$55,565
Overall	**$35,377**	**$4,940**	**$54,909**

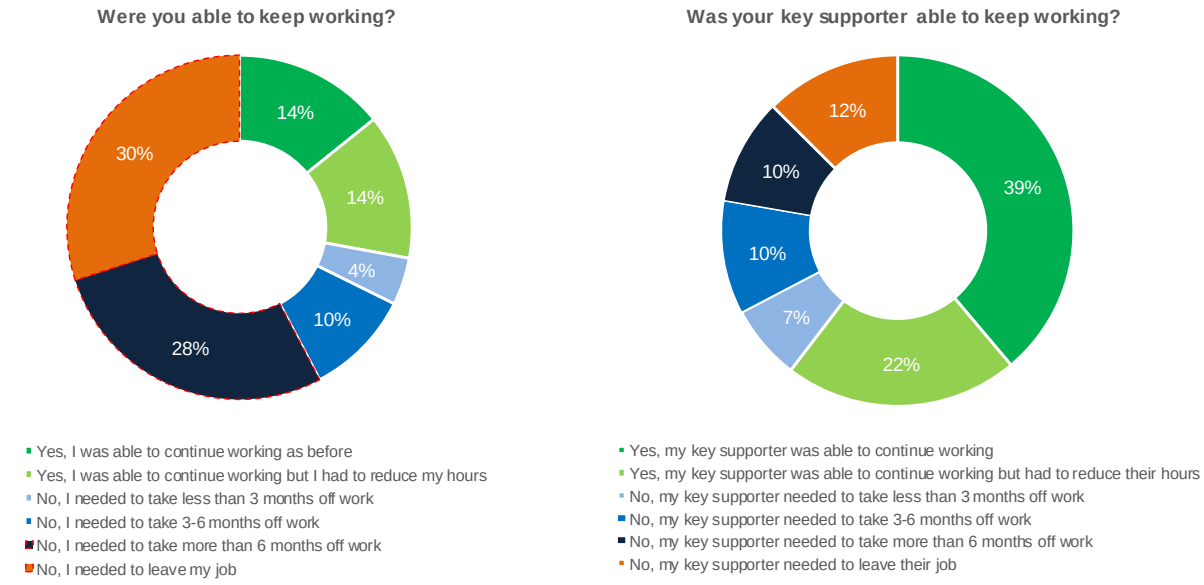
Source: Goldsbury DE, Yap S, Weber MF, Veerman L, Rankin N, Banks E, et al, 2018, *Health services costs for cancer care in Australia: Estimates from the 45 and Up Study*. PLoS One 13(7): e0201552, Table 2, with $2013 dollars inflated to $2018 dollars for consistency.

Although no effort was made to determine the average number of 'continuing phase costs per year', the healthcare costs roughly accord with the healthcare components of direct financial costs identified in the CanTeen and Cancer Council NSW studies in $2018 value terms, although the CanTeen costs for AML and ALL were substantially higher, which is consistent with other reports showing the cost of transplant for children being approximately double that of adults,[10] and the longer time frame over which period childhood cancer survivors were likely to receive treatment.

The productivity costs presented in the CanTeen and Cancer Council NSW reports are also consistent with the survey of people living with blood cancer, which showed that of the people who were not retired (1/3 were already retired), only 14 per cent were able to continue working as they had before, and nearly 60 per cent reported needing to either leave their job or take more than six months off work (Figure 2.6).

[10] Gordon R, Thompson C, Carolan JG, Eckstein G, Rostron C, 2009, *A Costing Study of Blood and Marrow Transplantation Services in NSW: Final Report*. University of Wollongong Australia: Centre for Health Service Development

Figure 2.6: Impacts on household income of blood cancer



Source: Survey of People Living with Blood Cancer 2018, See Appendix B.

The survey also shows the impact on carers was significant, too. Like people living with blood cancer, approximately one third were already retired. But of those who were working, one in five needed to leave their job or take more than six months off work.

A sudden change in employment and household income can lead to financial hardship for families. This, in turn, can adversely impact on survival and quality of life for people living with blood cancers. In total, approximately one third of respondents indicated they needed to seek financial assistance to cope with the impact on household income.

Taken together, this suggests a robust consensus valuation of the direct financial costs by the literature by sub-type for paediatric, AYA and adult populations using the CanTeen and Cancer Council NSW studies.

Estimating the lifetime financial costs of blood cancer

To estimate the lifetime financial costs of blood cancers for people diagnosed in 2018, the lifetime costs for AYAs estimated in the 2018 CanTeen study were applied to people 25 years and younger for the following sub-types: AML, ALL, NHL and Hodgkin lymphoma, and the lifetime financial costs estimated in the by the 2005 Cancer Council Australia study were applied to the sub-types for all other age cohorts.[11] The costs for leukaemia were applied to AML, ALL, CML and CLL, and the costs for lymphoma were applied to lymphoma and myeloma. MDS and MPN were not included in these costs, and therefore can be considered as a conservative estimate of the total costs of blood cancer to the community. These costs estimates are shown in Table 2.2 below.

[11] Note that because specific childhood costs for CML, CLL and Myeloma were not developed the costs of treating children with these diseases was assumed to be the adult rate. This will likely underestimate the costs for these persons but there are very few of them (including no children diagnosed with myeloma).

The interpretation of Table 2.2 is important; *it does not say* that the financial costs of blood cancer are $3.2 billion in 2018. Rather, it says that the total financial costs that will be incurred to treat people newly diagnosed in 2018 *over the remainder of their lives* will be $3.2 billion. Again, financial costs here are also defined to be more than just healthcare costs, and include the impacts to productivity, such as the loss of employment, and the impact on carers, as well as some transfer and taxation impacts. Importantly, these costs do not include the burden of disease arising from years of life lost and years of life lived with a disability (these are explored in the following section).

Table 2.2: Total lifetime financial costs by cohort from 2018 to 2035 ($ millions)

Cohort	Paediatric and AYA Leukaemia	Paediatric and AYA Lymphoma	Adults Leukaemia	Adults Lymphoma & Myeloma	Total Lifetime Financial Costs
2018	$0.59	$0.33	$1,182.07	$2,026.03	**$3,209.02**
2019	$0.63	$0.35	$1,273.80	$2,162.42	**$3,437.20**
2020	$0.68	$0.38	$1,374.08	$2,308.95	**$3,684.09**
2021	$0.73	$0.40	$1,484.35	$2,466.94	**$3,952.42**
2022	$0.79	$0.43	$1,606.91	$2,637.24	**$4,245.36**
2023	$0.84	$0.46	$1,739.34	$2,818.48	**$4,559.13**
2024	$0.91	$0.50	$1,883.52	$3,012.07	**$4,896.99**
2025	$0.98	$0.54	$2,040.58	$3,218.88	**$5,260.97**
2026	$1.05	$0.58	$2,212.11	$3,440.67	**$5,654.41**
2027	$1.13	$0.63	$2,399.76	$3,678.15	**$6,079.67**
2028	$1.21	$0.68	$2,603.55	$3,931.31	**$6,536.75**
2029	$1.30	$0.74	$2,825.52	$4,203.05	**$7,030.61**
2030	$1.40	$0.81	$3,067.65	$4,493.82	**$7,563.66**
2031	$1.50	$0.87	$3,332.96	$4,808.77	**$8,144.11**
2032	$1.62	$0.94	$3,622.57	$5,145.34	**$8,770.47**
2033	$1.74	$1.02	$3,937.49	$5,503.24	**$9,443.49**
2034	$1.87	$1.11	$4,280.42	$5,883.62	**$10,167.01**
2035	$2.01	$1.20	$4,654.13	$6,287.18	**$10,944.53**
Total (2018-2035)	**$20.96**	**$12.00**	**$45,520.81**	**$68,026.14**	**$113,579.91**
NPV (2018-2035, 3%)	**$15.13**	**$8.63**	**$32,648.26**	**$49,321.48**	**$81,993.50**

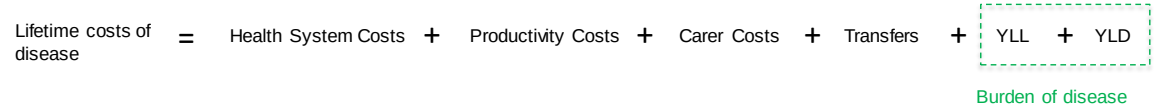
With that context one can see that the lifetime financial cost people newly diagnosed with blood cancer in 2018 is estimated to be $3.2 billion. This is projected to rise with increasing incidence to nearly $11 billion for people newly diagnosed with blood cancer in 2035. The total lifetime financial costs of people who will be diagnosed with blood cancer between 2018 and 2035 is expected to be roughly $82 billion in net present value terms ($113.5 billion in total).

These costs reflect both the high average cost of treatment for people living with blood cancer, and the number of people which is comparable to the 'big three' cancers: breast cancer, lung cancer and colorectal cancer.

2.4 Burden of Disease from 2018 to 2035

Critically, the above costs only value the direct financial costs of blood cancer; they do not consider the impact of the years of life lost or the impact of years lived with a disease (Figure 2.7).

Figure 2.7: Focus on direct financial costs



This section explores these costs.

Burden of disease based on the literature

The balance of the lifetime cost of cancer is the burden of disease which is sum of the value of years of life lost (YLL) and the years lived with a disability (YLD). By consistently applying the burden of disease values estimated in the CanTeen study to paediatric and AYA populations for AML, ALL, NHL and Hodgkin lymphoma, and the burden of disease estimates estimated in the Cancer Council NSW report to the other blood cancer cohorts, it is possible to estimate the total burden of disease. The estimates of burden of disease by cohort are shown in Table 2.3 below.

Like the estimation of direct financial costs, the interpretation of Table 2.3 is important. In particular, it *does not say* that the burden of disease for blood cancer in 2018 is $18 billion. It says that the total lifetime burden of disease costs that will be incurred by people newly diagnosed in 2018 will be $18 billion. These are the costs associated with living with the disease over the remainder of their lives, combined with the costs of premature death, or life not lived. Importantly, *these costs do not include the direct financial costs,* which were discussed in the previous section.

Table 2.3: Total lifetime burden of disease by cohort from 2018 to 2035 ($ millions)

Cohort	Paediatric and AYA Leukaemia	Paediatric and AYA Lymphoma	Adults Leukaemia	Adults Lymphoma & Myeloma	Total Lifetime Burden of Disease Costs
2018	$0.68	$0.29	$5,457.25	$12,730.53	**$18,188.75**
2019	$0.74	$0.31	$5,880.73	$13,587.57	**$19,469.34**
2020	$0.79	$0.33	$6,343.72	$14,508.24	**$20,853.08**
2021	$0.85	$0.35	$6,852.81	$15,500.97	**$22,354.98**
2022	$0.91	$0.37	$7,418.59	$16,571.08	**$23,990.96**
2023	$0.98	$0.40	$8,030.01	$17,709.88	**$25,741.27**
2024	$1.06	$0.43	$8,695.63	$18,926.30	**$27,623.42**
2025	$1.14	$0.46	$9,420.73	$20,225.79	**$29,648.13**
2026	$1.22	$0.50	$10,212.64	$21,619.43	**$31,833.78**
2027	$1.31	$0.54	$11,078.97	$23,111.66	**$34,192.47**
2028	$1.41	$0.58	$12,019.78	$24,702.35	**$36,724.12**
2029	$1.52	$0.63	$13,044.54	$26,409.85	**$39,456.54**
2030	$1.63	$0.68	$14,162.38	$28,236.86	**$42,401.54**
2031	$1.75	$0.73	$15,387.27	$30,215.86	**$45,605.62**
2032	$1.89	$0.79	$16,724.29	$32,330.71	**$49,057.67**
2033	$2.03	$0.85	$18,178.17	$34,579.60	**$52,760.65**
2034	$2.18	$0.92	$19,761.37	$36,969.67	**$56,734.14**
2035	$2.35	$1.00	$21,486.70	$39,505.44	**$60,995.48**
Total (2018-2035)	**$24.44**	**$10.16**	**$210,155.57**	**$427,441.79**	**$637,631.96**
NPV (2018-2035, 3%)	**$17.64**	**$7.33**	**$150,726.97**	**$309,911.19**	**$460,663.13**

With that context one can see that the lifetime burden of disease costs for people newly diagnosed with blood cancer in 2018 is estimated to be $18 billion. This is projected to rise with increasing incidence to $60 billion for people newly diagnosed with blood cancer in 2035. The total lifetime burden of disease for all persons diagnosed between 2018 and 2035 is expected to be roughly $460 billion in net present value terms ($637 billion in total).

Years of Life Lost from blood cancer

The above approach is consistent with burden of disease studies completed across the healthcare sector. To get an *annual* picture of disease burden as opposed to a *lifetime* burden of disease per cohort the YLL per annum were also identified and valued.

In total, approximately 187,000 people are expected to die from blood cancer between now and 2035, with more than 1.4 million years of potential life lost across all sub-types at an average of 81,000 years of potential life lost per annum. By 2035, the number of years of potential life lost per year are expected to reach more than 100,000, up from just over 50,000 per annum today.

This reflects that while some sub-types of blood cancer are highly associated with ageing population cohorts, blood cancers affect people of all ages.

A range of studies have been undertaken to estimate the value of a life and the value of a statistical life year in order to guide government decision-making, be it to weigh the costs and benefits of new safety regulations, the benefits of alternative health interventions or the value of infrastructure to support emergency services delivery. While in a very real sense a life or life year is invaluable, these estimates are practical tools to support government decision-making.

A wide range of values are applied to the value of a statistical life or life year. For example:

- The Office of Best Practice Regulation's current guidance for the value of a statistical life is $4.2 million and the value of a statistical life year is $182,000 in $2014, or $197,000 in $2018.[12]

- Similarly, a meta-review of the valuation of a statistical life year undertaken for the Australian Safety and Compensation Council found the mean value of a statistical life for Australia to be $5.7 million and a median value of $2.9 million, and the mean value of a statistical life year to be $433,437 and a median value of a statistical life year to be $119,589.

  Ultimately, the report recommended a value of statistical life of $6.0 million, with sensitivity analysis of $3.7 million and $8.1 million, and the value of a statistical life year of $252,014 in $2008, with sensitivity analysis of $155,409 to $340,219 in $2008 using a discount rate of 3 per cent over an estimated 40 years of remaining life.[13]

- Within the health space, the cost per quality-adjusted life year (QALY) gained is the general mechanism for valuing health interventions. Unlike other markets,

[12] Department of Prime Minister and Cabinet, 2014, *Best Practice Regulation Guidance Note, Value of a Statistical Life*.
[13] Australian Safety and Compensation Council, 2008, *The Health of Nations: The Value of a Statistical Life*.

however, the Australian Federal government does not publish explicit cost per QALY ranges to allow for judgement to be applied on a case-by-case basis. There is, however, some industry consensus that the cost per QALY paid is generally between $50,000 and $76,000. The origins of this range are based in part on a 2001 PharmacoEconomics article[14] that evaluated Pharmaceutical Benefits Advisory Council (PBAC) outcomes between 1991 and 1996 and identified that products were quite likely to be listed at a price of $46,000 per QALY and less likely to be listed at $76,000 per QALY gained. While this is quite old data, the valuations nonetheless persist; for example, the Lung Foundation of Australia recently valued years of life lost (YLL) at $50,000.

Moreover, the issue of '$50,000 per QALY' has also been the subject of debate in health communities more broadly, with at 2014 article in the *New England Journal of Medicine* indicating that the valuation of $50,000 per QALY was 'curiously resilient' and possibly too low.[15] The article recommended that regulatory systems and purchasers at least adopt a range of valuations at $50,000, $100,000 and $200,000 per QALY gained.

Applying a value of $50,000 to the expected YLL lost in 2019 puts the cost to the community of premature death at $2.7 billion (Table 2.4). Over time, this is expected to grow to more than $3.7 billion by 2035. The total cost in NPV terms to 2035 is expected to be in the order of $40 billion based on current incidence, prevalence and survival rates.

As shown in Table 2.4, if higher valuations per the value of a life year are used, the cost to the community is by definition also higher. For example, adopting the Office of Best Practice Regulation's (OBPR) valuation of a statistical life year of $197,000 would imply that the years of life lost in 2019 was in the order of $10.5 billion. Over time, this is expected to grow to more than $14 billion by 2035. The total cost in NPV terms to 2035, using the OBPR's valuation, estimates the expected costs to be in the order of $160 billion based on current incidence, prevalence and survival rates.

[14] George B., Harris A., and Mitchell A., 2001, 'Cost-Effectiveness Analysis and the Consistency of Decision Making Evidence from Pharmaceutical Reimbursement in Australia (1991 to 1996)', *PharmacoEconomics*, November 2001, Volume 19, Issue 11, pp 1103–1109, accessed at: https://link.springer.com/article/10.2165%2F00019053-200119110-00004

[15] Neumann P.J., Cohen, J.T., and Weinstein M.C., 'Updating Cost-Effectiveness — The Curious Resilience of the $50,000-per-QALY Threshold', *N Engl J Med* 2014; 371:796-797, DOI: 10.1056/NEJMp1405158.

Table 2.4: Valuing Years of Life Lost from Blood Cancer ($ billions)

		Valued at $50,000	Valued at $76,000	Valued at $188,000	Valued at $197,000
	Years of Life Lost	Lower bound PBS cost per QALY 1991-1996	Upper bound PBS cost per QALY in 1991-1996	Lower Bound Australian Safety and Compensation Council	Office of Best Practice Regulation - Current Guidance
2019	**55,802**	$2.8	$4.2	$10.5	$11.0
2020	**58,878**	$2.9	$4.5	$11.1	$11.6
2021	**61,943**	$3.1	$4.7	$11.6	$12.2
2022	**64,481**	$3.2	$4.9	$12.1	$12.7
2023	**67,575**	$3.4	$5.1	$12.7	$13.3
2024	**68,875**	$3.4	$5.2	$12.9	$13.6
2025	**71,408**	$3.6	$5.4	$13.4	$14.1
2026	**75,504**	$3.8	$5.7	$14.2	$14.9
2027	**77,832**	$3.9	$5.9	$14.6	$15.3
2028	**82,072**	$4.1	$6.2	$15.4	$16.2
2029	**85,450**	$4.3	$6.5	$16.1	$16.8
2030	**89,175**	$4.5	$6.8	$16.8	$17.6
2031	**94,597**	$4.7	$7.2	$17.8	$18.6
2032	**98,802**	$4.9	$7.5	$18.6	$19.5
2033	**104,058**	$5.2	$7.9	$19.6	$20.5
2034	**109,008**	$5.5	$8.3	$20.5	$21.5
2035	**114,360**	$5.7	$8.7	$21.5	$22.5
Total (2018-2035)	**1,379,819**	**$69.0**	**$104.9**	**$259.4**	**$271.8**
NPV (2018-2035, 3%)		**$40.7**	**$51.8**	**$78.7**	**$194.8**

2.5 The Total Economic Cost of Blood Cancer from 2018 to 2035

In total, the total lifetime economic cost of people diagnosed with blood cancer in 2018 is estimated to be more than $21.4 billion.[16] As shown in Table 2.5, this is comprised of $3.2 billion in lifetime financial costs and $18.2 billion in burden of disease costs.

As a result of new diagnoses of cancer in 2018 and currently prevalence of people living with blood cancer today approximately 7,400 people are expected to die from blood cancer in 2019, with more than 55,000 years of potential life are expected to be lost.

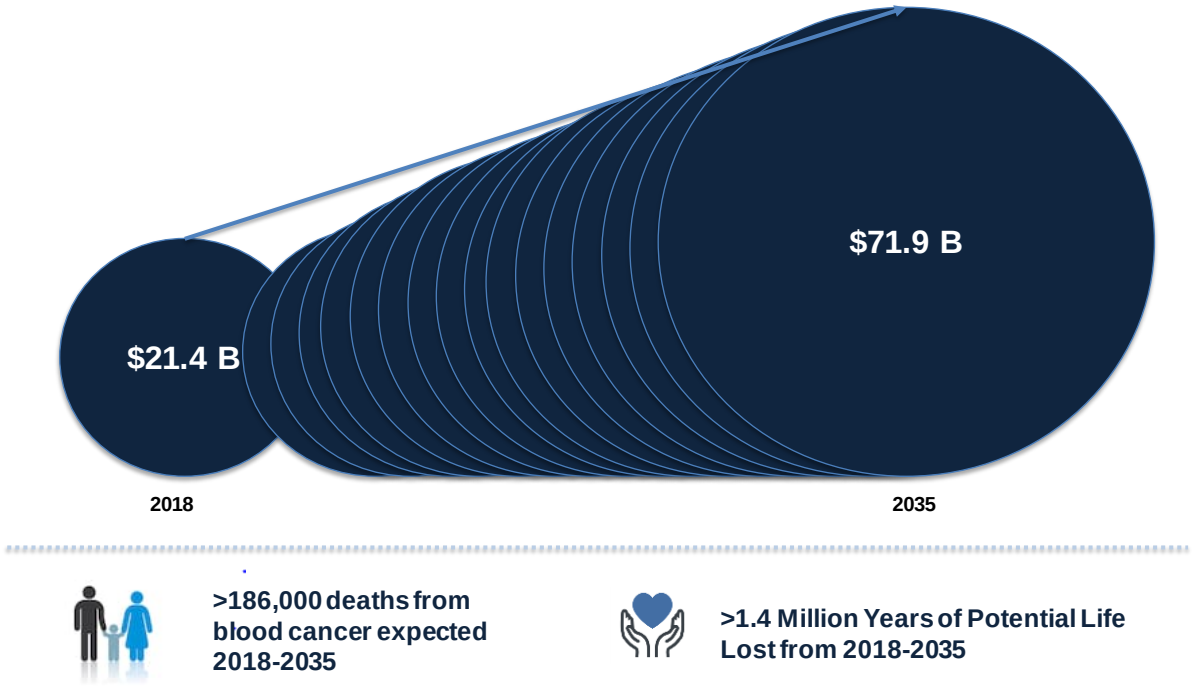
Table 2.5: Total lifetime burden of disease by cohort from 2018 to 2035 ($ billions)

Cohort	Direct Financial Costs	Burden of Disease	Total Economic Cost	Deaths	YLL
2018	$3.2	$18.2	**$21.4**	-	-
2019	$3.4	$19.5	**$22.9**	7,429	55,802
2020	$3.7	$20.9	**$24.5**	7,916	58,878
2021	$4.0	$22.4	**$26.3**	8,398	61,943
2022	$4.2	$24.0	**$28.2**	8,660	64,481
2023	$4.6	$25.7	**$30.3**	9,154	67,575
2024	$4.9	$27.6	**$32.5**	9,353	68,875
2025	$5.3	$29.6	**$34.9**	9,703	71,408
2026	$5.7	$31.8	**$37.5**	10,257	75,504
2027	$6.1	$34.2	**$40.3**	10,585	77,832
2028	$6.5	$36.7	**$43.3**	11,156	82,072
2029	$7.0	$39.5	**$46.5**	11,616	85,450
2030	$7.6	$42.4	**$50.0**	12,121	89,175
2031	$8.1	$45.6	**$53.7**	12,845	94,597
2032	$8.8	$49.1	**$57.8**	13,412	98,802
2033	$9.4	$52.8	**$62.2**	14,113	104,058
2034	$10.2	$56.7	**$66.9**	14,776	109,008
2035	$10.9	$61.0	**$71.9**	15,489	114,360
Total (2018-2035)	**$113.6**	**$637.6**	**$751.2**	**186,900 deaths**	**1.4 million YLL**
NPV (2018-2035, 3%)	**$82.0**	**$460.7**	**$542.7**		

By 2035, these costs are expected to grow to more than $70 billion for people diagnosed in that year (Table 2.5 and Figure 2.8).

[16] Due to limited data, the economic costs of people diagnosed with MDS and MPN are not included, and these estimates are likely to be conservative.

Figure 2.8: The per annum economic costs over 2018-2035 and total number of deaths and Years of Life Lost



In present value terms the sum of these costs to 2035 is expected to exceed $540 billion,[17] with more than 186,000 deaths and 1.4 million years of potential life lost (Table 2.5 and Figure 2.8).

Taken together, these data highlight the significance of blood cancer to the community and indicates the need for action to address the health and economic risks arising from blood cancers.

[17] Noting again that these costs do not include the costs of MPN and MDS.

Chapter 3

Existing and Emerging Challenges for People Living with Blood Cancer

The Leukaemia Foundation has a vision to cure blood cancer and a mission to care for people living with blood cancer and their families. This chapter systematically identifies the range of challenges that exist or are emerging to improve survival outcomes and quality of life for people living with blood cancer and their families.

3.1 Overview of the Challenges to Zero Deaths from Blood Cancer

Today, blood cancer is the most frequent cause of non-preventable cancer death.

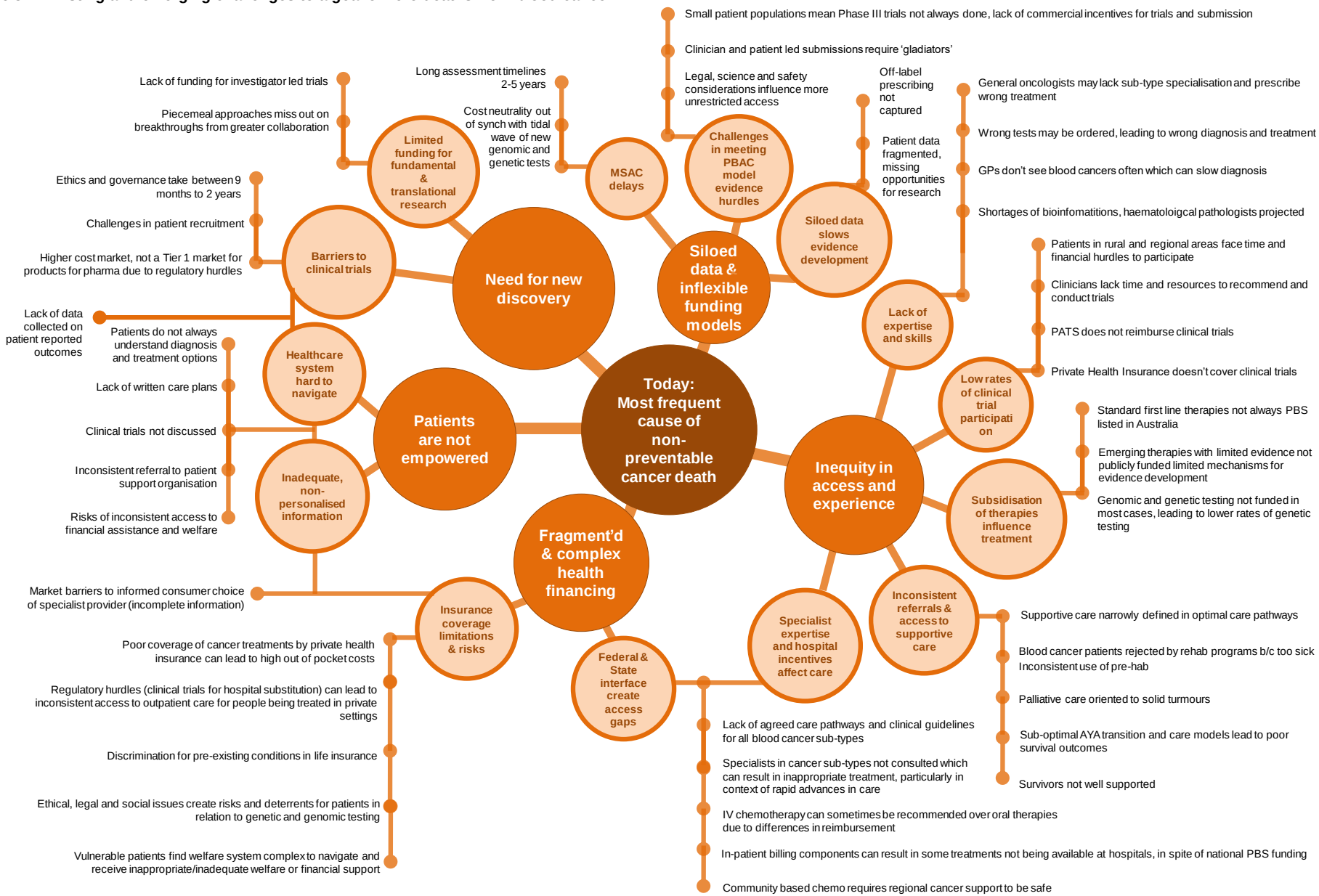
As other cancers are increasingly controlled through education campaigns (lung cancer) and screening programs (colorectal cancer), it is likely that blood cancer will become the leading cause of cancer death in time without action to improve the survival outcomes and quality of life.

Reducing deaths from blood cancer to zero will require stakeholders to address a complex set of issues encompassing health system reforms and investments in research for cures. Figure 3.1 below summarises the existing and emerging challenges that exist to improving the survival outcomes for all blood cancer sub-types and quality of life for people living with blood cancer. These include:

- Incomplete understanding of the causes of blood cancers, and requirements for new discovery
- Inequity in access and experience for people living with blood cancer
- Lack of empowerment for people living with blood cancer to engage in their treatment
- Data silos and market barriers that slow evidence development and the listing in the context of traditional regulatory models
- Fragmented health systems and complex financing arrangements.

These issues are explored in turn, drawing on evidence from an analysis of optimal and current care pathways in Australia and overseas (See Appendix A), a statistically significant survey of more than 3,200 people living with blood cancer (See Appendix B), consultations with more than 65 stakeholders and secondary research review of available literature and data (See Appendix E).

Figure 3.1: Existing and emerging challenges to a goal of zero deaths from blood cancer



3.2 Incomplete Understanding of the Cause of Blood Cancers

Perhaps one of the most significant barriers to reducing mortality from blood cancer is that the causes of different types of blood cancer are not yet fully understood.

While there have been significant advances in some blood cancer sub-types, clinicians nationally indicated that realising the goal of zero deaths from blood cancer will require new discovery:

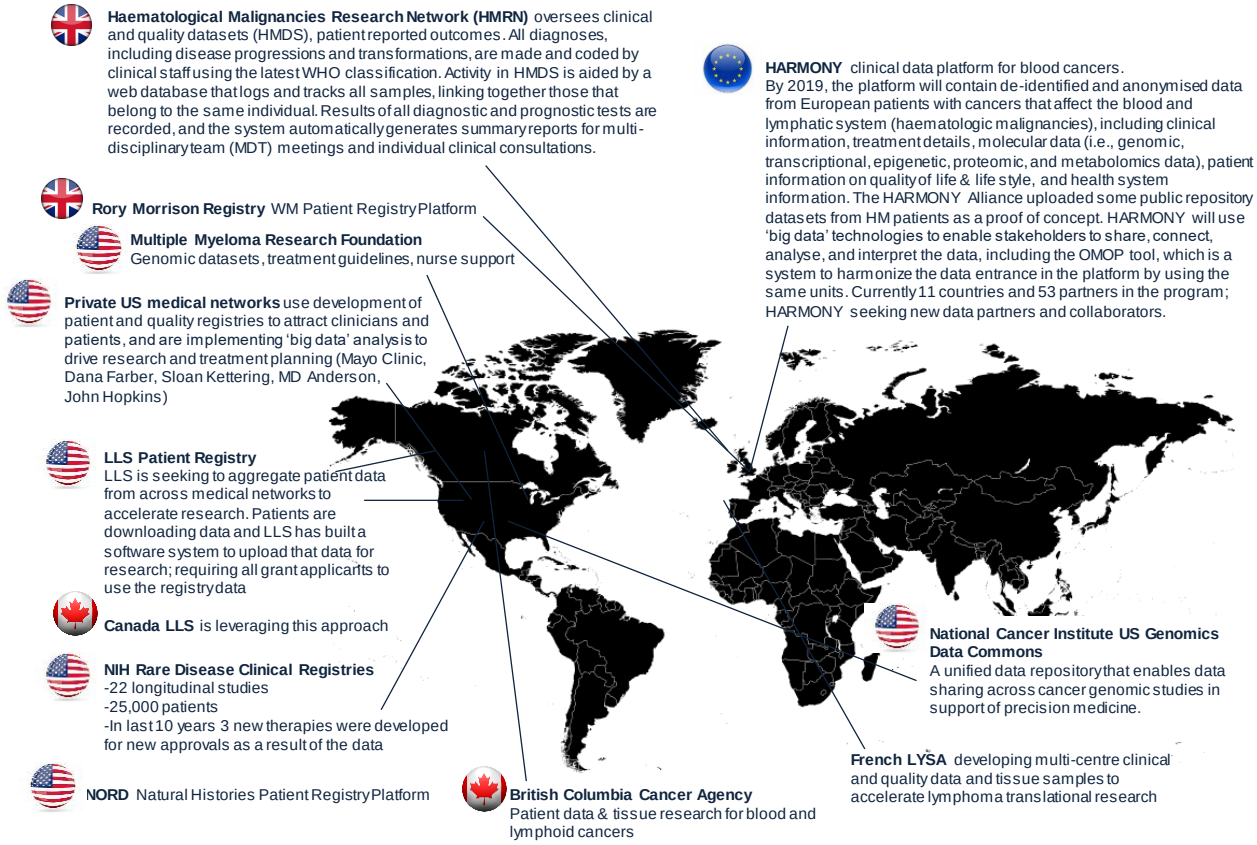
> *"We could probably reduce the number of lives lost today by a 1/3 if we uniformly implemented world's best knowledge. This includes education of specialists, providing access to currently known drugs and consistent health service delivery. The other 2/3 will require new discovery. This will require more funding for clinical trials and research into a range of abnormalities."*
>
> *— Prof John Seymour, Peter MacCallum Cancer Centre*

As the genetic and genomic complexity of blood cancers is becoming clearer, the barriers to research breakthroughs arising from an uncoordinated approach are also coming into sharp relief. More than ever, new discovery in blood cancer treatments will be dependent on research collaboration and the effective collection, sharing and analysis of 'big data'.

In particular, international research collaboration can accelerate the time to a cure through the more effective aggregation of sub-type populations based on genetic and genomic variations in the tumour and the patient. While there may be only a small handful of people with a blood cancer sub-type in one market, globally there may be many more. Putting these patients together through international research collaboration can better explain non-responders to therapies and accelerate new treatments for these sub-types.

As a consequence of the increasing understanding of the complexity and opportunities inherent to the precision medicine paradigm, governments in developed nations have been investing in systems for the integration of disparate data and funding for research is increasingly focused on cross-border research collaborations (Figure 3.2).

Figure 3.2: Investing in systems for big data and research collaboration: international trends



Participating in this global push for a cure is particularly important for a small market like Australia. Linking Australian patients into global research initiatives has the potential to accelerate research outcomes, and it also enables access by Australians with blood cancer to novel therapies.

The need for Australia to make itself an attractive location and partner in international research efforts is evident in a number of examples, including recent examples related to patients with chronic myeloid leukaemia in blast crisis and acute myeloid leukaemia (Box 3.1).

Box 3.1: Barriers to international research collaboration in Australia – case studies

Novel treatments for patients with CML in Blast Crisis

Chronic myeloid leukaemia progresses in three stages of disease. Most patients are diagnosed early and there are effective treatment options for these patients in the form of tyrosine kinase inhibitors (TKIs), which, since their development in 2001, have transformed CML from a highly fatal disease to a condition that can be chronically managed through a daily oral drug therapy.

For patients that progress to CML in blast crisis, however, there are currently no available drug therapies, although some patients may be eligible for an allogenic stem cell transplant.

Overseas, however, a new trial has been established at MDAnderson in the US to test the use of venetoclax for these patients. While venetoclax was developed in Melbourne, with funding support from the Leukaemia Foundation, at the time of writing it is still not publicly subsidised in Australia.

One of Australia's leading research centres in CML had discussed the potential for participation in the clinical trial. Due to challenges in patient identification and recruitment, however, the research clinician indicated that there may be only one patient identified at the treatment centre in their State over the course of a year, and currently there are not good mechanisms for identifying other patients with the required characteristics in Australia.

Ultimately, it was decided that the costs of opening an international trial site for potentially only a single patient was not worth the effort and the potential Australian trial site was not included in the MDAnderson trial.

Overcoming the barriers to Australia's participation in these types of trials is essential for new discovery and enabling Australian patient access to novel therapies.

Novel treatments for patients with AML

Acute myeloid leukaemia is the most common type of acute leukaemia in adults. Despite intensive chemotherapy and transplantation strategies, the 3-year relapse free survival for adult AML patients under 60 years old is 50%, with most patients relapsing in the first year of diagnosis. The standard of care for eligible patients with newly diagnosed AML involved induction treatment with intensive chemotherapy, typically involving cytarabine and an anthracycline-based drug, which is aimed at achieving complete remission. The escalation of chemotherapy dose intensity during induction or consolidation is clinically challenging. AML is still fatal in about half of younger patients and about 80 per cent of patients over the age of 60 years old. Consequently, there is a need for more specific and less toxic drugs that are rationally designed to target leukaemia specific abnormalities.

Current drug development strategies in AML are frequently unsuccessful, excessively costly and make inefficient use of the global research resources available among the AML academic community. New drugs are often piloted in the setting of relapsed/refractory AML, rather than the first line setting, which amplifies the risk of development failure.

To this end, a global Phase III trial is in development to investigate the use of a new therapy, ivosidenib, for AML. Phase I and Phase II research published in the New England Journal of medicine in 2018 reported ivosidinib have produced durable remissions for patients with specific gene mutations (IDH1). The stratification of the AML patient population by gene mutations makes participation in the global trial essential for these patients and to support evidence development for listing on the PBS.

Australia faces challenges in being able to participate, however, because one of the drug therapies involved in the trial (daunorubicin) is TGA registered but not PBS listed for the AML indication. This presents a significant hurdle to participation because the additional cost of this medicine, even though it is not the primary focus of the trial. By contrast, these drugs are available and used as standard of care internationally. In order to ensure comparability of outcomes, the trial participants must be globally consistent. Without access to this medicine, AML patients with IDH1 mutations will not be able to participate in this globally study.

Source: CML case study is based on research interviews and the AML case study is based on information provide by the ALLG.

The CML in blast crisis and AML IDH1 mutation examples highlights the challenges for Australia in progressing research in blood cancers today. With only two or three per cent of the world's population, Australia has always been a small market, but the challenges of its size are compounded in the context of precision medicine:

- The further fragmentation of small patient populations can increase the difficulties in attracting international research funding for clinical trials, because companies or research institutes may not want to open a trial in Australia if it is hard to identify patients for research, especially if the cost per patient meets or exceeds other developed nation prices.[18]

- Australia lacks effective mechanisms for identifying patients for recruitment into clinical trials. This adds to long ethics and governance timelines, which exceed international trial timeline targets.

- Moreover, it adds to the challenges to win funding from traditional Australian research funding sources for investigator-led trials, such as the National Health and Medical Research Council (NHMRC), with patient populations appearing smaller because precision medicine is more advanced compared to other cancer types.

Critically, the most significant issue is that patients don't get access to new treatments. In the case of CML in blast crisis, there are no alternative treatments; in the absence of access to a clinical trial, or potentially some sort of compassionate access program, mortality from CML is an effective certainty for this cohort.

The pursuit of a cure for blood cancers will therefore require greater international collaboration in research than ever before, and is arguably more important for Australians than other, larger markets. Ensuring Australian patients and researchers are

[18] See MTPConnect by LEK, 2017, *Clinical Trials in Australia: the Economic Profile and Competitive Advantage of the Sector*, p 43, accessed at https://www.mtpconnect.org.au/Attachment?Action=Download&Attachment_id=54

integrated into international research efforts, however, will require Australia to address, *in a more innovative way*, the very persistent challenges to the conduct of clinical trials while at the same time ensuring it does not truncate essential fundamental and translational research endeavours. These issues are considered in turn.

Challenges to clinical trial research

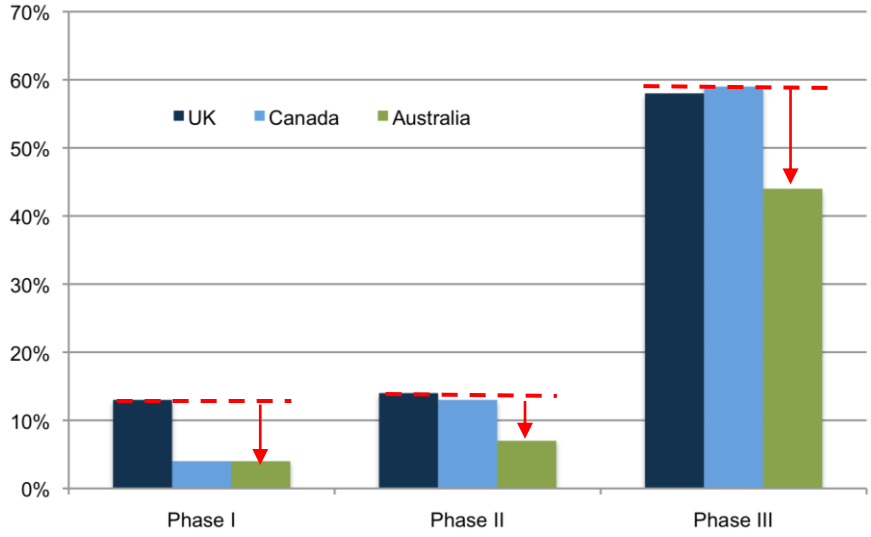
Clinical trials are an integral part of the research and development of new treatments or tests, and the refinement of existing standards of care and clinical practice. To this end, they are a critical step in the path to reducing mortality from blood cancers.

The persistent and significant challenges to the conduct of clinical trials in Australia, however, present a formidable hurdle to the realisation of zero deaths from blood cancer. As shown in Figure 3.5 below, the survey of people living with blood cancer indicated that less than 20 per cent of patients participated in a clinical trial, and of those who did not participate 87 per cent of patients did not participate because either the trial was not discussed with them or there weren't any trials available.

Multiple reviews in Australian competitive advantage in clinical trials have identified the excellence in research quality and reputation for safety as major contributors to the conduct of clinical trial activity in Australia.

Nevertheless, Australia lags its international peers in participation in international clinical trial research. A recent review by MTPConnect found that Australia lagged the United Kingdom and Canada in its participation in industry-sponsored international clinical trials for all phases of clinical trial research except for Phase 1, where Australia was on par with Canada but lagged behind UK participation rates (Figure 3.3). Within oncology, Australia lagged the UK by 17 per cent in participation in multi-country trials.

Figure 3.3: Australian participation in international clinical trial research by phase of study



Source: Report to MTPConnect by LEK, 2017, *Clinical Trials in Australia: the Economic Profile and Competitive Advantage of the Sector*, p 43, accessed at https://www.mtpconnect.org.au/Attachment?Action=Download&Attachment_id=54

To understand the challenges associated with clinical trial activity, it is important to first understand how they are conducted and who is involved. Clinical trials see a range of stakeholders come together to progress research; these include:

- *Industry stakeholders* — Pharmaceutical, biotechnology and medical device companies, which are usually referred to as 'industry' stakeholders. These

companies fund the vast majority of clinical trial activity globally and in Australia. When a trial is funded by pharmaceutical industry it is generally referred to as an 'industry-led' trial. Pharmaceutical and biotechnology companies may out-source the conduct of clinical trials to Contract Research Organisations (CROs), who are specialists that design plan and manage clinical trials on behalf of the company or 'sponsor'.

- *Medical Research Institutes* — Medical Research Institutes, which focus solely on medical research and typically specialise in one or more therapy areas. Medical Research Institutes generally partner with hospitals, universities and clinical trial networks in the conduct of clinical trials. Examples of Medical Research Institutes with a focus on blood cancers in Australia include the Walter and Eliza Hall Institute in Victoria, the Garvan Institute in New South Wales, the South Australian Health and Medical Research Institute, and the Diamantina Institute and Queensland Institute for Medical Research in Queensland.

- *Healthcare providers* — Hospitals (public and private), private clinics and GP practices serve as 'trial sites' that host trials and provide the necessary clinical staff for the conduct of the clinical trials. Hospitals can also fund a clinical trial, as well as conduct clinical trials on behalf of another sponsor (such as industry) through recruiting, treating and monitoring patients. Private clinics are less likely to sponsor trials but can support in the recruitment and conduct of trials that are funded by other stakeholders, such as industry.

  Within the hospital, treating clinicians conduct clinical trials in addition to seeing their patients. While hospitals can receive revenue from the trial to cover administrative costs and may also receive funding for the treatment of patients, there are generally limited incentives for the conduct of clinical trials outside of patient care.

  - Public hospitals that are active in the conduct of blood cancer research include the Victorian Comprehensive Cancer Centre, Alfred Hospital and Royal Melbourne Hospitals in Victoria, Westmead Hospital in NSW, the Princess Alexandra Hospital in Queensland, Perth Children's Hospital, and the Royal Adelaide Hospital in South Australia.

  - Private hospitals that are active in the conduct of blood cancer research include ICON Cancer Care and the Cabrini Hospital group.

- *Universities* — Universities are not usually trial sites, but partner and collaborate with Medical Research Institutes and hospitals in research, often in early stage trials or in trials related to clinical practice (implementation science). Examples of universities that are active participants in blood cancer research include Monash and Melbourne University in Victoria.

- *Clinical Trials Networks* — Clinical Trials Networks are groups of researchers, clinicians and academics that share infrastructure to conduct multi-centre clinical trials and facilitate knowledge sharing between researchers in the field. In blood cancer, there is the Australasian Leukaemia & Lymphoma Group (ALLG), which supports the conduct of 3-4 clinical trials per year, of which 1-2 are international trials in partnership with industry and researchers based in the European Union, Canada and the United Kingdom. Currently, the ALLG does not pursue international clinical trials in the United States due to regulatory requirements by the FDA which impose a compliance burden that was reported to exceed the current capacity of the network.

These stakeholders come together for the conduct of two main types of trials:

- *Industry-led trials*, which are sponsored, funded and managed by pharmaceutical, biotechnology and medical device companies for the purpose of developing intellectual property that can be commercialised into a product. These trials must be executed in a way that meets the regulatory requirements of the market(s) in which the company would ultimately like to sell a product. In Australia the relevant regulators are the Therapeutic Goods Administration (TGA), which ensures that products to be sold in Australia meet required safety and efficacy standards. The equivalent to the TGA in the United States is the Food and Drug Administration (FDA) and in the EU it is the European Medicines Agency (EMA).

- *Investigator-led trials*, which are initiated by clinicians and researchers at hospitals and Medical Research Institutes. These trials are conducted for the public good and focused on answering a clinically-relevant research question irrespective of its commercial value. Investigator led trials tend to be funded through a variety of sources, including government (such as through the National Health and Medical Research Council (NHMRC)), philanthropic donors (such as the Leukaemia Foundation, Snowdome and the Lions Club) and research institutions, including Medical Research Institutes and universities. Some also receive funding from industry.

Currently the vast majority of clinical trials conducted in Australia are industry-led trials, which account for 66 per cent of activity by numbers of trials. Investigator-led trials account for the remaining 33 per cent of trials.[19]

In the pursuit of a cure for blood cancers, both types of trials are essential, and there are barriers to the conduct of both.

The challenges and issues facing clinical trials have been well documented over a decade or more. Australian Federal and State Governments, in consultation with the clinical trials sector, have responded over time by implementing a number of activities aimed at improving Australia's ability to initiate and deliver clinical trials. Even with these reforms, however, National Aggregate Statistics (NAS)[20] for clinical trials conducted in public health institutions indicate that Australia still lags its international peers in the conduct of clinical trials. For example:

- KPIs for ethics approvals indicates that less than half (46 per cent) of ethics applications are approved between 0–60 days and 88 per cent within 120 days. This compares with international comparison of targets of 60 days in Europe and England; 30 days in United States, Canada and Korea; and 145 days in China.

- In addition to ethics, there are also site governance approvals which must be obtained, and the processes for patient recruitment to the trial. While ethics were overall seen to have been substantially streamlined through the development of centralised approval processes, site governance challenges were reported to have mushroomed in response:

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[19] Clinical Trials Jurisdictional Working Group Framework for National Aggregate Statistics (NAS), *Second Activity Report on Clinical Trials in Australian Public Health Institutions*, 2015-16, accessed at: https://www.health.gov.au/internet/main/publishing.nsf/Content/EE207D978A44E4B8CA257FA90081B212/$File/NAS%20Second%20Activity%20Report.pdf

[20] *Ibid*.

- NAS data indicate that only half of the trials at public institutions saw site governance approvals at '*at least one site*' completed within 60 days following the ethics approval date. Critically, these were not clear measures of time to site governance approval for the trial, however, because these data do not measure the time to obtain approvals across all sites in a multi-site trial.
- Moreover, no data is currently collected in the NAS dataset for the time to meet patient recruitment.

Patient recruitment was reported by stakeholders to be incredibly challenging under current arrangements, with many trials closing due to an inability to recruit and retain patients. For example, a 2014 survey conducted by Clinical Trials Connect assessed the recruitment success for a range of clinical trials in Australia. The survey identified that only 20 per cent of trials met their recruitment deadline. Similarly, Medicines Australia indicated that more than 50 per cent of sites did not meet their recruitment requirements, pointing to fragmentation of the sector and the need for better coordination of effort at the national, state and territory level.[21] Also, an EY review of clinical trial performance for the Department of Health,[22] stakeholders identified a lack of streamlined infrastructure as a key barrier to recruitment and retention in Australian clinical trials. Trial site staff reported that finding participants that fit complex eligibility criteria is a major barrier to recruitment.

This was consistent with stakeholder interviews which, notwithstanding reforms to clinical trials over the past decade, consistently reported that the time to trial establishment was somewhere between 9 months and 2 years, well in excess of international target timelines. In the context of small patient sample sizes this substantially contributes to Australia lagging behind the UK and Canada in participation in global clinical trials in oncology (Figure 3.3 above).

Adding to these very substantial administrative inefficiencies, however, was an emerging consensus that there is an underlying lack of incentives for the conduct of clinical trials at hospitals, including in particular public hospitals. Multiple stakeholders saw this as the out-working of a long-term evolution in the role of the public hospital, with unintended consequences emerging for Australian research. While the transition to activity-based funding arrangements nationally may have brought efficiencies in service delivery, there have been other effects for public hospitals which have historically been the major engines of scientific excellence in Australia. Today, clinical trials are now seen as an 'add-on' (Figure 3.4) and are unsupported unless they can earn a hospital revenue either directly or indirectly.

[21] Report to the Clinical Trials Project Reference Group by EY, 2016, *Scoping and analysis of recruitment and retention in Australian clinical trials, Final report*, June 2016, accessed at: http://www.health.gov.au/internet/main/publishing.nsf/Content/Clinical-Trials

[22] EY, 2016, *Scoping and analysis of recruitment and retention in Australian clinical trials*, report to the Department of Health, accessed at http://www.health.gov.au/internet/main/publishing.nsf/Content/EE207D978A44E4B8CA257FA90081B212/$File/EY%20Final%20Report%20-%20Recruitment%20and%20retention%20in%20Australian%20clinical%20trials%2030%20June%202016.pdf

Figure 3.4: Barriers to clinical trials: stakeholder perspectives

As a result of these multiple barriers, few patients are enrolled in clinical trials. The *Cancer Action Plan* in Victoria suggests the number of patients enrolled in cancer clinical trials is possibly seven per cent in Victoria. Similarly, stakeholder interviews estimated the proportion of patients enrolled was likely to be less than 10 per cent, while the survey of people living with blood cancer found that less than one in five patients reported participating in a clinical trial.

The survey of people living with blood cancer (See Appendix B) indicated that the most common reason as to why people with blood cancer do not participate in trials is because it is not suggested by their specialist (Figure 3.5). For example, 68 per cent of people who did not participate in a clinical trial indicated it was because their specialist did not suggest it.

Figure 3.5: Reason for non-participation in a clinical trial

Source: Survey of People Living with Blood Cancer, see Appendix B.

Stakeholder consultations indicated the reasons for this could be several, including:

- A lack of time for specialists to devote to enrolling patients in a trial in addition to clinic workload
- Lack of hospital incentives for trials
- General haematologists or oncologists not wanting to 'lose patients'
- Lack of knowledge by some specialists
- Logistical and infrastructure-related challenges in identifying trials and patients.

One in five patients indicated they wanted to enroll and looked for a trial with their specialist, but there either weren't any trials available or they failed to meet eligibility criteria. A small percentage (2 per cent) reported concern for the riskiness of trials compared with standard treatments or required too much travel.

Challenges to fundamental and translational research

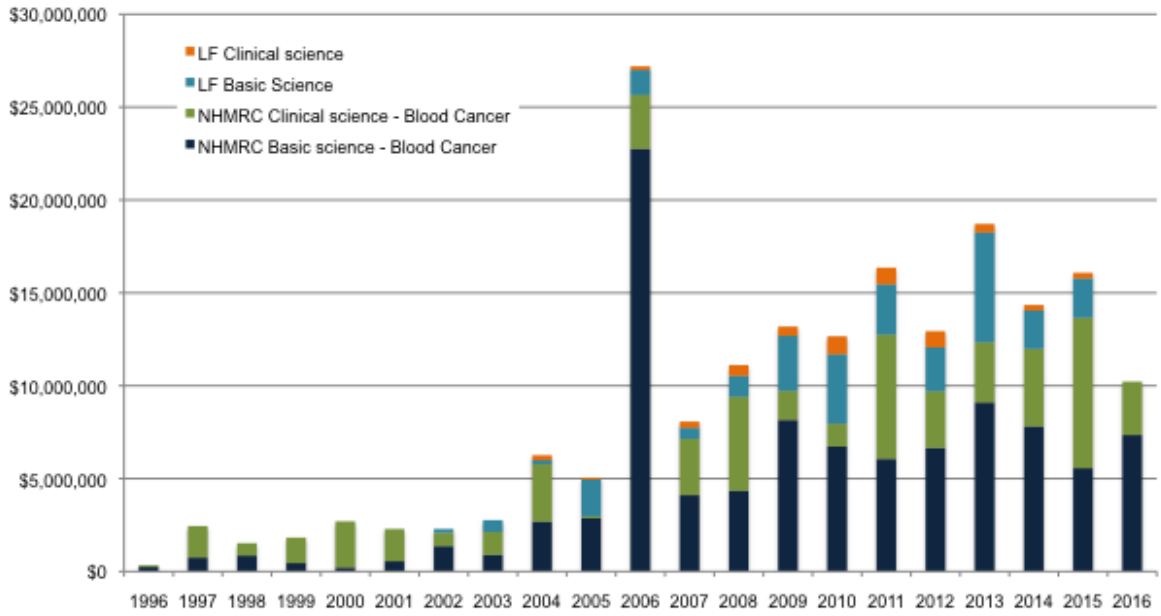
The AIHW's 2016 Australian Burden of Disease Study[23] found that cancer accounted for the highest proportion (19 per cent) of Australia's current burden of disease. Of this, blood cancers account for 10 per cent of the total disease burden. This accords with the 2005 cost of cancer which found that blood cancers accounted for nine per cent of the burden of disease from cancers, and nine per cent the total cost of cancer including economic costs.[24] This implies that blood cancers account for approximately two per cent of the total burden of disease, which is comparable to lung cancer (three per cent), colorectal cancer (two per cent) and breast cancer (two per cent).

Historically, however, NHMRC funding for blood cancer basic and clinical research has averaged 1.5 per cent of total NHMRC funding. Within Australia, the NHMRC funding for haematological tumours and haematology across basic and clinical science averaged

[23] AIHW, 2016, *Australian Burden of Disease Study: impact and causes of illness and death in Australia 2011*, https://www.aihw.gov.au/reports/burden-of-disease/abds-impact-and-causes-of-illness-death-2011/data, Table S13.5
[24] Access Economics, 2005, *The Cost of Cancer in NSW*, p vii

$8.7 million per annum over the 2000-2016 period (Figure 3.6). This has been topped up by other philanthropic donors, including the Leukaemia Foundation, which has provided an average of $3.5 million per annum for research since 2002.

Figure 3.6: NHMRC and Leukaemia Foundation funding for blood cancer (1996-2016)



Source: Analysis of NHMRC funding for haematology and haematological tumours and Leukaemia Foundation research funding.

While these investments have been important, and indeed provided the initial research funding for the development of venetoclax, the total funding for research in Australia is small compared to overseas investments and suggests research has been underfunded relative to the disease burden on average for nearly 20 years. For example, in the US, the Leukemia & Lymphoma Society (LLS) announced US$42 million in funding across 80 disease research teams in November 2018 alone.[25] in addition to US$1.5 billion in National Institutes of Health (NIH) funding for blood cancers in 2018 with a further US$1.4 billion planned for 2019.[26] Similarly, in the UK, Bloodwise UK allocated £10.9 million in 2018,[27] in addition to funding from Cancer Research UK, NHS England and funding for access to new medicines through the Cancer Drug Fund.

Stakeholders indicated the competition for funding for fundamental research, like investigator-led trials, created barriers to the continued understanding of the underlying genetic drivers of blood cancers, and that fundamental research was potentially undervalued in the current funding environment. For example, a number of stakeholders expressed concern that there had now been "such a dramatic right shift to translation that we are truncating that pipeline [of fundamental research that will deliver further gains]." Figure 3.7 summarises key stakeholder views on the need for continued investment in fundamental research alongside clinical trials.

[25] Chapman, M. 2018, 'Leukemia & Lymphoma Society Funding Next Wave of Blood Cancer', *Lymphoma News Today*, accessed at: Researchhttps://lymphomanewstoday.com/2018/11/28/leukemia-lymphoma-society-funding-next-wave-blood-cancer-research/
[26] NIH, 2018, *Estimates of Funding for Various Research, Condition, and Disease Categories* (RCDC), Hematology, 18 May, accessed at: https://report.nih.gov/categorical_spending.aspx
[27] Bloodwise, 2018, *Annual Report 2017/18*, p 43.

Figure 3.7: Stakeholder perspectives on fundamental research trends and implications for Zero by 2035

Indeed, comparing the average of NHMRC funding for basic and clinical science from 2011-2016 to funding from 2006-2010 indicates these anecdotes are true. To explain: the total annual funding for haematology and haematologial tumour research has stayed steady at around $12 million per annum across the two periods. Total funding per annum from 2006-2010 averaged $12.0 million per annum and total funding per annum from 2011-2016 averaged $11.8 million per annum. However, fundamental research's share of this has been in decline. The percentage of funding for basic science declined from an average of 72 per cent of total funding over the 2006-2010 period to 61 per cent in the 2011-2016 period.[28]

3.3 Inequity in Access and Experience

Stakeholder consultations, the literature review, survival outcome data by State and the survey of people living with blood cancer indicate that there are variations in treatment and care for Australians nationally. These inconsistencies in practice can translate into variable survival outcomes for people depending on where they live, their wealth, and who provides their treatment.

The main drivers for inequity in access and experience for people living with blood cancer based on consultations and the literature review are:

- Inconsistencies in workforce expertise and skills for the diagnosis and treatment of blood cancers
- The lack of public subsidy for novel treatments through the Pharmaceutical Benefits Scheme and Medicare Benefits Scheme, which can cause inequities of access
- Variation in service delivery nationally
- Inconsistent referrals to clinical trials

[28] Analysis of NHMRC grants from 1996 to 2016 for haematology and haemtological tumours fields of research.

- Inconsistent referrals and access to supportive care, broadly defined.

These issues are considered in turn.

Inconsistencies in workforce expertise and skills for the diagnosis and treatment of blood cancers

Issues in workforce education and skills availability exist across care settings from primary care through to tertiary hospitals.

Perhaps one of the most commonly identified issues was a lack of understanding of blood cancers by the GP. It was consistently reported by stakeholders, patients and in the literature that GPs can be slow to identify blood cancers compared to other conditions, particularly for chronic or indolent cancers where the symptoms at presentation could indicate a number of potential diseases.

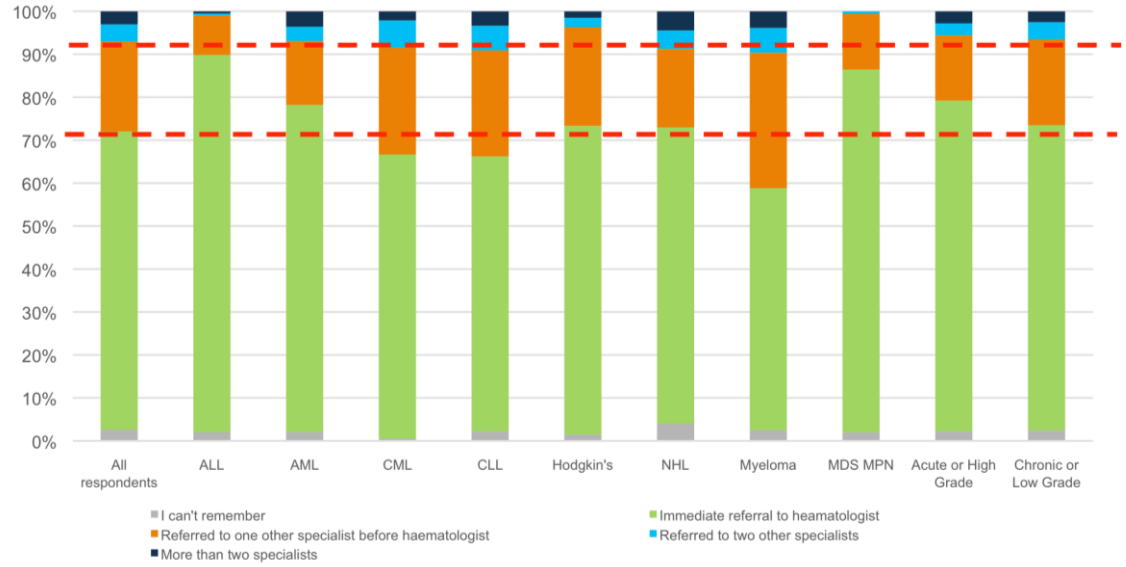
The lack of GP understanding of blood cancers was reported to lead to inefficiencies in health service delivery, through misdiagnosis and referrals to the wrong specialist, and delays to treatment:

> *"GPs are not well equipped to identify blood cancers, they may see one to two patients over the course of their career. It can delay diagnosis."*
>
> *— Researcher*

> *"Sometimes there is anxiety to get the result. They need a nurse supporting them to say, "Take the time to get the exact diagnosis". If you embark on the right diagnosis it changes the outcome… misdiagnosis is an issue. Are they doing the right tests?"*
>
> *— Oncology nurse*

For example, survey results show that while most people with blood cancer were immediately referred to a haematologist, a significant majority (30 per cent) were referred to one or more other specialists before ultimately being referred to a haematologist (Figure 3.8). Nearly one in 10 people were referred to two or more other specialists before being referred to a haematologist. The survey results also indicate that there was a higher likelihood of referral to other specialists ahead of a haematologist for chronic or 'low grade' blood cancer sub-types compared to acute sub-types.

Figure 3.8: Number of specialists seen before the haematologist



Source: Survey of People Living with Blood Cancer, see Appendix B. The red lines show key thresholds for the average across all blood cancers as discussed in the text and allow for variation by sub-types to the average to be more easily observed.

These inappropriate referrals are an expensive inefficiency in the healthcare system. If approximately 15,000 new patients are expected to be diagnosed each year (and growing), and 20 per cent are referred to one other specialist inappropriately, and just under 10 per cent referred to two or more, then assuming a minimum cost of a specialist visit is $130 to the government[29] and $64 to patients on average,[30] this costs the community just over $1.1 million every year in health system waste, with government bearing roughly 67 per cent of that cost, and households bearing the other 33 per cent.

More importantly, however, the lack of skills to diagnose a blood cancer may contribute to the sometimes-substantial delays between presentation to the GP with symptoms and referral to the haematologist. Survey results suggest some patients are not getting referred to a haematologist fast enough, with nearly one in five reporting more than two months between their presentation to the GP and the first appointment with a haematologist (Figure 3.9).

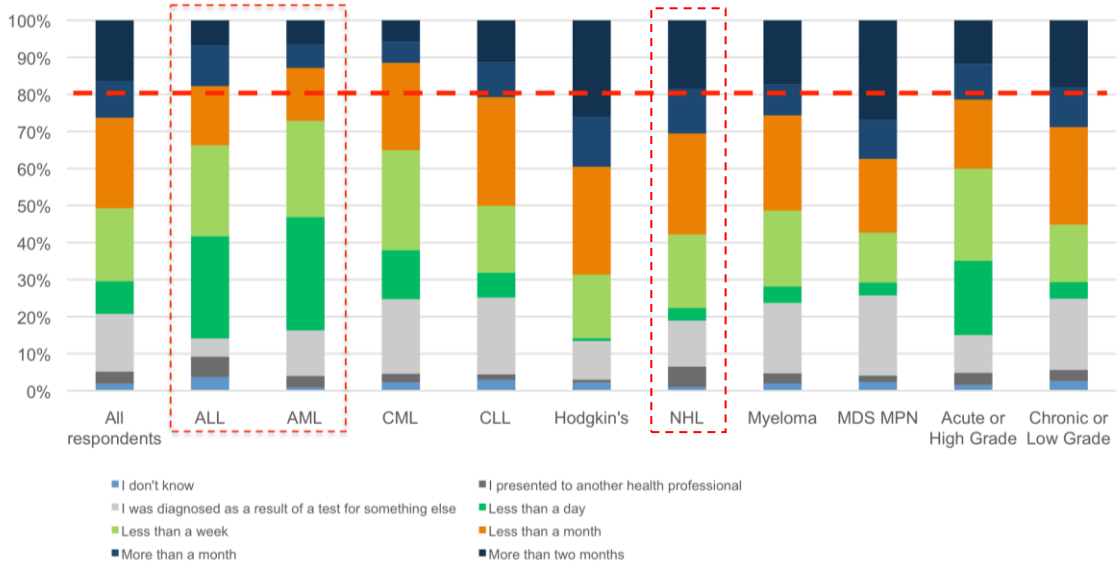
Potentially more concerning, the optimal care pathway for AML provides guidance that patients should be seen by haematologist within 24 hours and survey results suggest less than half of patients met this recommendation (See Appendix A, Section A.1). The optimal care pathway for Non-Hodgkin lymphoma also recommends referral to a

[29] The MBS item fee would vary depending on the specialist to whom the patient was referred. The estimated cost of $153 is taken from MBS item number 110 in group A4, Consultant Physician Attendances To Which No Other Item Applies; a benefit of 85% was applied assuming it was a specialist service. In geriatric medicine (category A28), however, an initial consultation lasting 30 minutes would attract an MBS item fee of $287, for example. Given the complexity of blood cancers it is highly likely that the visits would take longer and be charged at a higher rate, and therefore this is considered a conservative estimate of cost. See MBS Online published 1 December 2018 accessed at: http://www.mbsonline.gov.au/internet/mbsonline/publishing.nsf/Content/04AA67013FD6E6C0CA25834700038565/$File/201812-MBS.pdf.

[30] The AIHW reported in 2018 the median out of pocket charge for specialist consultations to patients in 2016-17 to be $64 per visit. See AHIW 2018, Patients' out-of-pocket spending on Medicare services 2016–17 accessed at: https://www.aihw.gov.au/reports/primary-health-care/mhc-patient-out-pocket-spending-medicare-2016-17/contents/summary AIHW, 2018, Patients' out-of-pocket spending on Medicare services, 2016–17 accessed at: https://www.aihw.gov.au/getmedia/f6dfa5f0-1249-4b1e-974a-047795d08223/aihw-mhc-hpf-35-patients-out-of-pocket-spending-Aug-2018.pdf.aspx?inline=true and Choice, 2018, *How to avoid health care out-of-pocket costs*, accessed at: https://www.choice.com.au/money/insurance/health/articles/how-to-avoid-out-of-pocket-health-expenses.

haematologist within two days for people with symptoms, and within four to six weeks for all other patients (See Appendix A).

Figure 3.9: Time between presentation to the GP and first appointment with a haematologist



Source: Survey of People Living with Blood Cancer, see Appendix B. The red lines show key thresholds for the average across all blood cancers as discussed in the text and allow for variation by sub-types to the average to be more easily observed.

Other workforce concerns related to the currency and supply of specialist skills for the effective treatment of blood cancers, including in particular that:

- General oncologists may lack expertise in blood cancer sub-types, which may result in the wrong diagnosis and treatment of patients
- There is an existing and growing shortage of bioinformaticians, medical oncologists and haematological pathologists projected.

The first factor, the expertise of some clinicians in blood cancers sub-types, was attributed by stakeholders in part to the rapid pace of innovation and the infrequency with which some specialists may see patients with relevant disease characteristics. For example, the challenges of sub-type specialisation were noted by multiple health professionals:

> *"What appears to look like one kind of lymphoma can turn out to be very different… Small differences in the diagnosis of the disease can make a big difference in the treatment plan. I have to tell people who it's better to wait to get the diagnosis right."*
>
> *— Oncology Nurse*

> *"We will do blind reviews – one person with expertise [in one sub-type of blood cancer] and the other person with expertise [in another sub-type of blood cancer]. And we both missed things. If you don't have disease-specific expertise you don't have anything. You don't know what you're looking for. You have to know what you're looking for."*
>
> *— Researcher*

These sentiments were echoed by other stakeholders, and are not unique to Australia; indeed, in the UK the National Health Service in its recent guidance on *Improving Outcomes for Haematological Cancers* has recommended that all patients with a blood

cancer should be 'managed by a multidisciplinary team serving populations of 500,000 or more', and that:

> *"In order to reduce errors, every diagnosis of possible haematological malignancy should be reviewed by specialists in the diagnosis of haematological malignancy. Results of the test should be integrated and interpreted by experts who work with local haemato-oncology MDTs and provide a specialised service at a network level."*[31]

In addition, a 2009 study into the medical oncologist workforce by the Medical Oncologists Group of Australia (MOGA) found there were risks of an emerging shortage of key skills to support cancer care. In the context of increasing incidence and prevalence in blood cancers this, too, could adversely impact on the reduction in mortality and morbidity from blood cancer, with less time for clinicians to support clinical trial activity and potentially impacts to patient care.[32] A persistent shortage of bioinformaticians and computational biologists was also reported, which may impact on the ability for Australia to successfully transition to more systematic genomic and genetic testing to inform diagnosis and treatment.

The availability of public subsidy for therapies influence treatment plans

Another factor contributing to inequity in access to treatment and care is the lack of public subsidy for some therapies, including not only drug therapies but also tests to support diagnosis and treatment selection.

There was a clear consensus that if a drug therapy was not PBS listed, it was likely that this would not typically be considered as a treatment option, and specialists would not discuss these treatments with patients (Figure 3.10).

Figure 3.10: Stakeholder perspectives on public subsidy access challenges

[31] National Institute for Clinical Excellence, National Health Service, 2016, *Guidance on Cancer Services, Improving Outcomes in Haematological Cancers*, The Manual, accessed at: https://www.nice.org.uk/guidance/ng47/evidence, p 7.
[32] Blinman PL, Grimison P, Barton MB, Crossing S, et al, 2012, 'The shortage of medical oncologists: the Australian Medical Oncologist Workforce Study', *Med J Aust* 2012; 196 (1): 58-61. || doi: 10.5694/mja11.10363.

More than ever, patients are more aware about treatments that may be in use overseas. In the survey of people living with blood cancer, Google was the third most frequently cited source of information behind their haematologist (#1) and the Leukaemia Foundation (#2). In addition, patients reported traveling overseas to participate in international conferences, to hear about evidence and emerging treatment options. The trend for patients accessing information, and potentially mis-information, is increasing.

This paradigm shift to more empowered consumers is changing the way expectations for health services. For example, in its recent White Paper *Shifting Gears: Consumers Transforming Health* released in November 2018, the Consumer Health Forum (CHF) underlined the new expectation for consumer centred care:

> *"Consumers will assume a 'new power'. They will command convenience and access to high value, modern, personalised services that meet their needs. They will expect to have choice and control over the services they pay for. They will be activated more than ever with access to burgeoning information and innovations that will assist them to say well, self-manage and access quality care tailored to them."*
>
> — *Consumer Health Forum, 2018*

This sentiment was echoed by the Productivity Commission's *Shifting the Dial: 5-Year Productivity Review* which called for the re-configuration of the health system around the principles of patient-centred care, and the OECD which called for health service reforms that 'deliver improvement that matter to patients and their changing care needs.

Combined, this is increasing pressure on governments to address potential gaps in access to services compared to international comparator markets.

Of course, one must exercise caution when comparing access across health systems. In the US, the FDA approves medicines for use and this is not equivalent to the provision of a public subsidy as occurs in Australia; purchasing decisions are made by health provider groups and highly dependent on means. Interviews with international experts in the US consistently indicated that financial toxicity is a serious concern for people in the US, with one stakeholder indicating 'patients are cutting tablets, basically not compliant because of the cost'. Similarly, the National Cancer Institute (NCI) SEER Program data (Surveillance, Epidemiology and End Results Program) indicate substantial differences by race and geography in the US depending on means.[33] In particular, one government stakeholder pointed out that: 'When you see the triple, quadruple combination therapies [of high cost medicines], I mean, no government can afford that'.

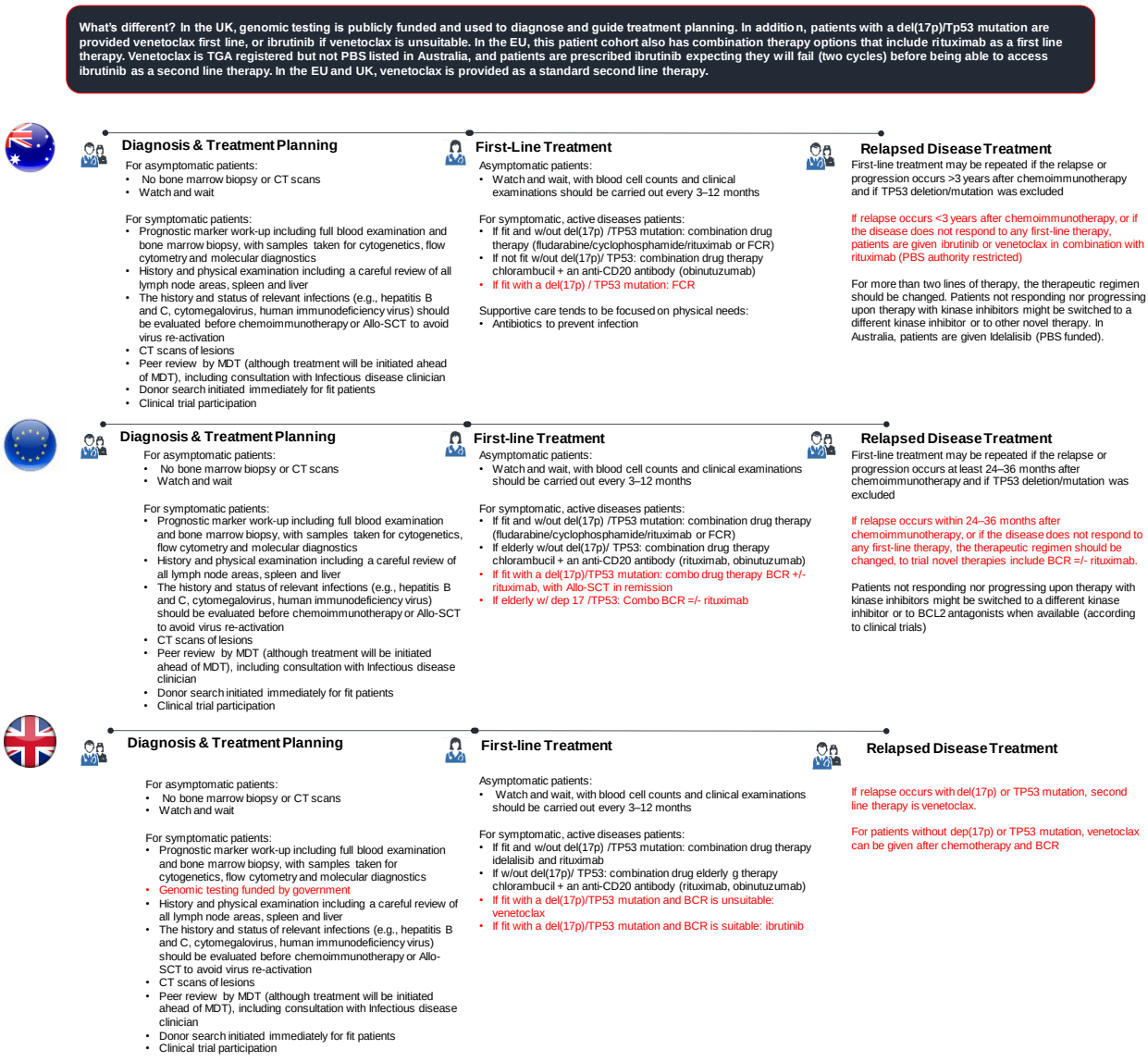
Nevertheless, for each blood cancer sub-type, with the exception of CML, a comparison of clinical guidelines in international comparator markets — The National Institute for Clinical Excellence (NICE) in the UK and European Society for Medical Oncology (ESMO) in the EU — with Australian subsidised therapies identified differences in both first-line and second-line treatment options.

For example, as shown in Appendix A and in Figure 3.11 below, in Australia, people diagnosed with CLL with del(17p)/TP53 mutations must fail at least two rounds of chemotherapy before they can access ibrutinib with a public subsidy. Alternatively,

[33] See data at NCI SEER Program accessed at: https://seer.cancer.gov.

patients can seek a clinical trial or privately fund the therapy. In Australia today clinicians prescribe the chemotherapy, at a cost of approximately $3,350 per cycle[34], or nearly $7,000 in total, expecting it will fail and then switching patients to ibrutinib. By contrast, in the UK and EU, ibrutinib is first-line therapy for patients with del(17p)/TP53 mutations. Moreover, in the UK, venetoclax is first line therapy for del(17p)/TP53 mutations where other drug therapies are not appropriate. Venetoclax is also available in the UK for relapsed and refractory disease, and combination therapies are recommended for second line therapies in the EU.

Figure 3.11: International Benchmarking – Chronic Lymphocytic Leukaemia



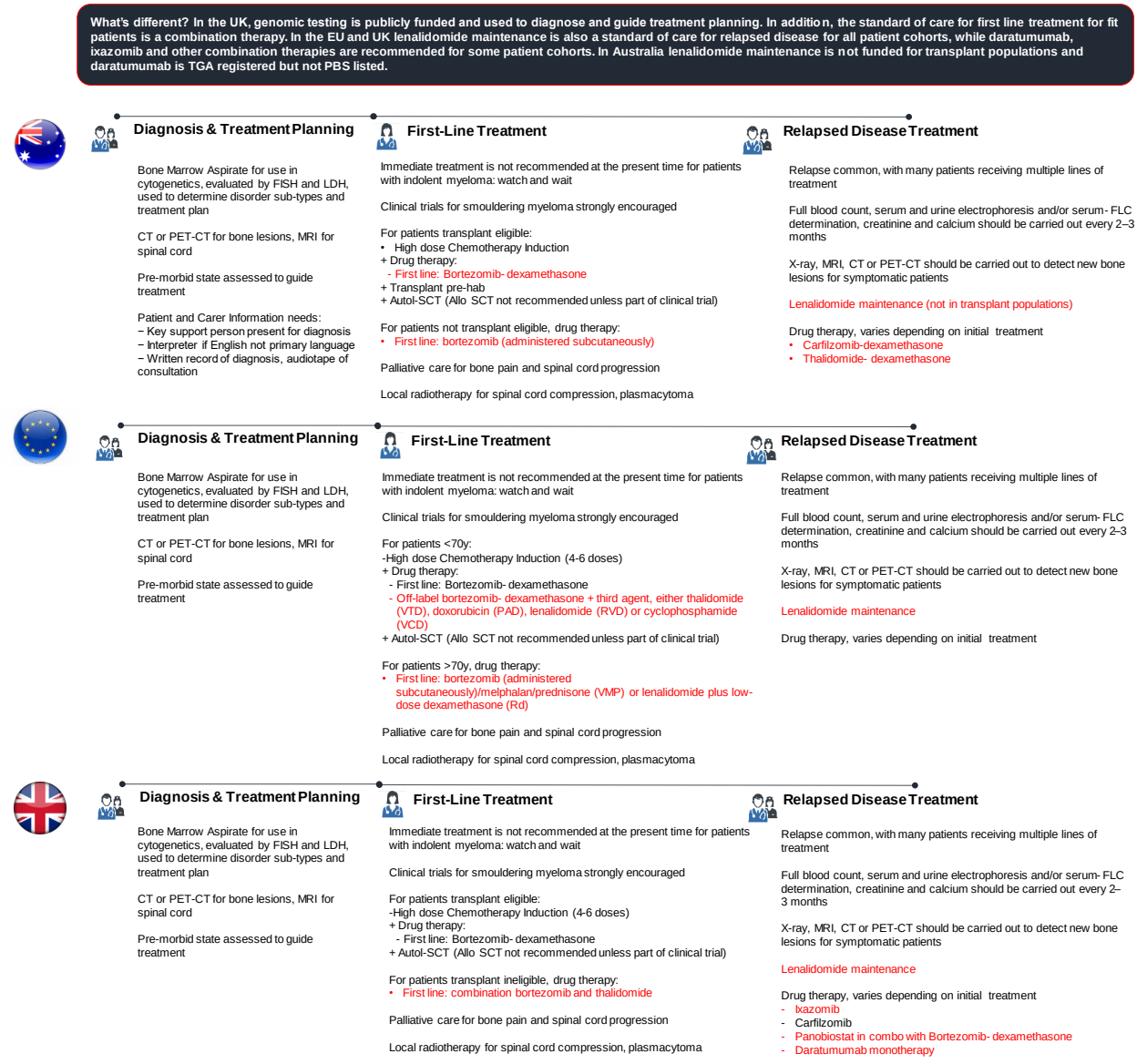
Sources: National Institute for Health and Care Excellence, 2018, First line treatment and treatment for relapsed or refractory disease; ESMO Clinical Guidelines for CLL, accessed 8 Sept at https://watermark.silverchair.com/; PBAC, 2018, PBAC Meeting Positive Recommendations, November accessed at: www.pbs.gov.au, eviQ, and consultations with clinicians in Australia regarding current standards of care as part of national stakeholder consultations. Draft Care pathways were also reviewed in collaboration with clinicians as part of the consultation process.

Similar issues exist for other blood cancer sub-types as well. For example, Figure 3.12 shows therapies for myeloma that are standard in the UK and EU which are not

[34] See eviQ, 2018, Chronic Lymphocytic Leukaemia FCR (fluarabine, CYCLOPHOSPHamide rituximab), ID 496 v.5, accessed at eviq.org.au

available in Australia. At the time of writing, patients in the UK and EU are delivered bortezomib in combination with thalidomide or lenalidomide, which has been shown to improve survival outcomes.

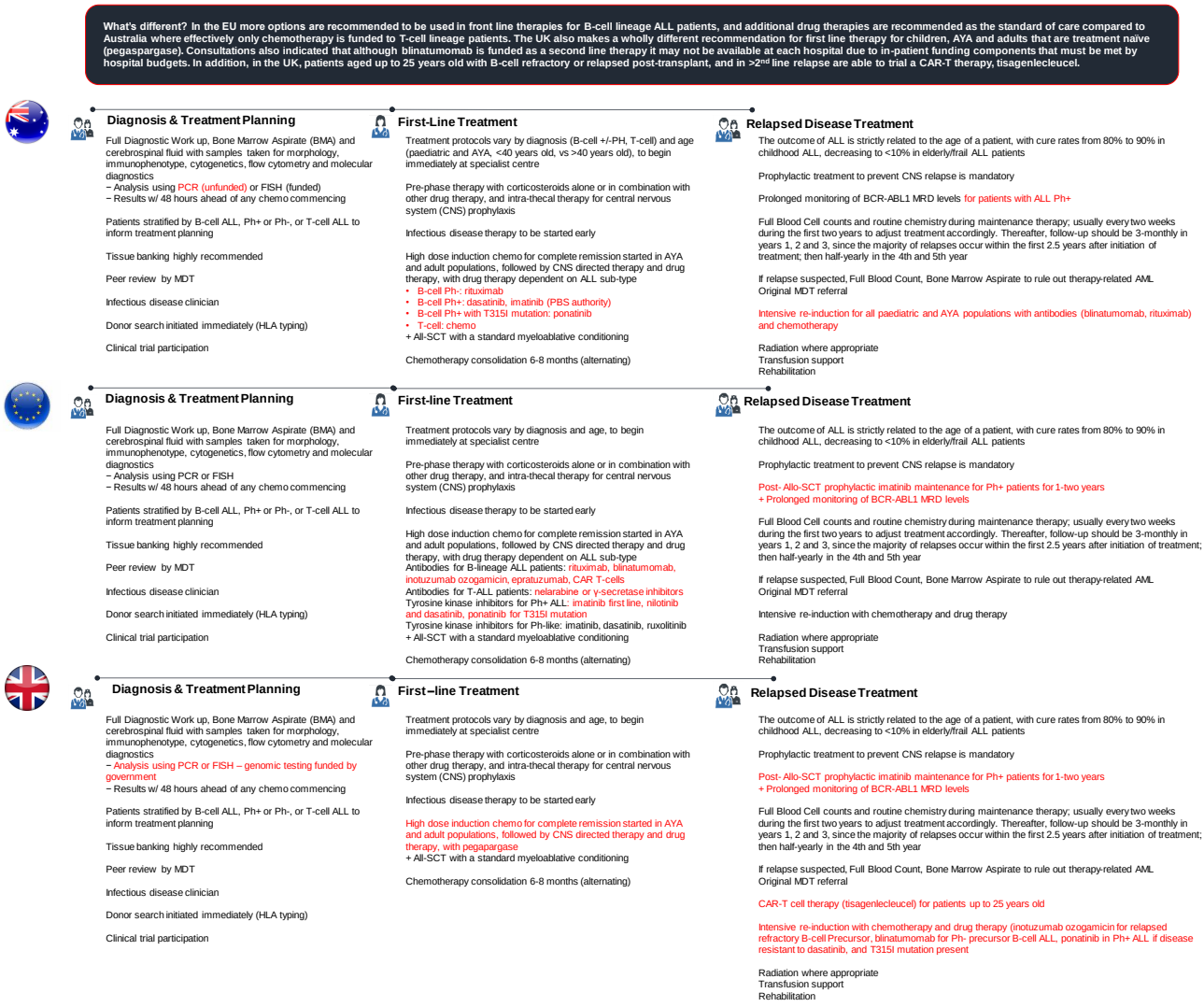
Figure 3.12: International Benchmarking – Myeloma



Sources: Clinical Guidelines Myeloma Australia; National Institute for Health and Care Excellence, 2018, First line treatment and treatment for relapsed or refractory disease; ESMO Clinical Guidelines for Myeloma, accessed 8 Sept at https://watermark.silverchair.com/; eviQ guidelines for Myeloma. Draft Care pathways were also reviewed in collaboration with clinicians as part of the consultation process.

Differences between Australian and international approaches to treatment are also evidence in ALL (Figure 3.13). Compared to recommended standards of care by ESMO in the EU and NICE in the UK, fewer drug therapies are PBS listed in Australia putting many of these options out of reach for most patients.

Figure 3.13: International Benchmarking – Acute Lymphoblastic Leukaemia



Sources: National Institute for Health and Care Excellence, 2018, First line treatment and treatment for relapsed or refractory disease: ALL; ESMO Clinical Guidelines for ALL, accessed 8 Sept at https://watermark.silverchair.com/; eviQ guidelines for ALL. Draft Care pathways were also reviewed in collaboration with clinicians as part of the consultation process.

As shown in Appendix A, at the time of writing[35] differences could be seen across effectively every blood cancer sub-type.

Over time, these issues tend to be resolved. But where research intensity is high, the risk for potential differences increases. But as noted by one government stakeholder, however, it has been increasingly recognised that 'patients afflicted by a malignancy face greater urgency in treatment than compared with patients with high blood pressure, where time and the risk of mortality is not such a significant issue'. Moreover, in the context of shifting consumer expectations for the health care system, this creates new challenges for governments.

Like cancer, the issues underlying these differences are complex. Oftentimes 'access' is discussed as if it is one single issue, when in fact there are a range of challenges to evidence development and public funding (Figure 3.14) and requires a range of policy responses to meet the complexity of the challenge.

[35] December 2018

Figure 3.14: Unpacking complex issues in drug therapy access to support consumer and community engagement with government

Access consideration	Therapy in use for other indications but very little evidence (Pre-clinical or Phase I) for blood cancer indication	Therapy approved and/or in use for other indications or overseas for blood cancer indication, but limited evidence (Phase II)	Novel therapy is standard of care overseas but no submission to Australian market due to market failures and/or does not meet Australian cost-effectiveness thresholds (Phase II or Phase III data)	Combination therapies are standard of care overseas but does not meet Australian cost-effectiveness thresholds and/or no sponsor submission due to market failures or submission risks (Phase II or Phase III data)
Current state-of-play for Australian patients	Access dependent on: 1) Pharma opening a clinical trial site, or 2) Funding for investigator led trial While Australian research quality consistently cited, pharma not always willing to bring trials to Australia and funding for investigator-led trials limited - Complicated and long lead times for ethics and governance - Inconsistent testing, siloed data slows patient recruitment - Contributes to cost Safety issues limit options for 'tele-trial' innovations	Where market incentives are inadequate to develop evidence and/or seek listing, clinicians and/or patient organisations must prepare submission. But this relies on access to data, so patients can be caught in catch-22. No formal mechanisms for capturing real world data (e.g., of off-label use) and potentially heroic 'gladiator' type model assumptions for clinicians to champion products through regulatory processes. If medicine/service not listed, cost is generally unobtainable for most Australians. This creates risk of a two-tiered system where patients with means access therapies in Australia or by travelling overseas and other patients do not.	Where market incentives are inadequate to develop evidence and/or seek listing, clinicians and/or patient organisations must prepare submission. But this relies on access to data, so patients can be caught in catch-22. No formal mechanisms for capturing real world data (e.g., of off-label use) and potentially heroic 'gladiator' type model assumptions for clinicians to champion products through regulatory processes. If medicine/service not listed, cost is generally unobtainable for most Australians. This creates risk of a two-tiered system where patients with means access therapies in Australia or by travelling overseas and other patients do not.	Where market incentives are inadequate to develop evidence and/or seek listing, clinicians and/or patient organisations must prepare submission. If medicine/service not listed, cost is generally unobtainable for most Australians. This creates risk of a two-tiered system where patients with means access therapies in Australia or by travelling overseas and other patients do not. Low level of understanding among patients and community regarding benefit cost trade-offs being made by government.
Examples	Venetoclax for CML in blast crisis; currently no therapy for these patients. RAH sought participation in trial running at MD Anderson but pharma reluctant to open site with only single patient likely to present at RAH over year	Off-label medicines & compassionate access • Venetoclax for Ph+ALL, AML • TKIs for ALL(dasatinib and ponatinib just listed at Nov meeting after long delay) • CAR-T for AML • PD-1 checkpoint inhibitors for AML	Off-label medicines & compassionate access • Ibrutinib for 1st line CLL, Waldenstrom's • Venetoclax for add'l CLL indications • Daratumumab for multiple myeloma • Blinotumumab 1st line for ALL	Off-label medicines & compassionate access Combination therapies for multiple myeloma (lenolidomide, daratumumab, carfilzomib), leukaemias, lymphomas
Government & clinician concerns	• Patient safety • Need for a clear signal of benefit (e.g., MRD outcomes, safety in at least 5 patients)	• Does not meet PBS/MBS evidence requirements • Equity concerns • Patient safety • How to advance science and not pursue 'scattergun' approach	• Equity concerns • PBAC/MSAC are submission driven • May exceed PBS cost-effectiveness thresholds • Co-dependent diagnostic challenges • Evidence for cellular therapies as services • Risk of high costs, particularly for targeted therapies which patients must take for the rest of their lives	• Risk of astoundingly high costs, particularly for targeted therapies which patients must take for the rest of their lives, which exceed PBS cost-effectiveness thresholds • Co-dependent diagnostic challenges • Evidence for cellular therapies as services • Equity concerns • PBAC/MSAC are submission driven • Challenges when multiple companies involved

As can be seen in the Figure, issues include:

- The maturity and quality of the evidence
- Market incentives for research and evidence development
- Market incentives for registration (with the TGA) and listing (on the PBS and MBS), with pharmaceutical industry considerations for global price benchmarks that influence applications for first vs subsequent lines of therapy
- Pressure on public hospitals budgets
- Pressure on broader Federal budget
- High costs of therapies, including in particular combinations of high cost therapies.

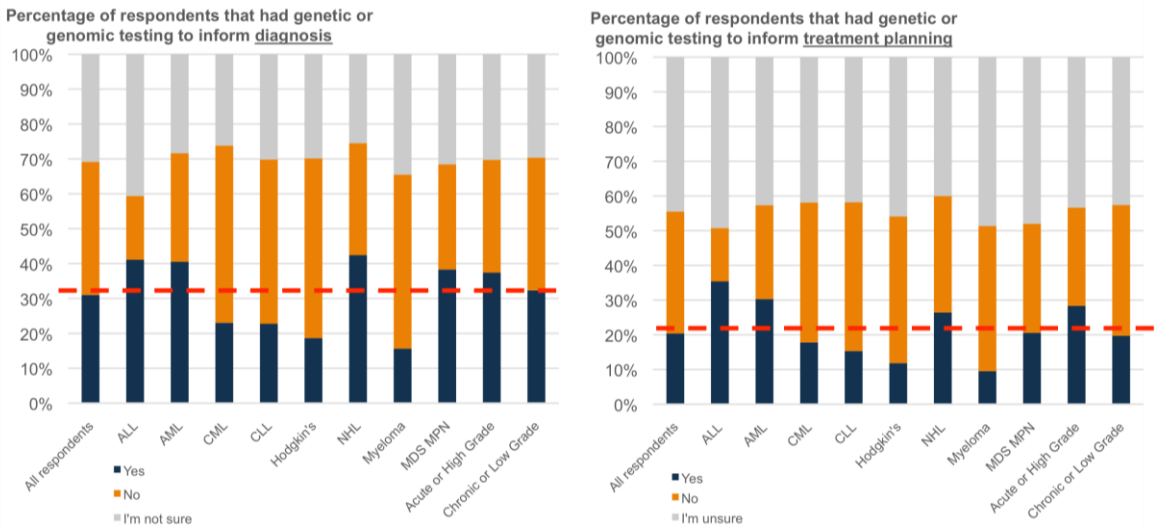
As patient populations fragment to a greater and greater extent there are increasing risks that commercial incentives to navigate the regulatory and funding system also attenuate. Australia's regulatory system, combined with its small market size, may contribute to delays by industry in submissions to the TGA and PBS. For example in the Senate Inquiry into *Availability of new, innovative and specialist cancer drugs in Australia*, the Department of Health reported that between 2009-2014 industry submitted cancer medicines to the TGA on average 38 weeks after submission to FDA and EMA.[36] Unlike applications for listing on the PBS, which can accept clinician or patient led submissions, only drug sponsors are permitted to lodge an application for a new indication with the TGA. The Medical Oncology Group of Australia (MOGA) also reported that there is inadequate coverage of new indications that are outside TGA approved indications, despite the availability of evidence to support new indication.[37]

Critically, the issue is not limited only to drug therapies. A number of genetic, genomic and other tests are not funded and this likely contributes to low rates of take up compared to what might otherwise be the case (See Appendix A for clinically important but unfunded tests by sub-type). As a consequence, Australia is behind its international peers in the use of genetic and genomic testing to guide treatment. Consistent with stakeholder consultations, the survey of people living with blood cancer indicated that a genetic or genomic test was used to confirm a diagnosis in only a third of patients and only one in five patients were confident a test had been used to inform treatment selection (Figure 3.15). Testing for chronic conditions was lower than for acute sub-types.

[36] Senate Community Affairs References Committee, 2015, Availability of new, innovative and specialist cancer drugs in Australia, Commonwealth of Australia 2015, p 17 accessed at: https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs/Report

[37] Ibid, p 21

Figure 3.15: Genetic and genomic testing is not routine



Source: Survey of People Living with Blood Cancer, see Appendix B. Note the red line shows the average across all blood cancer sub-types for people who indicated they had received a genetic or genomic test to inform their diagnosis and/or treatment plan.

For some sub-types, this may result in the wrong treatment, contributing to poorer health outcomes for patients and health system inefficiencies (see Case Study: Next Generation Sequencing in Chapter 4).

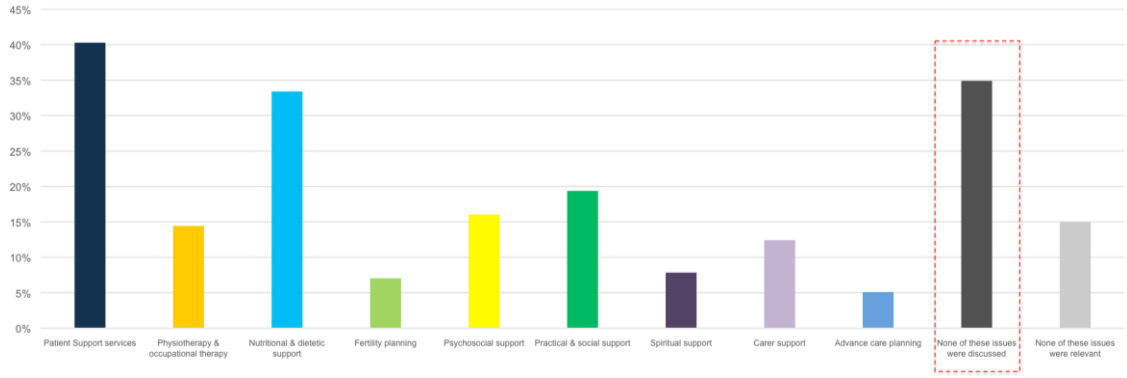
Without public subsidy, patients must either privately fund, seek compassionate access to a clinical trial, or forego the therapy. But accessing the therapy also depends on patients knowing about their treatment options. Consultations indicated that in most cases the option for the novel treatment was not discussed if it was not listed. But some patients with means are able to bridge the gap, raising concerns for equity of access. A recent survey of 68 medical oncologists by the National Oncology Alliance indicated that potentially 6,000 Australians are not able to afford the treatments they would recommend (across all cancers, or approximately four per cent of 2017 incidence of total cancer), and that 3,500 patients are privately funding access to cancer medicines (3 per cent of 2017 incidence). Data by cancer type were not provided.[38]

Inconsistent referrals to supportive care

Consistent with stakeholder consultations, discussions of supportive care were reported in the survey to be inconsistently and infrequently discussed. In the survey of people living with blood cancer, more than a third of respondents indicated that no supportive care was discussed at treatment planning (Figure 3.16).

[38] National Oncology Alliance, 2018, *Calls to make cancer drugs more affordable*, accessed at: https://nationaloncologyalliance.org.au/2018/08/14/calls-to-make-cancer-drugs-more-affordable/

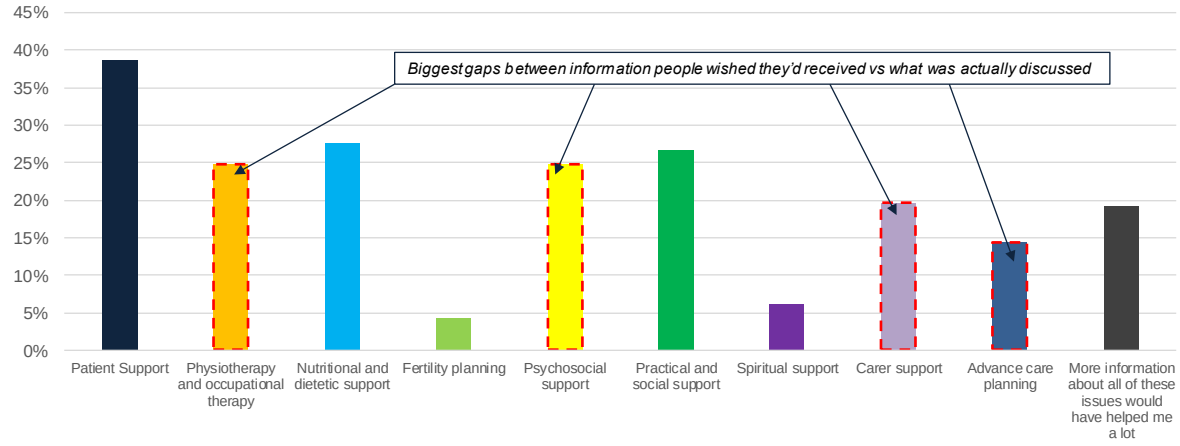
Figure 3.16: Percentage of patients reporting discussion of supportive care at treatment planning



Source: Survey of People Living with Blood Cancer, see Appendix B

The survey indicated that more consistent referrals to patient support services was important to people living with blood cancer. This is perhaps intuitive because more consistent referral to patient support can provide a useful gateway and partner for navigating the healthcare system and understanding options. While 40 per cent of survey respondents indicated patient support services had been discussed (Figure 3.16), it was also the most frequently cited issue that people living with blood cancer wished had been discussed at diagnosis and treatment planning, with nearly 40 per cent of people indicating they wish it had been discussed (Figure 3.17).

Figure 3.17: In hindsight, what information about supportive care do you wish you'd received more of?



Source: Survey of People Living with Blood Cancer, see Appendix B

The survey also indicated that more consistent discussion and referrals to physical support, including physiotherapy and occupational therapy as well as nutritional and dietetic support, psychosocial support, carer support and advanced care planning were the areas where there the biggest differences between what people wished had been discussed, compared to what was actually discussed at treatment. At least a quarter of respondents indicated they wished they had received more information regarding:

- Physiotherapy and occupational therapy
- Psychosocial support
- Nutritional and dietetic support
- Practical and social support.

The review of optimal care pathways, clinical guidelines and stakeholder consultations also indicated that for specialists, 'supportive care' tends to be narrowly defined to physical care, and within this the needs varied by sub-type, with infection management and rehabilitation the most commonly identified supportive care needs by clinicians. By contrast, the optimal care pathways developed by the Cancer Council for AML and Hodgkin/Diffuse Large B-Cell Lymphoma included a comprehensive definition of supportive care including thinking about a patient's:

- Information needs
- Physical care needs, defined to include physiotherapy and occupational therapy, nutritional and dietetic support and fertility planning
- Psychosocial support needs
- Practical support needs, including child care and in-home support, and financial planning support
- Spiritual care needs
- Advanced care planning.

While every person's needs are different and may change over time, both the survey and stakeholder consultations indicated the major gaps in supportive care are in access to rehabilitation and psychosocial supportive care (Figure 3.18).

Figure 3.18: Stakeholder perspectives on the gaps in supportive care

Both clinicians and patients alike indicated that more could be done to enable access to rehabilitation. Rehabilitation is important for managing fatigue and other co-morbidities or side-effects of treatment. For example:

- The most frequently reported symptom in cancer survivors is cancer-related fatigue, which is defined by the National Comprehensive Cancer Network as 'a

distressing persistent, subjective sense of physical, emotional and or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning.' The National Cancer Institute in the US estimated that fatigue occurs in up to 96 per cent of cancer survivors who have been treated for cancer.[39] Other studies indicate that at least 60 per cent of cancer patients experience fatigue.[40]

- A substantial body of emerging research has shown that patients have reduced cardiorespiratory fitness as a result of the direct toxic effects of anti-cancer treatment. This reduced cardiorespiratory fitness is associated with heightened symptoms, functional dependence and possibly an increased risk of cardiovascular morbidity and mortality.[41]

The major challenge identified is that rehabilitation programs have been historically developed for people recovering from surgery, such as hip or joint replacements, and cancer patients are too sick following treatment and so rejected from these programs. This is in spite of research showing that pre-habilitation before chemotherapy and surgery and rehabilitation after can substantially improve patient outcomes. For example, a 2014 study found that a 3-month program comprised of a one-hour program with a cancer exercise specialist three days per week for people living with blood cancer saw statistically significant improvements including:

- A 20 per cent increase in aerobic capacity (VO2 peak)
- A 7 per cent improvement in resting heart rate
- A 32 per cent improvement in mean fatigue levels.[42]

This is consistent with a study for leukaemia patients that found a 20-week specialised cancer rehabilitation program improved patient strength by (52 per cent vs 38 per cent before the intervention), aerobic capacity (51 per cent compared to 5 per cent before the program) and quality of life.[43] Similarly, a Roundtable Consensus Statement of the Benefits of Exercise for Cancer Patients in the US conducted a systematic review of the benefits of exercise for cancer patients, which found that two randomised controlled trials (RCT) and one post-intervention study found exercise for blood cancer patients that did not receive a transplant delivered significant improvements in aerobic fitness and fatigue. One RCT also found a positive impact on depression. For blood cancer patients that had received a transplant, exercise was found to be safe by more than six RCTs, improve aerobic fitness or halt a deterioration in fitness, and reduce fatigue.[44] The Roundtable made further recommendations based on the outcomes for the systematic literature review for a blood cancer-specific rehabilitation program.

Critically, low aerobic capacity and low levels of physical activity are associated with all-cause mortality across cancer populations, whereas exercise may be associated with reduced risk of recurrence and cancer death. For example, a 2014 systematic review and

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[39] National Cancer Institute, 2013, Information from PDQ for patients.
[40] Wagner LA, Cella D, 2004, 'Fatigue and cancer: causes, prevalence and treatment approaches', *Br J Cancer*, 2004;91:822-828
[41] Lakosko SG, Eves ND, Douglas PS, and Jones LW, 2012, 'Exercise rehabilitation in patients with cancer', *Nat Rev Clin Oncology*, 2012 Mar 6: 9(5): 288-296.
[42] Repka CP, Peterson BM, Brown JM, et al, 2014, 'Cancer type Does Not Affect Exercise Mediatied Improvements in Cardiorespiratory Function and Fatigue', *Journal of Integrative Cancer Therapies*, Volume 13 issue: 6, p 473-481.
[43] Durak E, Lilley P, Hackworth J, 1999, 'Physical and psychosocial responses to exercise in cancer patients: a two year follow up survey with prostate, leukemia, and general carcinoma', *JEP Online*.
[44] Schmitz KH, Courneya KS, Matthews C, et al, 2010, 'American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors', *Medicine & Science in Sports & Exercise*, July 2010: Volume 42 Issue 7, p1409-1426.

meta-analysis of cardiorespiratory fitness as a predictor of cancer mortality found that increased cardiorespiratory fitness was a strong predictor of decreased total cancer mortality risk. Improving cardiorespiratory fitness from a low level to an intermediate or high level of fitness was related with a statistically significant decrease in summary relative risk of total cancer mortality of 0.80 and 0.55, respectively.[45] This means that people who had an intermediate level of fitness were 20% less likely to die from cancer than people with a low level of fitness and people who had a high level of fitness were 45 per cent less likely to die from cancer. This corresponds with the age-based survival data available from the State Cancer Registries which show consistently across sub-types that more fit patients have higher survival rates than persons with lower levels of fitness.

The other very significant issue in care consistently identified through all stakeholder consultations was the more consistent discussion of psychosocial support. For example, data reported from a CART-Wheel Patient Reported Database for Waldenström's found that 12 per cent of patients experienced stress at same levels as people with PTSD.[46] This is consistent with research that has similarly found higher rates of depression among cancer patients.[47] A 2015 study found that more than 10 per cent of patients diagnosed with cancer experience depression and clinically significant levels of anxiety.[48] Other studies have reported the rate of depression in cancer patients to be three times higher than the general population[49]. Depression leads to a poorer quality of life, and compromises patient outcomes, with research showing that depression also contributes to higher rates of mortality in cancer. A 2009 meta-analysis found that minor or major depression increases mortality rates by up to 39 per cent, and that patients displaying even few depressive symptoms may have a 25 per cent increased risk of mortality.[50] Similarly, the impact of mood and mental wellbeing on cancer progression is considered important by clinicians and people living with blood cancer, with 70 per cent of oncologists in the US and 85 per cent of patients believing that mood affects the progression of cancer,[51] although a 2009 meta-analysis found that while depression can affect cancer morbidity it does not affect cancer progression.

Consultations indicated that for patients with chronic conditions where care is community based, the probability that people will 'fall through the cracks' is increased:

> *The supportive care needs are different by acute diseases – your AML, your ALL, your high-grade lymphomas. You might be sick, and the doctor gives you antibiotics, and 3-4 days later you're worse, so you go back. Order the blood test and that afternoon you're diagnosed. Then it's all guns blazing, and these patients are immediately into survivorship mode. There is often not a lot of time for psychosocial support [at first], but over time nurses and staff catch these patients by osmosis. For chronic patients it is different…CLL, CML, B-Cell lymphomas, follicular, indolent. They take medication daily, there is no pathway through the hospital, in and out, to be seen by doctors. There are no real ways to 'catch' these patients [for referral to psychosocial support].*
>
> – *Oncology Nurse*

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[45] Schmid D, and Leitzmann MF, 2015, *Cardiorespiratory fitness as a predictor of cancer mortality*

[46] Patient reported outcomes in CART-Wheel for Waldenström were reviewed and found 80 per cent concordance with clinician entered data.

[47] Couper, JW, Pollard AC, Clifton DA, 2013, 'Depression and Cancer', *Medical Journal of Australia*, 199 (6 Suppl):S13-S16.

[48] Smith H, 2015, 'Depression in cancer patients: Pathogenesis, implications and treatment (Review)', *Oncology Letters*, 2015 Apr; 9(4): 1509–1514.

[49] Linden W, Vodermaier A, Mackenzie R, Greig D. 'Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age'. *J Affect Disord*. 2012;141:343–351. doi: 10.1016/j.jad.2012.03.025.

[50] Satin JR, Linden W, Phillips MJ. 'Depression as a predictor of disease progression and mortality in cancer patients: a meta-analysis'. *Cancer*. 2009;115:5349–5361. doi: 10.1002/cncr.24561.

[51] Lemon J, Edelman S, Kidman AD. 'Perceptions of the "Mind-Cancer" Relationship Among the Public, Cancer Patients, and Oncologists'. *J Psychosoc Oncol*. 2004;21:43–58. doi: 10.1300/J077v21n04_03.

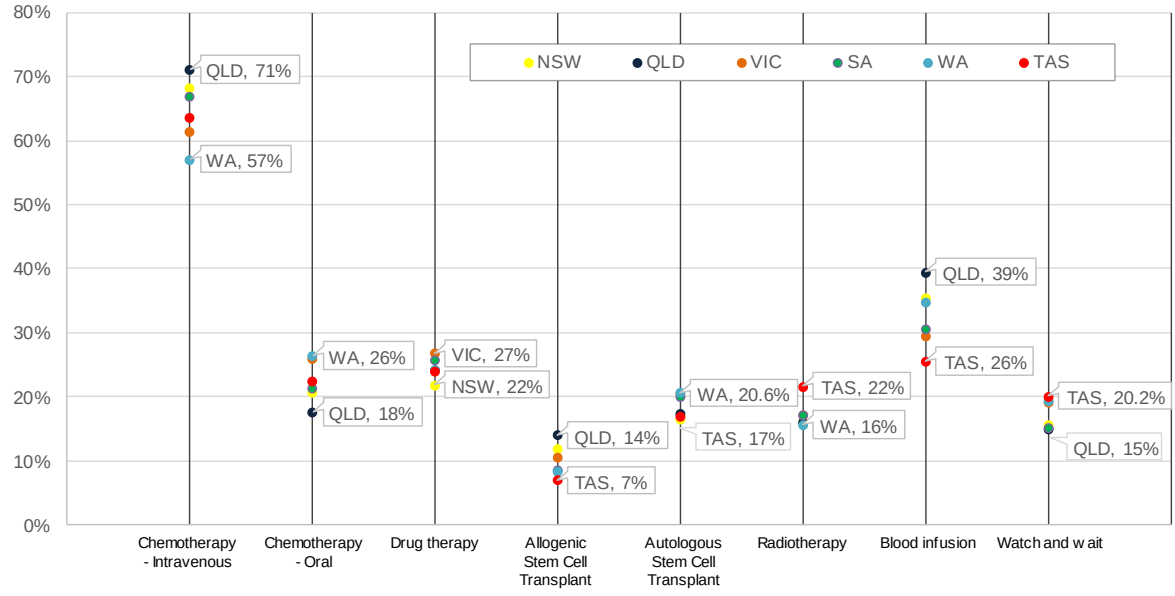
This is also reflected in the care pathways and clinical guidelines for these blood cancer sub-types: as one treating clinician noted there was not an automatic screening or referral to psychosocial support for patients on watch and wait, and this would be an improvement. The Leukaemia Foundation has similarly found in its research for the CLL My Way strategy that anxiety with 'watch and wait' treatment is very high among patients.

Variation in services and inconsistent referral to clinical trials nationally

Available literature and data, as well as stakeholder consultations and the survey of people living with blood cancer also indicated there are substantial variations in treatment and care depending on the State a patient lives in, whether they live in a metropolitan area or regional area and whether they are treated in a public or a private hospital setting (or both).

For example, consistent with stakeholder consultations, the survey showed variation in service delivery depending on where you happened to live. For example, people living in Queensland reported receiving intravenous chemotherapy more frequently compared to other jurisdictions, including NSW (68 per cent), Victoria (61 per cent), and Western Australia (57 per cent). Conversely, people living in WA and Victoria reported receiving oral chemotherapy more frequently. Victoria also prescribed drug therapy more frequently than other jurisdictions (27 per cent of respondents), with only 22 per cent of people in NSW reporting receiving drug therapy.

Figure 3.19: Variation in service delivery by State as reported by people living with blood cancer



Source: Survey of People Living with Blood Cancer, see Appendix B.

Some of this variation is likely due to clinician expertise and preferences, some due perhaps to the lack of clinical guidelines for some sub-types, and some due to variable reimbursement for different types of therapies at the hospital level. These results are consistent with the literature and data review and related to the Senate Inquiry into

Access to Innovative, Novel and Specialist Cancer Medicines which also concluded that that public hospital and/or State hospital formularies may influence treatment choice.[52]

This is particularly true where there are in-patient cost components in addition to the PBS costs. For example, due to the risks inherent to the use of some medications the product information may recommend an admission to the hospital, and the hospital or State formulary may decide the budget cannot afford these bed-days. As explained by one industry stakeholder:

> *"There are in-patient components that sit alongside PBS components, like recommended hospital stays, and even if a medicine is approved nationally it might be rejected by a particular hospital… The FDA has just approved six new in-patient medicines for AML. It is only going to get worse. If you can't bill for it then patients aren't getting right care."*

Therefore, even if a medicine is PBS listed it may not be available or used in every hospital which contributes to variation in services. This issue was also identified by the Senate Inquire into New, Innovative and Specialist Cancer Medicines:

> *The committee also notes concerns raised about the availability of cancer medicines through public hospital formularies. Access to subsidised medicines for admitted public patients in public hospitals is dependent on the formulary of individual hospitals and in Queensland, the state-based formulary. The decision to list pharmaceuticals on the formulary of Australian hospitals is a consideration for the drug committees of individual hospitals or States and territories.*
>
> *The committee heard that as there is no single streamlined process across institutions and jurisdictions to assess proposed formulary listing of a medicine, the timeframe of each listing process is variable. Requests to prescribe drugs outside a hospital's list of approved medications, such as new anti-cancer therapies, usually involves an application to the hospital executive or jurisdictional advisory body.[53]*

Variation is not only observed in chemotherapy and drug treatments, but other therapies. The survey indicated substantial variation in blood transfusions and transplant rates, which accord with available research. For example, recent research through the IMPROVE project found that a substantial percentage (45 per cent) of transplant eligible patients with newly diagnosed myeloma do not proceed to autologous stem cell transplant as recommended by published clinical guidelines.

Patients also face variable hurdles to care and participation in clinical trials. The Patient Assisted Travel Scheme has received scrutiny by multiple Senate Inquiries, and has been criticised for providing variable and inadequate rates of subsidy for regional patients. Moreover, as PATS does not cover the costs to participate in clinical trials this may also serve as a barrier to consistent clinical trial participation, although the primary challenge was identified to be inconsistent discussion and referral to trials.

Variations in treatment, in combination with other factors, contribute to variable survival outcomes for patients nationally, and appear to impact disproportionately on people living in regional areas — defined by the State Cancer Registries as 'inner regional' and 'outer regional' areas. When looking across all blood cancer sub-types it is possible to see that while there are some minor differences in outcomes at the 1-year survival mark, by year five there are marked differences in survival between people

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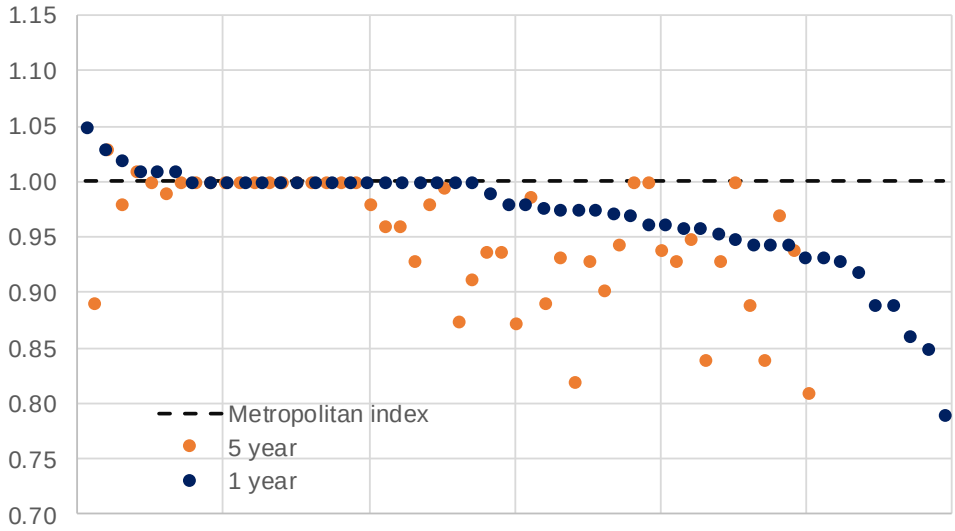
[52] Senate Community Affairs References Committee, 2015, *Availability of new, innovative and specialist cancer drugs in Australia*, Commonwealth of Australia 2015, p 47 accessed at: https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs/Report

[53] *Ibid*, p 70.

living in metropolitan and regional areas. Figure 3.20 shows the differences in survival at 1-year and 5-years for people in capital city areas compared to regional areas. These data were based on survival outcomes by region reported by State Cancer Registries.

The way to read the graph is the following: let's say the survival outcome in the metropolitan area was reported as 95 per cent survival at 1-year and the survival outcome in the regional area was 93 per cent at 1-year. In this case, the survival outcome for the regional area was approximately two per cent lower than the metropolitan area and in this graph it would be shown as the 0.98 relative to the metropolitan outcome. Obviously, there will be a multitude of factors influencing the outcomes of any one region over a particular time period, but in aggregate they tell a story of consistent regional disadvantage.

Figure 3.20: Deviations in regional survival outcomes from metropolitan areas – 1-year and 5-year survival outcomes



Source: Analysis of State Cancer Registry data. Note that some outcomes may be based on a small number of cases. Note that in this case 'regions' were defined to be 'inner regional' and outer regional' areas, compared with metropolitan capital cities.

The reasons underlying the metro-regional divide appear to be complex, including factors such as fewer blood cancer specialists in regional areas and barriers to treatment and care created by time and distance from major specialist centres. In reviewing differences between the metropolitan and regional respondents to the people living with blood cancer survey, it was found that:

- Regional people experienced longer delays in seeing a haematologist:
  - 24 per cent less likely to be seen in less than a day
  - 32 per cent more likely to be seen by a haematologist more than a month after presentation to a GP
  - 19 per cent more likely to be seen by a haematologist more than two months after presentation to a GP
- Diagnosis and treatment for regional people was less likely to be informed by genetic or genomic testing or cytogenic analysis:
  - 7 per cent less likely to receive a genetic or genomic test to guide diagnosis
  - 7 per cent less likely to receive a genetic or genomic test to guide treatment

  - 15 per cent more likely not to have had a bone marrow biopsy
- Regional people reported receiving different treatments protocols
  - 14 per cent less likely to report receiving an oral chemotherapy
  - 10 per cent less likely to report receiving a drug therapy
- Regional people were less likely to feel in control
  - 22 per cent more likely to report they felt completely uncertain about their diagnosis
  - 33 per cent more likely to report they felt completely uncertain about their treatment plan
  - 25 per cent more likely to report they did not know where to go if they had questions, and more information would have been helpful
- Regional people were less likely to have discussed supportive care interventions that can improve wellness and survival…
  - 9 per cent less likely to have discussed psychosocial support
  - 10 per cent less likely to have discussed practical and social support

  ….but more likely to have discussed end-of-life planning and spiritual support
  - 28 per cent more likely to have discussed spiritual support
  - 26 per cent more likely to have discussed advanced care plans

  …and ultimately not receiving supportive care interventions
  - 18 per cent more likely to report wishing they had received psychosocial support during treatment
  - 14 per cent more likely to report wishing they had received practical and social support during treatment
- Regional patients were more likely to want interventions to support social connection, access to telemedicine and help with finances
  - 23 per cent more likely to say that tools to connect cancer survivors was a high priority
  - 17 per cent more likely to say telemedicine to reduce travel was a high priority
  - 12 per cent more likely to say that telemedicine to monitor symptoms remotely was a high priority
  - 13 per cent more likely to say that tools to help me manage my finances was a high priority.

3.4 Patients Are Not Empowered

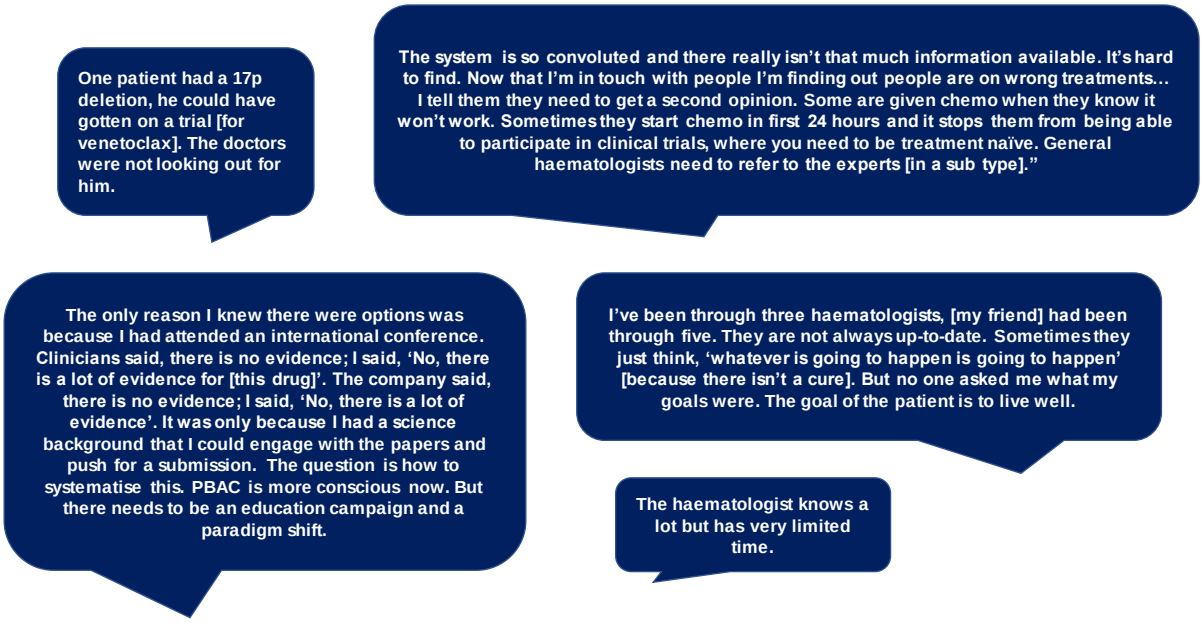
In a 2018 presentation on the value of patient registries for the National Organisation for Rare Disorders (NORD), Janet Woodcock, Director of the Centre for Drug

Evaluation and Research at the FDA in the US, noted that increasingly, and particular for patients with less common and chronic diseases, patients are the experts in their disease:

> *"It is important for patients to get together. Patients understand the nuance of the disease…. Patients know all the medical jargon, all the laboratory terms, they have lived that disease and have expertise to contribute."*

More than ever before, the power of the patient to transform care is recognised as an essential tool for reducing disease mortality and morbidity. In the past, patients tended to accept treatments without question; today it is understood that the aggregation of information about patient goals and side-effects can help to improve research and treatment. But in Australia, there continue to be hurdles to the meaningful engagement of consumers and the community in product appraisals, treatment decisions, and priority setting (Figure 3.21).

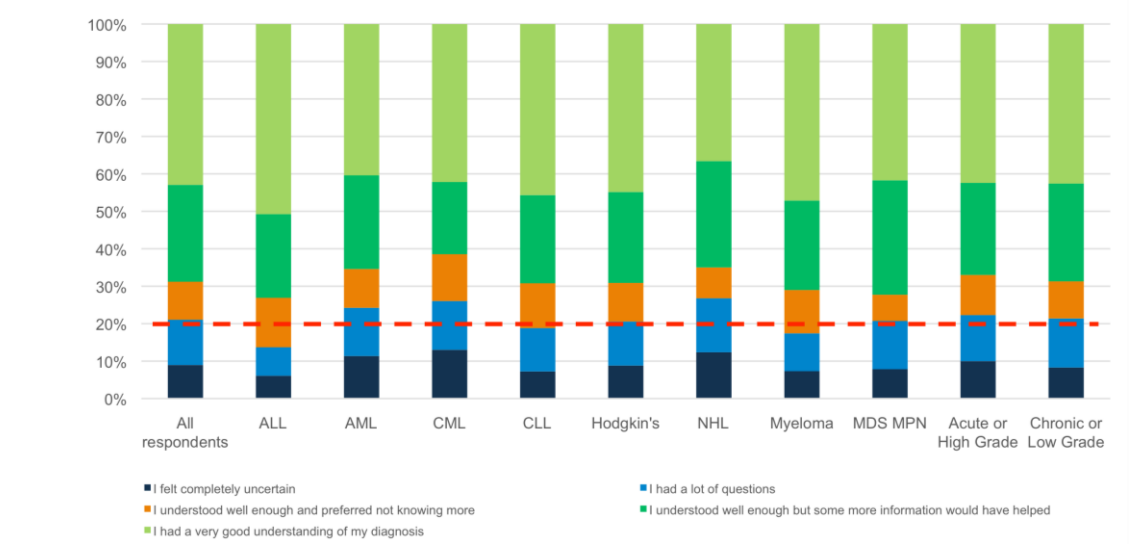
Figure 3.21: Stakeholder perspectives on the need to address barriers to patient empowerment



One of the most significant barriers to the empowerment of people living with blood cancer is the complexity of the Australian healthcare system. Patients and their families lack effective tools for finding timely, personalised information to support informed conversations. It starts with the selection of their specialist, the understanding of their diagnosis and treatment options, and progresses through to how to get the right supportive care for themselves and their families that help them to not just survive, but also live well.

For example, one of five people living with blood cancer report feeling "completely uncertain" or having "lots of questions" about their diagnosis (Figure 3.22).

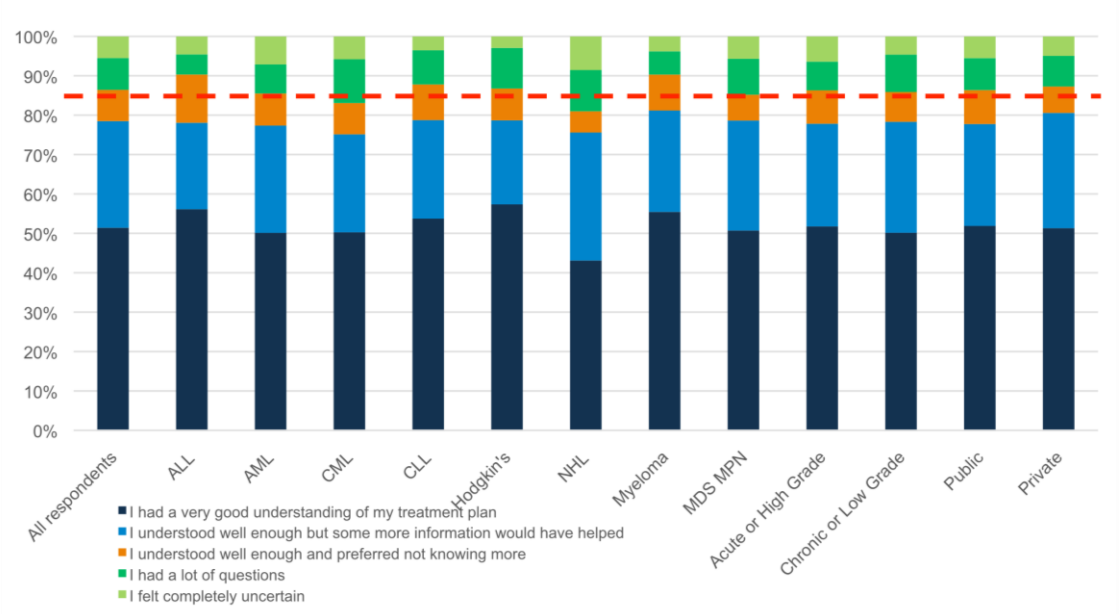
Figure 3.22: More to be done to help patients understand diagnosis



Source: Survey of People Living with Blood Cancer, see Appendix B. The red lines show key thresholds for the average across all blood cancers as discussed in the text and allow for variation by sub-types to the average to be more easily observed.

Most patients reported having a good understanding of their treatment plan, better than they reported understanding their diagnosis, but more than 10 per cent report having "a lot of questions" or "feeling completely uncertain." Understanding was marginally poorer among people living with Non-Hodgkin lymphoma but otherwise consistent across blood cancer sub-types and care settings.

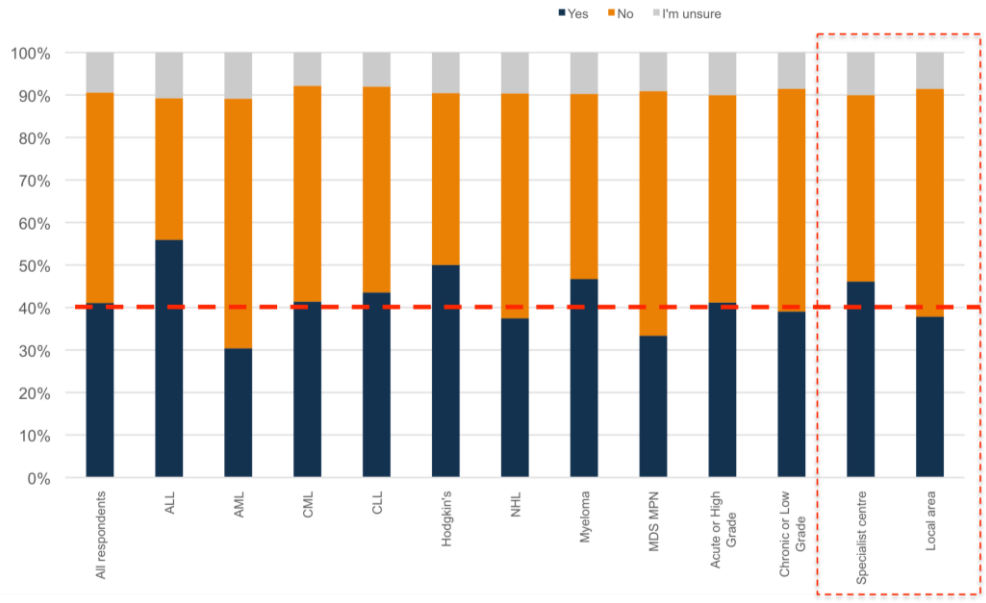
Figure 3.23: More to be done to help patients understand treatment



Source: Survey of People Living with Blood Cancer, see Appendix B. The red lines show key thresholds for the average across all blood cancers as discussed in the text and allow for variation by sub-types to the average to be more easily observed.

Part of this may be due to the lack of written care plans.[54] For example, less than half of patients reported receiving a written care plan, which is substantially inconsistent with recommended clinical best practice and optimal care pathway recommendations. People treated in local areas were less likely to receive a written care plan than people treated at a specialist treatment centre (Figure 3.24).

Figure 3.24: Percentage of patients with a written care plan



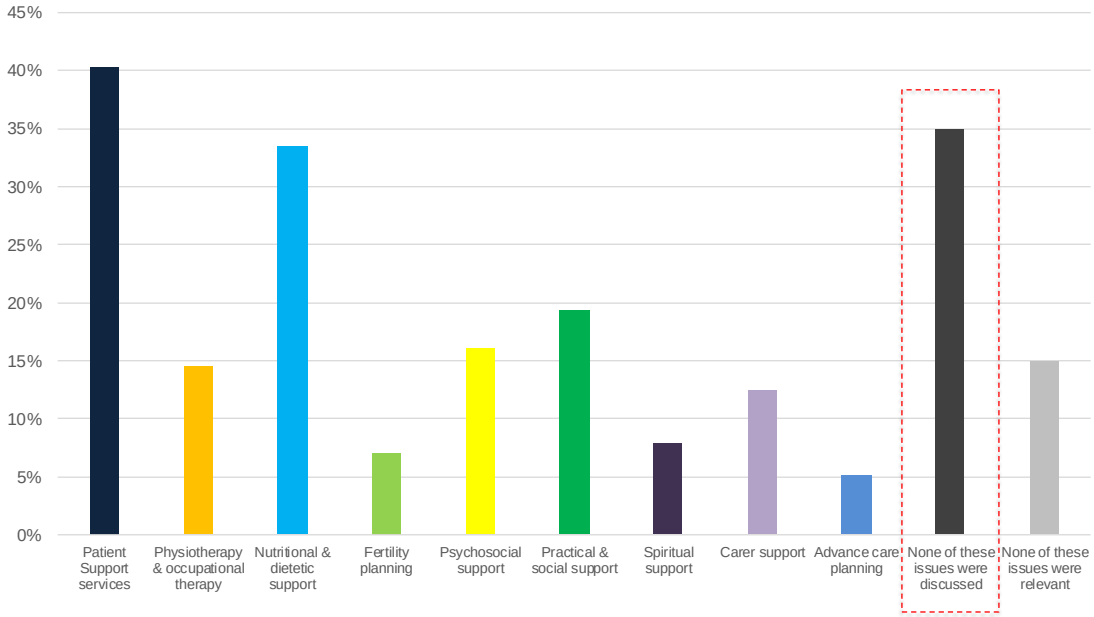
Source: Survey of People Living with Blood Cancer, see Appendix B. The red lines show key thresholds for the average across all blood cancers as discussed in the text and allow for variation by sub-types to the average to be more easily observed.

Without a written care plan, it is very hard for patients to understand the information that is being given to them. For example, the Leukaemia Foundation's empathy mapping for blood cancer sub-types highlighted the vulnerability of most people at diagnosis. While all people experience diagnosis and treatment differently, the Foundations' research indicated that often times people hear the word 'cancer' and find it hard to retain or process any other information.

Patients are also not empowered to understand their treatment options for supportive care. Consistent with feedback from stakeholder consultations, discussions of supportive care were reported in the survey to be inconsistently and infrequently discussed. More than a third of respondents indicated that no supportive care was discussed at treatment planning (Figure 3.25).

[54] Written care plans are for people with an illness who have several healthcare professionals working with them. A written care plan puts down in writing the treatment plan that will be delivered and makes sure that everyone knows who is responsible for what and when. The patient is an important part of this team and should be fully involved in the written care plan. The written care plan might also include what to do in a crisis or to prevent relapse.

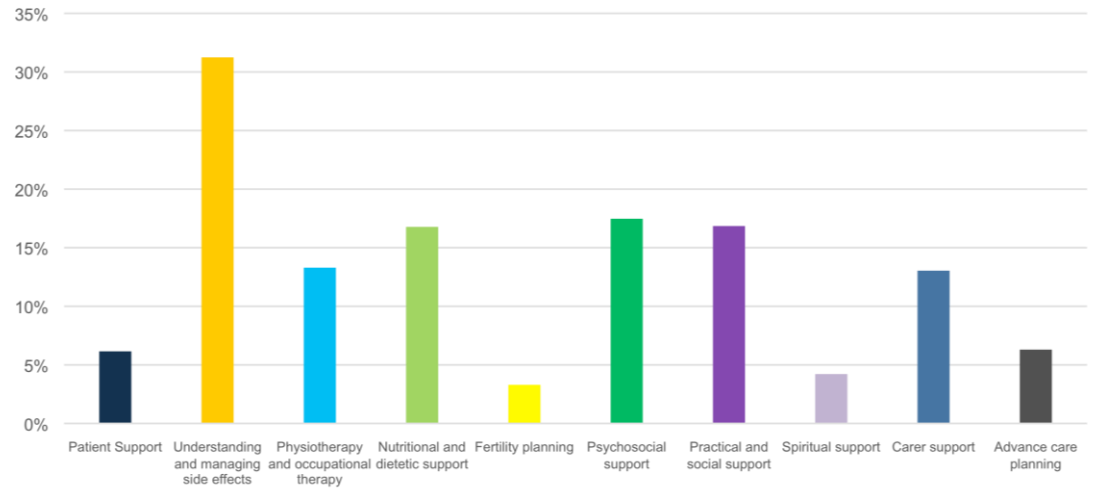
Figure 3.25: Percentage of respondents indicating supportive care had been discussed at treatment planning



Source: Survey of People Living with Blood Cancer, see Appendix B.

In hindsight, more than one third of patients reported wishing they had understood the side-effects of their treatment and how to manage these. They also reported wishing they had discussed psychosocial support, practical and social support, nutritional and dietetic support and physiotherapy and occupational therapy.

Figure 3.26: In hindsight, what do you wish had been discussed?



Source: Survey of People Living with Blood Cancer, see Appendix B.

3.5 Siloed Data & Inflexible Funding Models Slow Evidence Development

Australians have benefited from a high-quality regulatory system that sets a high standard of evidentiary rigour to ensure patient safety and product efficacy while also realising value for money in general.

Historically, the challenges for meeting the high evidentiary standards governing the listing of new services, devices or drugs on the MBS and PBS have not been so great as to substantially delay access to new therapies. Historically, however, therapies could be

developed for an entire population under a 'one size fits all' model of medicine development. As a result, the 'big diseases' received a great deal of research focus by the public and the private sector combined, and consequently many major conditions, such as cardiovascular disease or breast cancer, are increasingly well controlled, with good access to therapies and services through both the PBS and MBS.

In a world of precision medicine, however, these regulatory systems can come under pressure as evidence development for smaller, more fragmented populations is costlier. In the case of cancer, the challenges are further complicated due to the long time to demonstrate overall survival outcomes, and ethical issues that complicate trial design and the development of comparator groups, which can lead to greater uncertainty in the data compared to a world where cross-over trials were not allowed. This can mean a long-time to evidence development and listing of therapies for different sub-types. Ultimately, the costs of evidence development may exceed the potential benefit, such that there is not a market incentive for the private sector to act or the private market may be slower to act than in other markets with different evidence standards or funding systems.

Where evidence hurdles are high, and tolerance for uncertainty is low, this can lead to growing gaps between therapies being recognised as routine or best practice care and their registration with the TGA and/or availability of public subsidy through the PBS or MBS. It can also lead to increasing use of off label prescribing. While statistics of off-label prescribing are not available, one government stakeholder indicated it could be 'in the thousands'. This is also consistent with the National Oncology Alliance (NOA) data, which indicated that potentially 3,500 patients were privately funding access to novel therapies.

Of course, off-label medicines may have less supporting evidence and undergone less scrutiny than medicines registered by the TGA and/or listed on the PBS or MBS.

In a world of precision medicine, however, it is hard to overlook the fact that there are tools available to improve the treatment of patients and health system efficiency. This leads one to a moral question: if there is emerging knowledge of clinically important genetic or genomic differences between people, and an attempt is not made to provide a service or therapy that reflects this knowledge, then is the health system in fact doing harm?

This creates a moral case for reform to our regulatory systems, particularly in relation to genetic and genomic testing. In addition to the moral impetus for reform, these tests should improve health system efficiency, creating an associated economic case for change.

There is then a related, second order question focused on who bears the responsibility for providing access, and in a federated health system cost-shifting can lead to blame-shifting and people falling between the cracks. Ultimately, in a system of mixed financing the solution would need to be the option which provides for the greatest equity and efficiency across public and private, in-patient and out-patient care settings.

To this end, genetic and genomic testing is increasingly recognised as part of routine care overseas; for example, the UK has now made genomic testing part of the standard of care, as have many US medical groups. In Australia, not all tests that are recognised as clinically important are used, and stakeholders indicated that this was in large part due to a lack of public subsidy through the MBS, although other stakeholders noted this was once the remit of public hospitals but in an era of activity-based costing nothing that is not funded is done.

Clinicians engaged in the consultation process stressed the value of maintaining high standards for evidence development (Figure 3.27), as the engine of good science and ensuring patient safety; the question is how to overcome the barriers to evidence development in an innovative way that does not compromise patient safety through imprudent shortcuts. It was noted that MSAC required between two to five years of data to support a consideration for listing. In the next two to five years, between 31,000 and 85,000 people will be diagnosed with a blood cancer, and between 15,000 and 41,000 will die from blood cancer.

Figure 3.27: Stakeholder perspectives on evidence requirements

An example of new tools to guide treatment is the use of next generation sequencing at the Christine and Bruce Wilson Centre for Lymphoma Genomics at Peter MacCallum. The test can be used to evaluate a panel of 29 genes to support the diagnosis and treatment of people with blood cancer. To date the test has been used in the evaluation of more than 1,000 patients with some form of lymphoid malignancy, including lymphomas, myelomas, CLL and ALL. Within this cohort it was found (based on data as at December 2018):

- In 31 per cent of patients the test provided mutation data that directly influenced a correct diagnosis. In some cases, this was as profound as proving that a person had lymphoma as opposed to a severe infective process. Other patients were identified to have an entirely different sub-type of lymphoma from a previous diagnosis, such as a B-Cell lineage Lymphoma rather than a T-Cell lineage Lymphoma, or the identification of an aggressive lymphoma as opposed to an indolent lymphoma. All of these clarifications provide clarity for a different treatment path. (See Appendix A for examples of treatment choices by sub-type)

- In 44 per cent of patients the test provided information to guide the prognosis of the patient, which would in turn influence therapy through choice of the aggressiveness of therapy and/or decisions around stem cell transplantation. The avoidance of stem cell transplantation in inappropriate cases alone has the potential to deliver very substantial health system efficiencies, as well as potentially sparing the patient from a difficult intervention for little health gain.

- In 12 per cent of patients it provided a directly targetable therapeutic lesion. This allows for greater targeting of patients, which would be expected to improve survival outcomes by ensuring responders are given the right drug therapy and reducing the time for non-responders to be provided with an alternative therapy.

Currently this test is not funded, however. Consequently, even though more than 12,000 patients could potentially benefit in a year, only patients who happen to be in the right State, at the right treatment location, have access to this test. In the time to develop evidence to the required hurdles for wider listing between 25,000 and 69,000 will be diagnosed with a blood cancer that could have potentially benefitted from the more precise understanding of their disease.

Compounding these challenges are issues of:

- Barriers to data availability
- Policies for cost neutrality
- A reliance on 'gladiators' to champion evidence development and submissions.

Barriers to data for evidence development

The siloed nature and incomplete nature of data collection slows evidence development.

There are a number of patient registries collecting data on patient outcomes nationally. The major registries include the ALLG National Blood Cancer Registry, which collects data for AML, ALL and uncommon lymphomas, and the more recently established Lymphoma and Related Diseases Registry (LaRDR) and Myeloma Registry, which are now more systematically collecting data to support research and clinical trials.

Historically, registries have collected data for only a subset of patients, but a number of registries are now systematically collecting data for every new patient diagnosed and treated at participating hospitals. For example, the Lymphoma and Related Diseases Registry collects clinical data for all new cases of Hodgkin and Non-Hodgkin lymphomas, including:

- Health at diagnosis
- Demographic details
- Laboratory and imaging results at diagnosis
- Therapy decisions, including pre-therapy benchmarking, chemotherapy, autologous and allogenic stem cell transplantation, and maintenance and supportive therapies
- Outcomes (overall and progression free survival, duration of response and time to next treatment)
- Long term outcomes.[55]

Moreover, the focus of registries is on clinical data. Patient experience, which is essential to inform valuations of the quality of life benefits and side-effects of treatments

[55] Lymphoma and Related Diseases Registry, 2018, accessed at lardr.org.

is not systematically captured, and neither are natural history data, although services such as Biogrid offer the potential to integrate these data in a de-identified manner for secondary research. The MyHealthRecord provides an obvious, centralised mechanism for the collection of patient experience and natural history data but concerns for privacy and very real administrative hurdles are slowing the development of this as a tool for research and evidence development. In the absence of action with the MyHealthRecord, some patient groups are attempting to fill the void with their own patient reported outcome registries, such as the WhIMSICAL database developed in partnership with CART-Wheel by the Waldenström's Macroglobulinemia patient group, WMozzies, which is a similar model to the National Organisation for Rare Disorders (NORD) patient entered data registries for rare disorders in the US. Figure 3.28 provides stakeholder pictures on data capture and availability.

Figure 3.28: Stakeholder perspectives on evidence requirements

Policies for cost neutrality

To help rein in the very substantial growth in healthcare costs against a backdrop of an increasing and ageing population, as well as increasing consumer expectations for health services, Government has generally sought to implement cost neutrality and offset policies to support new listings to MBS. To the extent that policies for cost neutrality unnecessarily slow the uptake of new diagnostic tests such as genetic, genomic or other tests this will also frustrate progress towards reducing mortality from blood cancers. Government considerations for cost neutrality and offsets, while important tools for containing overall expenditure growth, can also create challenges to accessing emerging technologies; as one stakeholder put it:

> *"This is entirely unsustainable in the context of the tidal wave of new genetic and genomic testing coming down the pipeline."*

Reliance on clinical 'gladiators' for submissions

The other major barrier to evidence development and listing is the expectations for clinicians to prepare all submissions for listing. In many ways it would appear that all roads lead back to the clinician: they bear responsibility for participation in clinical trials, for the development of care pathway and clinical guidelines, for the preparation of regulatory submissions, in addition to actually treating patients. While clinicians must

be a driving force and integral stakeholder to all of these activities, at some point the sustainability of this model must be reviewed.

3.6 Fragmented Health Systems and Complex Financing Arrangements Lead to Inequity

The other major challenge for people living with blood cancer is the fragmented and complex nature of healthcare financing in Australia. Fragmented health care systems create incentives for cost-shifting that impact on patient care and cumulatively contribute to significant out of pocket costs and financial hardship for patients.

Complex State and Federal funding arrangements and cost shifting impact on patient treatment

Risks to patient care resulting from cost shifting was identified in the Senate Inquiry into Access to Cancer Medicines, which found that access to medicines was not always consistent across at all hospitals and in all States due to the specific hospital and state procurement practices and budget choices leading to unique formularies nationally, even when medicines are PBS listed. Looking forward, there may be an emerging issue in particular for AML patients with new FDA approvals for AML medicines that also include in-patient stay components which hospitals may not want to fund. Similarly, specialists indicated that hospitals face dis-incentives to use medicines that can be delivered at home, because the hospital would incur the costs of the drug, but would receive no revenue for treating the patient because hospitals are funded on an activity basis.

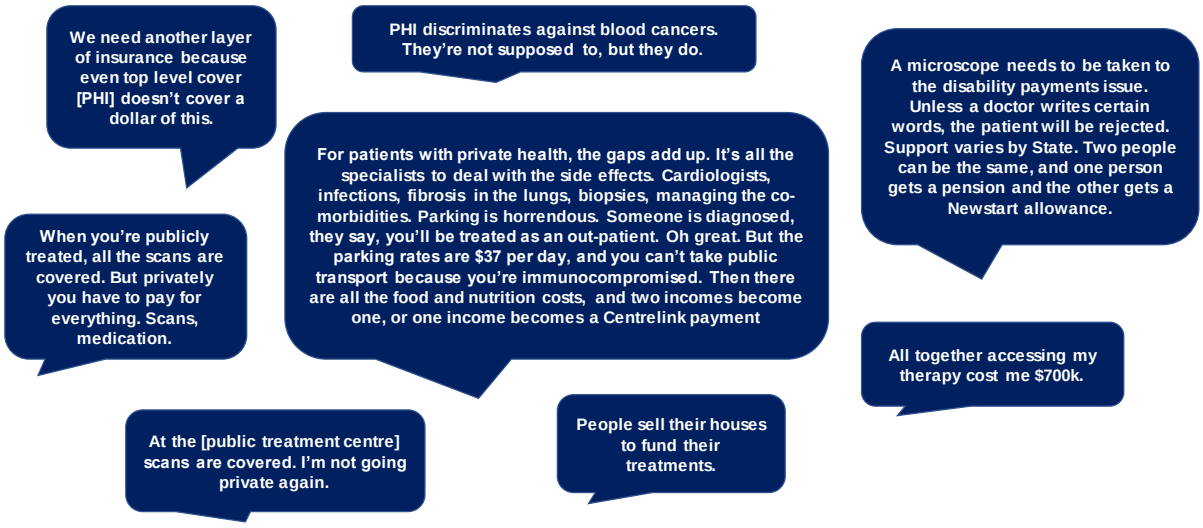
Cost shifting is also evident in testing, with tests that may once have been theoretically included as an in-patient service now not being covered, and without MBS listing even publicly-treated patients are left to pick up the costs.

The underlying fragmentation is arguably a significant cause of much of the variability in service delivery and experience observed nationally, which frustrates progress towards implementation of current best practice.

Poor coverage of private health insurance can contribute to significant cumulative out of pocket costs

In addition, the coverage of private health insurance of services for blood cancer was reported to be low, and the cumulative impact of specialist visits, tests and scans, and other medical services creating substantial stress for people and their supporters (Figure 3.29).

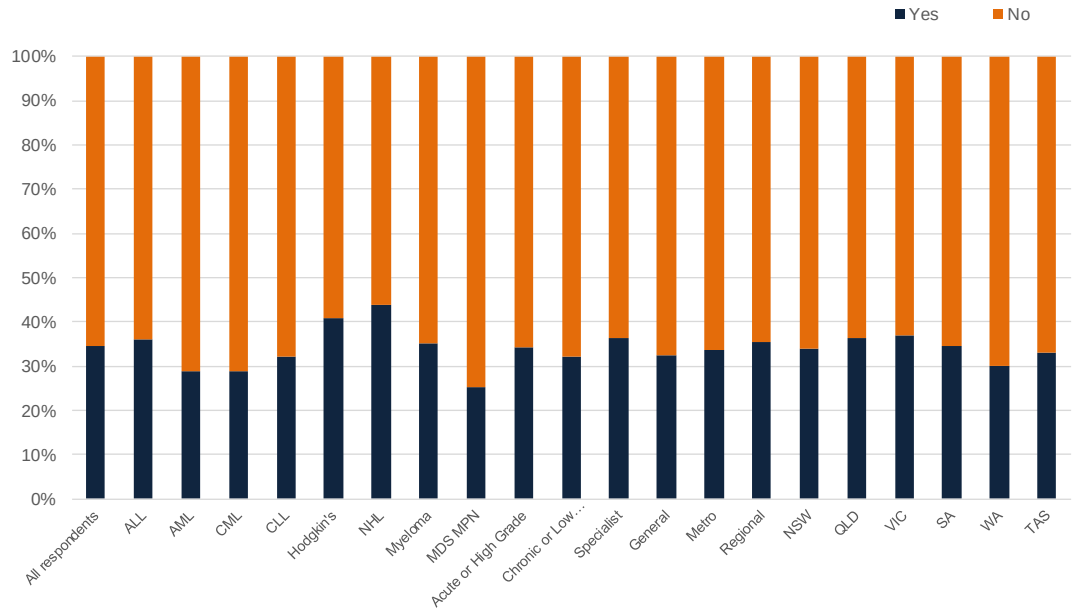
Figure 3.29: Stakeholder perspectives on complex financing, cost shifting and out of pocket costs



Private health insurers point to regulatory hurdles preventing the coverage of out-patient services, with potentially only the largest funds able to fund the clinical trials for hospital substitution. The sequitur of these arrangements, it is argued, is that patients in regional areas, potentially enrolled with a regional private health insurer that cannot fund such trials, would not be able to access more community-based services covered by private health insurance.

Just over 30 per cent of respondents reported incurring out of pocket costs, and this was roughly consistent across all sub-types, with lymphomas having a higher overall percentage (>40 per cent) compared to other sub-types. There was no substantial variation across geographic regions or hospital types (Figure 3.30).

Figure 3.30: Percentage of patients facing out of pocket costs

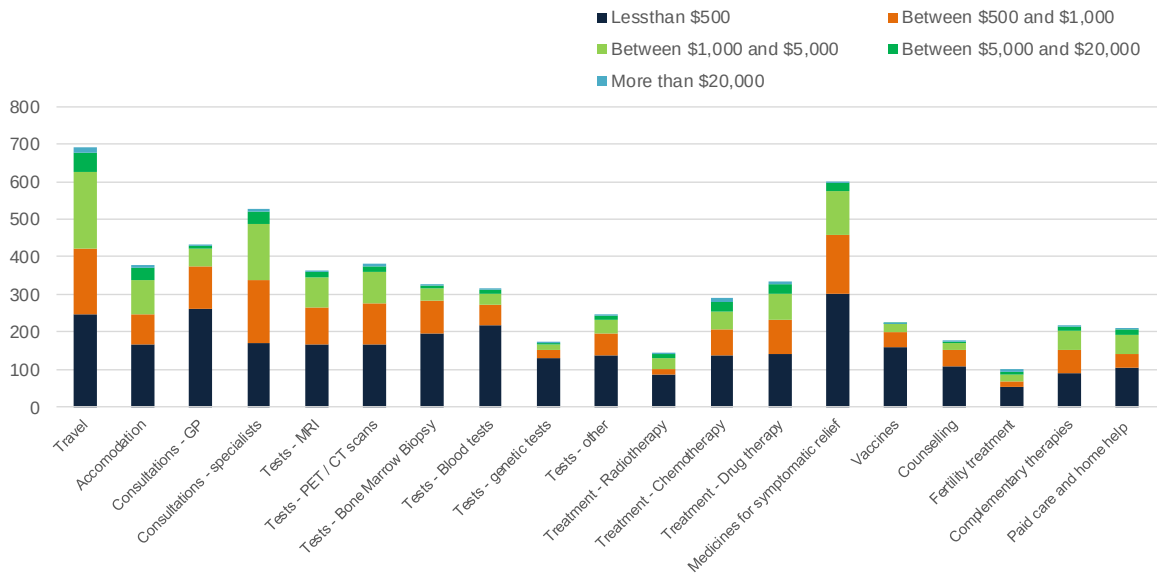


Source: Survey of People Living with Blood Cancer, see Appendix B.

The most significant types of out of pocket costs include travel costs, medicines for symptomatic relief (e.g., anti-nausea and analgesics) and specialists (Figure 3.31). These categories were more significant in terms of overall frequency as well as magnitude of

spend, with more people reporting expenditure in the ranges of '$1,000 to $5,000', '$5,000 to $20,000' and 'More than $20,000'.

Figure 3.31: Frequency and magnitude of out of pocket costs by category for people living with blood cancer



Source: Survey of People Living with Blood Cancer, see Appendix B.

Approximately seven per cent of patients who indicated they incurred out of pocket costs reported they had spent more than $5,000 on chemotherapy or drug. In addition, patients with private health insurance were between two and eight times more likely to report incurring costs in the '$5,000 to $20,000' cost band across a range of service.

Risks of financial hardship and challenges in navigating welfare systems impact patient outcomes

The survey of people living with blood cancer indicated that approximately one third of patients also required financial assistance as a result of their cancer. Financial hardship reduces the likelihood of survival and has similarly been identified by the Cancer Council:

> *A change in financial situation is a significant concern for people affected by cancer. Patients are often unaware of their options, such as financial assistance, and hardship arrangements, and have trouble accessing available welfare on their own. This inability to act can place people into financial hardship. Our interest in this matter is centred on the reality that Australians in the lowest socio-economic quintile are 30% more likely to die from their cancer than those in the highest socio-economic group, even when controlling for type of cancer and stage at diagnosis. Poverty and financial hardship directly impact on whether someone will survive from cancer.*[56]

The major issues identified by the Cancer Council and Oncology Social Work Australia in relation to accessing payments from the Centrelink, the National Disability Insurance

[56] Cancer Council and Oncology Social Work Australia, 2018, *Submission to the Independent Review of the Public Service*, p 1.

Scheme and My Aged Care programs were reported in their submission to the Independent Review of the Public Service, included the following:[57]

- *Practical challenges to accessing support*
  - *Requirements for computer literacy*: Highly digital benefit application systems require people to call automated voice systems or have access to a computer. This assumes a degree of computer literacy, numeracy skills and clarity of mind as it also requires recall of personal log in, pin codes and passwords.
  - *Risks and challenges related to immunosuppression*: Visiting the Centrelink office is time consuming and overwhelming for many people, but particularly difficult for people affected by mobility issues due to illness or treatment. People unwell from cancer are least able to tolerate an extended visit to an office. Often people affected by blood-based cancers are immune-suppressed and on medical advice, must avoid public settings, at times for months.
  - *Challenges for CALD people*: Limited availability of interpreters for people where English is not their first language.
- *Complex and confusing application processes*
  - Each Government welfare program is administered in isolation of other schemes, requiring individual applications and assessment.
  - Difficulty accessing appropriate welfare options despite lodgement of written letters of support from health professionals about the diagnosis and, or the effects of the condition on employment. Terminology used by the doctor is critical to the success of the claim and wrong terminology may mean starting again.
  - Time delays in welfare access can be compounded by the need to submit further documentation.
  - No transparency of the estimated wait time and/or status of applications within the review process.
  - No emergency assistance available to high need applicants during the review process.
  - Information about the reason for rejection or the processes for appeal are not routinely provided. People report that advice of an alternative claim option is not provided, which leads them to believe they have no entitlement to income or other support.
  - Interaction with multiple Centrelink officers, leading to telling the story over again, and can create high levels of discouragement in the application process and sometimes abandonment.
  - Difficulty obtaining an appointment with Centrelink social workers. A claims issue can be solved quickly by a hospital social worker with

[57] Cancer Council and Oncology Social Work Australia, 2018, *Submission to the Independent Review of the Public Service,* p 2.

assistance of a Centrelink Worker or Community Liaison Officer but these resources seem limited.

- Expiration of a medical certificate and discontinuation of payment without warning. This is particularly problematic for people who are unwell, hospitalised for long periods, geographically isolated and away from home, as well as for socially marginalised and vulnerable population.

Many clients are unaware of their eligibility for assistance. Confusion about eligibility can discourage a low-income patient from considering an application for assistance. Alternatively, people who are already receiving unemployment or income support may have their eligibility status change due to illness.

3.7 Conclusions

There are a number of existing and emerging challenges to the diagnosis, treatment and care of people living with blood cancer and hurdles to realising a cure across all sub-types. Major issues include a lack of consistent approaches to the diagnosis and treatment of patients using currently available Australian best practice, and the magnitude of this variation on regional patients in particular over time. Ensuring consistent access to treatment and care has the potential to deliver substantial improvements in survival outcomes and quality of life today. Empowering patients with the tools to engage with their haematologist and the wider healthcare system are foundational steps towards improving the lives of people living with blood cancer.

The full realisation of a goal for zero deaths from blood cancer, however, will require new discovery and to that end, Australians living with blood cancer must participate in international research by blood cancer sub-types.

The next chapter considers the opportunities to address these barriers.

Chapter 4

Opportunities to Improve Outcomes and Quality of Life

More than ever, there are compelling reasons to be optimistic about the future for people living with blood cancer. This chapter identifies the opportunities for governments, healthcare providers, clinicians, researchers, industry and most importantly, people living with blood cancer and their families, to work together to improve survival outcomes and the quality of life for people living with blood cancer and their families.

4.1 Overview of Opportunities

Through focused and strategic collaboration around a common goal, mortality from blood cancers can be reduced and quality of life substantially improved.

By implementing currently known best practice it will be possible even in the short term to improve survival rates and address quality of life challenges related to fatigue, anxiety and other side-effects of treatment.

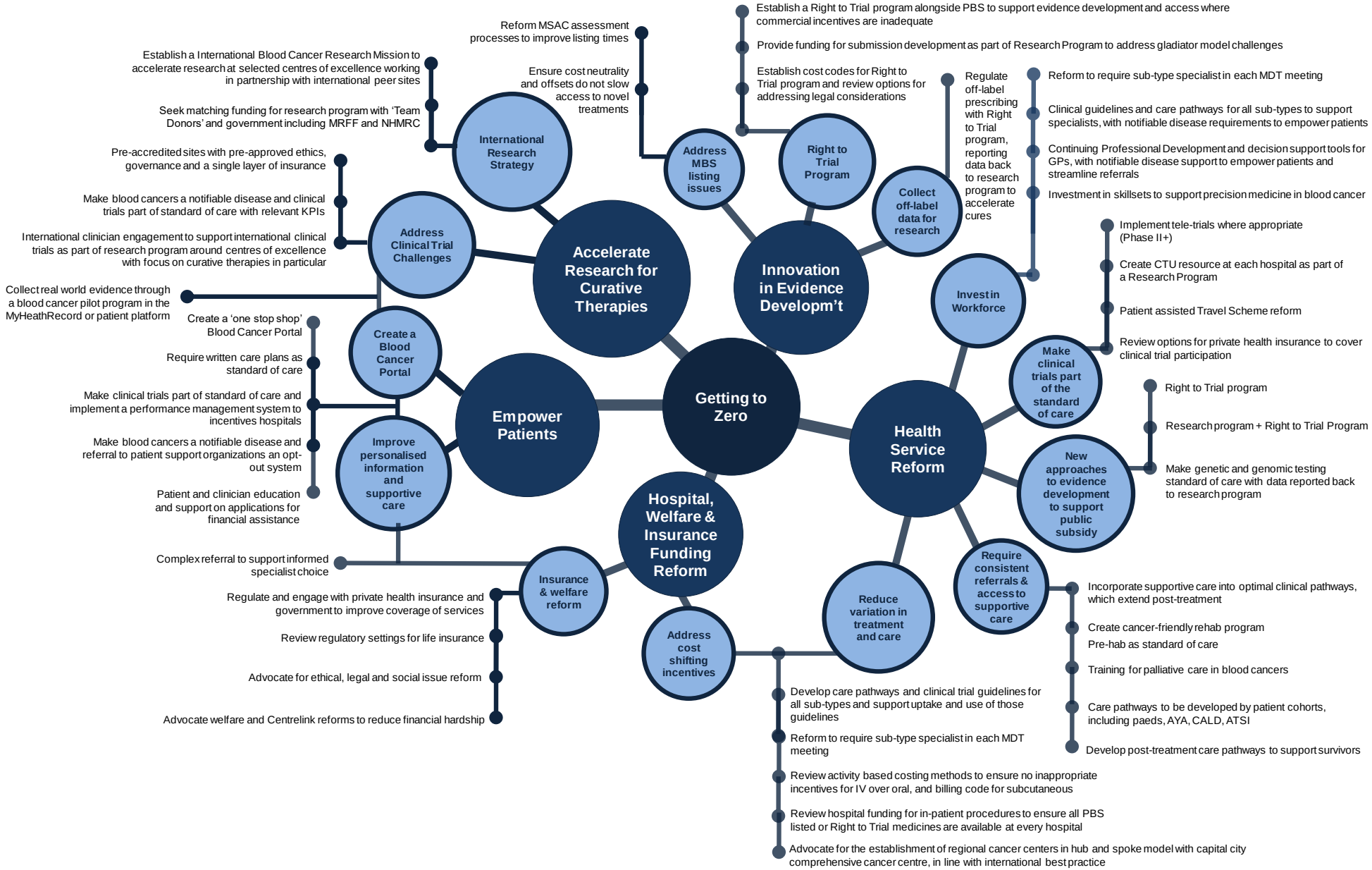
And through enhanced integration into international research substantial advances towards a cure for all blood cancer sub-types can be realised by 2035, while also delivering improved access to novel therapies today.

This chapter identifies a range of opportunities to improve the lives of people living with blood cancer, including:

- Empowering patients and their families
- Improving the consistency and use of evidence based best practice
- Implementing new approaches to support evidence development and access to novel therapies
- Accelerating research in curative therapies through the development of a national research strategy focused on blood cancer
- Reviewing hospital, welfare and insurance financing arrangements to address incentives for inconsistencies and inequities in care, and risks for financial hardship.

The range of opportunities are summarised in Figure 4.1 and discussed in turn.

Figure 4.1: Opportunities to improve survival outcomes and quality of life on the path to zero deaths from blood cancer



4.2 Empower Patients and their Families: *nothing about us without us*

Improving survival and wellness starts with the person who is diagnosed. Supported by their families, the patient knows their history and goals better than anyone else. Getting to an outcome that is best for that person requires their empowerment through information to act. Critically, many people find the healthcare system complex and confusing, and there can be substantial barriers to accessing information that enables a person to make an informed choice. Empowering people with information and tools is a necessary foundation to reducing deaths from blood cancer.

In addition, by working strategically and together, blood cancer patients can come together to advocate for change. The path to improved survival and wellness begins with the people living with blood cancer.

To this end, there are a number of potential opportunities to better meet patient expectations for information and to empower patient choice; these include:

- Make blood cancers a non-infectious notifiable disease
- Make referrals to blood cancer patient support organisations opt-out to ensure people do not 'fall through the cracks'
- Create a portal to support people living with blood cancer and their families, informed by a broader digital strategy for how to best to connect people living with blood cancer and the wider blood cancer support network, including clinicians and researchers
- Collect real world data on patient experience through the MyHealthRecord or a patient-entered database to support more effective engagement with regulatory authorities and research into new therapies
- Develop a complex referral MBS item and referral support tool to enable more effective referral pathways.

Make blood cancers a non-infectious notifiable disease

As precision medicine becomes an ever more meaningful paradigm for the treatment of blood cancers, the importance of input from sub-type specialists also increases.

To this end, most health systems are seeking greater controls over the treatment of blood cancers, to ensure input to treatment planning by sub-type specialists.

Within Australia, the very consistent theme was that sub-type specialist input was not always received and that this may adversely impact health outcomes, as well as frustrate recruitment to clinical trials, as the Clinical Trial Networks simply 'cannot find the patients'.

One opportunity would be to make blood cancers a notifiable disease, not just in the sense of required reporting of incidence and mortality to State Cancer registries, which already occurs, but similar to a communicable disease paradigm, where diagnoses of conditions on a notifiable disease list triggers action by health services. This is similar to reforms in the UK, which require treatment of blood cancer sub-types at hospitals serving a particular number of patients (to improve outcomes through higher throughput) and consultation by a sub-type specialist in the MDT. Similarly, in the US, cancers are one of a selected number of notifiable non-infectious diseases mandated by the Centers for Disease Control and Prevention (Box 4.1).

Box 4.1: Notifiable non-infectious diseases

In the USA the National Notifiable Disease Surveillance System (NNDSS) is responsible for sharing information regarding notifiable disease. As of 2017, the Centers for Disease Control and Prevention in the US have mandated in addition to notifiable infectious (communicable) disease a selected number of notifiable non-infectious diseases. Notifiable non-infectious diseases in the US include:

- Cancer
- Carbon monoxide poisoning
- Elevated blood levels of lead
- Pesticide related illness and injury
- Silicosis.

Source: Centers for Disease Control and Prevention, *2017 National Notifiable Conditions*, available at: wwwn.cdc.gov

An opportunity exists not just to report cases to State Cancer Registries, but to empower the patient with guidance on accessing a specialist in their sub-type. In the case of blood cancer, it could be as simple as an email, letter or text from the MyHealthRecord or other health service encouraging the patient to seek a complex referral consultation with their GP (see below), providing an opt-out referral to a patient support organisation and/or linking the patient to key information and questions to know.

This could also support the identification of people for enrolment in clinical trials, with opt-out consent to be included in a national clinical trial database. The NORD database captures information on patients willing to participate in a clinical trial to support patient recruitment.

The benefits of such a policy would be:

- Reductions in service delivery variation, improving survival outcomes and quality of life
- More targeted treatments matched to the genetic and genomic profile of the patient and their tumour, improving survival outcomes and quality of life
- Increase in clinical trial activity through reduced time and cost to identify patients.

Implement opt-out referrals to patient support organisations

Patient support organisations are a vital node within the blood cancer ecosystem. Patient support organisations:

- Help patients understand their disease, which is essential in the context of time-poor clinicians
- Help connect patients to each other as a mechanism of social support
- Help connect patients with services or, in some cases, actually provide services to improve the wellbeing of patients and their families; the Leukaemia Foundation, for example, provides transport and accommodation services, psychosocial support and nutritional and dietetic support programs.

Stakeholder consultations and the survey indicated that although 40 per cent of patients discussed patient support with their haematologist through the course of diagnosis and treatment, the remaining 60 per cent did not. To this end, earlier referral to patient support was seen as an important priority by people living with blood cancer to better support patients through their journey.

Similar to the ideas of making blood cancer a notifiable disease, it would be possible for a diagnosis to automatically trigger an email, letter or text from the MyHealthRecord or other health service with an opt-out referral to a patient support organisation. This more systematic referral to patient support could serve to substantially address the gaps in patient information needs and help people to more effectively navigate the healthcare system, including knowledge of and access to:

- Services to support the management of fatigue
- Psychosocial support to manage anxiety and depression
- Practical and social support
- Financial and employment support and advanced care planning.

More systematic use of supportive care by people who need help can substantially improve patients quality of life and in turn survival outcomes. As discussed in Chapter 3, patients who experience less depression and who are more fit are more likely to have a better survival outcome than people suffering from mental illness, fatigue and poor fitness. In addition, a number of studies analysing survival outcomes for different sub-types, including AML and myeloma, using SEER data showed that married people were more likely to survive blood cancer than single people and significantly more so than divorced people status. A person's insurance status was also a significant predictor of outcome, which in the US is a proxy for access to treatment.[58] Taken together these studies suggest that social connection is also important to both survival and living well.

Support the development of patient reported outcomes

While blood cancers combined are as common as other major cancers like breast cancer or lung cancer, in many ways patients with particular sub-types experience some of the challenges associated with 'rare' or 'less common' diseases. In particular there may not be evidence to support listing of new therapies for their specific indication, and also the 'lived experience' of their disease may be less well understood by their doctors than say a person with breast cancer.

For people with rare diseases the need to champion patient reported data is paramount to reducing mortality and improving quality of life by providing industry and researchers with a 'roadmap' for their disease: what are the issues that need to be better managed, what are the side-effects of treatments, what is the day-to-day experience of the disease.

Currently while there are a number of clinical data registries available for different sub-types of cancer, there are no databases of patient reported outcomes. Overseas there has been a significant investment by the NIH, FDA and NORD organisations to address these barriers through the development of natural history registries and patient-entered data. Closer to home WMozzies has trialled an innovative approach to patient-entered data leveraging the CART-Wheel platform developed by the Centre for Analysis of Rare Tumours.

These efforts reflect the cost challenges associated with entering patient data. For a clinician to enter all of the data there would be no time to see patients. By contrast patient-entered

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[58] See: Jamy O, Xavier AC, et al, 2018*, Impact of Insurance Status on Survival of Patients Diagnosed with APB in the US*, ASH Annual Meeting, San Diego and Costa, LJ, Brill IK, Brown EE, 2016, *Impact of martial status, insurance status, income and race/ethnicity on the survival of younger patients*; Costa LJ, Brown EE, 2015, 'Insurance Status, Martial Status, Income but not Race-Ethnicity Affect Outcomes of Younger Patients Diagnosed with Multiple Myeloma in the US', *Blood Journal*, vol 126, Issue 23, p 633

outcome data takes this burden away from time-poor clinicians and is highly cost effective: NORD estimated in 2018 that for the NIH to manage a patient-reported outcome registry it would cost in the order of $1 million to $2 million per annum, whereas the patient-entered registries cost only $15,000 per disease to run. While there may be skepticism currently regarding the quality of the data, initial concordance studies have also found the data can be accurate and good quality. For example, WhiMSICAL reported 80 per cent concordance in its initial pilot with clinical data and as a result of the pilot identified new approaches to support patients with the entry of more challenging parameters. Box 4.2 provides a summary of the NORD and WMozzies WhiMSICAL databases.

Box 4.2: Examples of Real World Evidence pilots of Patient Reported Outcomes

NORD Patient-Entered Registries

NORD patient-entry registries are a major innovation supported by the FDA, NIH, patient support groups, clinicians and researchers in the US to improve knowledge of the rare disorders to support the development of new therapies. This approach recognises the need to identify a path for industry to develop new products by identifying the needs and issues for people with rare disorders.

The development of patient-entered registries are important because of the significant cost reduction. As noted by NORD Chairman Marshall Summar in 2018, large NIH clinical network registries can cost between $1 million and $2 million per year to run, but a patient-entered registry can cost only $10,000 to $15,000 to run.[59] He went on to indicate that patient entered data had been of good quality. The NORD Registry platform has the following features:

- It is a cloud-based service that is mobile and easy to use for patients
- NORD funds a team of people to provide support and advice as needed
- Smart surveys target question participation and enable natural history data tracking
- The registry uses standardised data dictionaries
- Automated survey reminders have been built in to encourage long term user engagement
- Role-based permissions allow for flexible study design
- Analysis tools provide users with real time data for comparison to other patients.

The data collected addresses a knowledge gap, particularly for rare disorders, about the experience of the disease for patients.

WhiMSICAL Patient-entered database on the CART-Wheel platform developed

The WhiMSICAL database is designed to gain a better understanding of WM symptoms and correlation to pathology results, family history and genetics. The research also covers triggers to commence therapy, different treatments, their efficacy and tolerance, as well as disparities in treatment and access within countries and internationally.

Data is collected from patients internationally, including the US, Australia, Canada, the UK, NZ and the Netherlands. The registry provides a platform for big data analysis, with patients monitoring fatigue levels against haemoglobin levels, stress and other dimensions of patient experience.

A pilot study found 80 per cent concordance for Australian-entered data against data in the LaRDR registry. The registry also identified significant treatment diversity, with more than 37 unique first line therapeutic combinations entered by 180 patients.

Source: National Organisation for Rare Disorders, 2018, *IAMRARE Registry Program*, Summary by NORD Chairman Marshall L Summar, MD, on the need for registries in rare diseases, accessed at https://rarediseases.org/iamrare-registry-program/ and WMozzies, WhIMSICAL: A Global WM Registry for the Patient's Voice http://www.wmozzies.com.au/wp-content/uploads/2018/10/181126-WhiMSICAL-IWWM-10.png; Statistics on WhiMSICAL http://www.wmozzies.com.au/index.php/whimsical/; http://www.wmozzies.com.au/wp-content/uploads/2018/10/181007-WhiMSICAL-stats-geo.png

Patient data are important to support clinicians and regulators to understand what is going on in the day-to-day experience of the disease, to understand the secondary complications and co-morbidities of a treatment. As precision medicine becomes a new paradigm for

[59] National Organisation for Rare Disorders, 2018, *IAMRARE Registry Program*, Summary by NORD Chairman Marshall L Summar, MD, on the need for registries in rare diseases, accessed at https://rarediseases.org/iamrare-registry-program/

therapy development, these data become even more important. Importantly, this type of evidence could:

- Enable the more scientific and systematic engagement of patients in understanding the lived experience of disease as part of regulatory product appraisals, pricing decisions and priority setting
- Accelerate a regulatory review of a new therapy.

To this end, it may support the listings of more therapies, increased clinical trial activity or the identification of potential targets for a research strategy.

The most natural mechanism for the collection of these data would be the development of a patient reported outcomes module as part of the MyHealthRecord. If this proves too challenging, however, there could be opportunities to leverage and extend the CART-Wheel approach for Waldenström's for example.

Develop a complex referral MBS item and referral support tool to enable informed financial consent and more effective referral pathways

The other essential element to empowering patients is supporting their initial entry into the world of haematology. At diagnosis, patients are vulnerable. In the development of its *Inform Me* strategy, the Leukaemia Foundation engaged extensively with patients and found information processing in the early stages of finding out can be challenging for many people. Some people hear only the word 'cancer' and struggle to retain any other information. This was similarly reported by NICE in the UK as part of its *Improving Outcomes in Haematological Malignancies* strategy and the Cancer Council's Optimal Care Pathways, motivating recommendations for written care plans.

At the same time as processing their new reality, patients must also engage with their GP on a referral to a specialist, and as the literature and stakeholder consultations suggest, not all specialists may be current with the latest treatments in their sub-type. As discussed in Chapter 3, GPs also tend to have limited experience with blood cancers, but critically the initial referral can set into motion a path of events that have a substantial impact on the patient's probability of survival depending on their sub-type and disease staging.

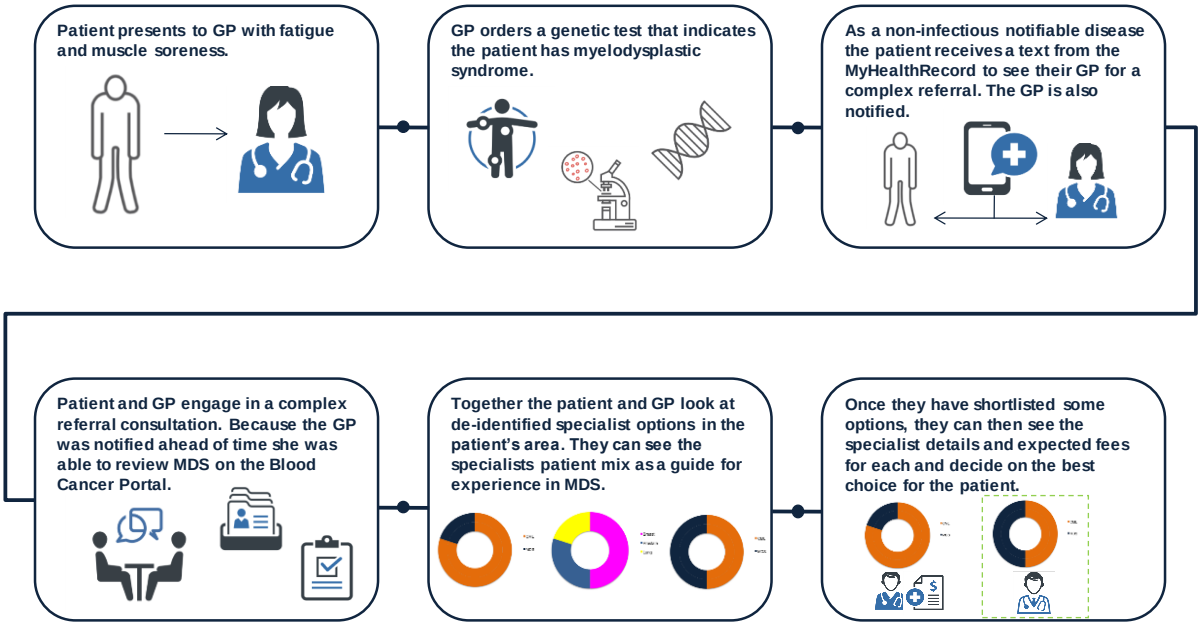
For private patients there are the out of pocket considerations as well. The survey showed that patients with private health insurance were eight times more likely to report incurring costs in the range of $5,000 to $20,000 across a range of services, which can add up to a very substantial impact to household income and financial security, and in turn, may affect overall survival outcomes (see SEER data analysis for AML and myeloma). Similarly, the Cancer Council, Breast Cancer Network of Australia, Prostate Cancer Foundation of Australia and CanTeen have developed a standard for informed financial consent to enable greater transparency around fees charged to enable patients to better consider the likely financial impact to them.[60]

An opportunity exists to empower patients and their GPs to select the best haematologist for them. A system could be developed to support a complex referral pathway. While 'quality' and 'outcome' data are always controversial and represent a major hurdle to decision support tools, 'throughput' is highly associated with quality; indeed, this is the principle underlying the Nationally Funded Centres (NFC) Program which seeks to improve patient

[60] See Cancer Council, 2018, *Informed Financial Consent – public consultation feedback*, December 5, accessed at: https://www.cancer.org.au/about-cancer/patient-support/informed-financial-consent.html.

outcomes for specialised services by regulating where these services may be provided nationally. A system that displayed de-identified specialist or treatment center options with simple pie charts or graphs of patient mix could still allow for patient choice but it would show whether a particular clinician or treating centre has had experience in treating a particular sub-type in the region of the patient. The doctor could then select one or more options for a detailed review, which would then bring up the specialist names and expected gap fees (Figure 4.2).

Figure 4.2: Complex referral support tools: how it could work



This would support the patient to make an informed decision and help patients to get to the right specialist for their sub-type sooner, which would be associated with improved health outcomes.

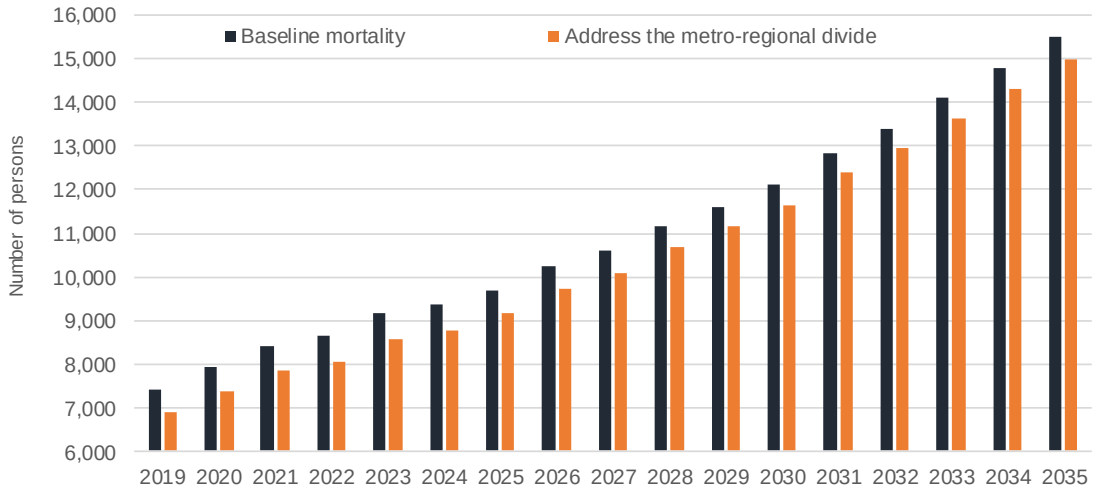
4.3 Catalyse Health Service Reform for Consistency and Equity in Treatment and Care

Once a person with blood cancer enters the healthcare system, there are further opportunities to improve the consistency and access to services.

There was consensus among stakeholders that with the more consistent application of what is already known to be best practice mortality and morbidity could be substantially reduced. Indeed, State Cancer Registry data indicate that if current best practice survival rates achieved in Australia today were realised nationally, without any variation between metropolitan and regional patients or between States, the number of deaths predicted by the blood cancer model would be substantially reduced.

For example, if the metropolitan-regional divide were addressed, approximately five per cent of deaths (more than 9,300 people) could potentially be avoided, preventing the loss of 200,000 years of life over the 2018 to 2035 period (Figure 4.3).

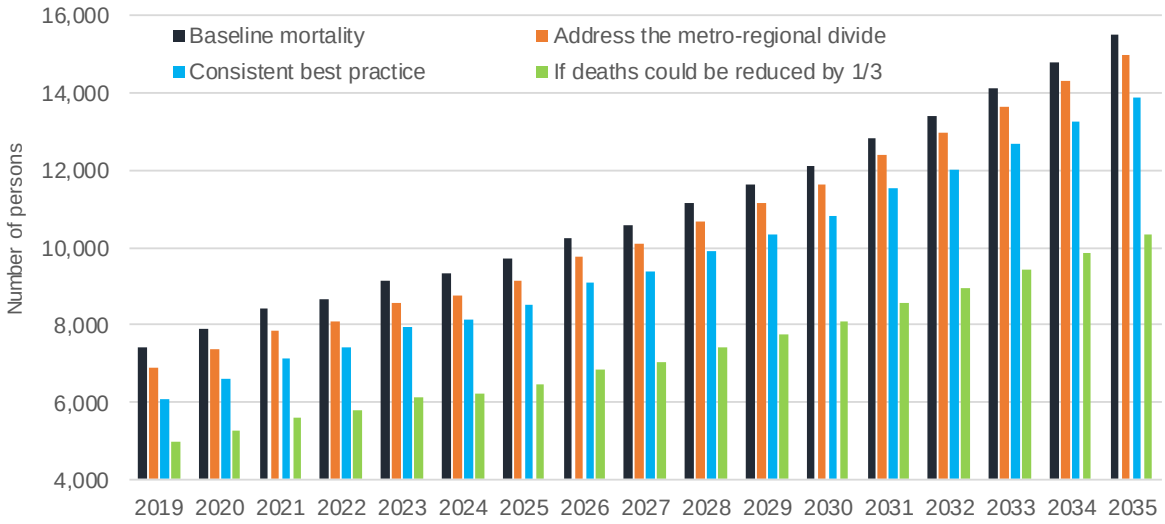
Figure 4.3: Reduction in deaths from blood cancer if there were no disparity in metro and regional survival outcomes



Source: Projections of Blood Cancer to 2035, See Appendix C.

In addition, if other variations in survival outcomes by State and territory were addressed, a further eight per cent of mortality could be reduced, yielding a total 13 per cent improvement on expected mortality based on current survival outcomes over the 2018-2035 period. [61] Compared to baseline projections, more than 22,000 deaths and more than 350,000 expected years of life lost could be prevented over the 2018 to 2035 period through more consistent implementation of currently available best practice (Figure 4.4).

Figure 4.4: Reduction in deaths from blood cancer if best practice in Australia consistently implemented, and potential to further reduce the number of deaths through further adoption of technology



Source: Projections of Blood Cancer to 2035, See Appendix C. Note the "Baseline" projections, "Address the Metro-Regional Divide" projections and "Consistent Best Practice" projections are based on AIHW and State Cancer registry data using technologies currently in use in Australia. The "1/3 reduction in deaths" is a scenario presented to show opportunities for further gains through adoption of other emerging technologies that are in use globally. Detailed analysis of technologies would need to be undertaken to more accurately assess this full potential.

[61] Note the years of life lost relative to the number of deaths for 'ensuring consistency in best practice' is lower than the years of life lost relative to the number of deaths for 'addressing the metro-regional divide'. This is a result of the 'mix' of blood cancers for which the differences in survival are reported, with outcomes for people living in rural areas tending to be reported for sub-types that impact on younger cohorts. Consequently, the death of a younger person equates to more years of potential life lost.

Even this could represent a conservative estimate for the potential reduction in the number deaths from blood cancer. While international survival benchmarking is not currently available, multiple stakeholders indicated that more consistent implementation of current best practice available globally, not just in Australia today, could reduce the number of deaths by potentially up to one third.

How can these benefits be realised? Ensuring more consistent implementation of consistent best practice will require a series of reforms and concerted action by blood cancer stakeholders. Fundamental, enabling opportunities include:

- Make blood cancer a non-infectious notifiable disease (discussed above)
- Reduce variation in treatment and care through the development of care pathways and clinical standards
- Make emerging genetic, genomic and other clinically important testing part of the standard of care
- Make consistent screening for supportive care referrals part of the standard of care
- Make clinical trials part of the standard of care
- Support the expansion of community-based care and tele-oncology
- Invest in workforce development.

These issues are considered in turn. Closely related to these issues are regulatory system reform and health financing reform, which are explored further in the following sections.

Address gaps in care pathways and clinical care standards

As noted by the Australian Commission on Safety and Quality in Health Care, clinical care standards can play an important role in delivering appropriate care and reducing unwarranted variation in service delivery, as they identify and define the care people should expect to be offered or receive, regardless of where they are treated in Australia.[62] To this end the Australian Commission on Safety and Quality in Health Care has developed a number of clinical care standards in Australia as part of its Clinical Care Standards Program; blood cancers are not currently included in this program.

Stakeholder consultations, available research and the survey of people living with blood cancer all point to potentially very significant variation in care leading to variations in survival outcomes, and quality of life. The survey indicated that depending on what State you lived in there would be potentially substantial differences in treatment choice (see Figure 3.18 in Chapter 3). Research in myeloma has similarly shown a patient's treatment setting influences whether transplant-eligible patients are recommended for transplant. In addition, the WhiMSICAL patient-entered database showed more than 37 unique first-line combinations of therapy for treating Waldenström's macroglobulinemia.

There is an opportunity for the Leukaemia Foundation to work with other blood cancer support groups, Federal and State governments, the Cancer Council and potentially the Australian Commission on Safety and Quality in Health to address extant gaps in care pathways and clinical standards of care.

[62] Australian Commission on Safety and Quality in Health Care, 2018, *Clinical Care Standards*.

It is important that in developing care pathways and clinical care standards that to improve not just survival but also quality of life that the pathways and standards incorporate recommendations that are evidence based for referrals to supportive care as well as post-treatment survivorship care pathways. (Evidence for closing key gaps in supportive care are discussed below).

Box 4.3: Opportunities to better support survivors

As more and more people survive their cancer, there is an increasing understanding of the need for supporting patients beyond active treatment.

When treatment ends, people often want life to return to normal as soon as possible, but may not know how, r they may want or need to make changes to their lives. Over time, survivors often find a new way of living. This process is commonly called 'finding a new normal' and it may take months or years.

The challenges related to survivorship include psychosocial challenges, financial challenges, nutritional challenges, managing side-effects and new needs for social and other practical support. For example:

- Emotional and family challenges — While most people adapt well over time to life after treatment, many people experience ongoing fears or concerns. Sometimes people find they need a lot of support – maybe even more than they did when they were diagnosed or during treatment. People can experience feelings of relief, isolation, fear, uncertainty, frustration, survivor guilt, anxiety, worry, lack of confidence, depression, heighted emotions, delayed emotions, and anger. After treatment is over, a person's family and friends may also need time to adjust. Research shows that carers can also have high levels of distress, even when treatment has finished. For children, they may struggle with the way family life changes after a cancer diagnosis. They may worry about the future or find it difficult to understand why life can't go back to the way it was before the cancer.
- Coping with side-effects — It can take time to recover from the side-effects of treatment. Side-effects can be both physical and emotional. They can vary depending on the cancer type and stage, and the treatment used. Some people experience late side-effects. These are problems that develop months or years after treatment finishes. They may result from scarring to parts of the body or damage to internal organs. Major concerns often include fatigue, pain, sleep problems, tingling or numbness in the hands or feet, and memory problems, as well as long term risks for cardiovascular problems, developmental delays (in children), immunosuppression and other late effects.
- Financial challenges — After any serious illness, people may have concerns about financial issues, insurance policies, superannuation and work. For many people, cancer treatment can be a financial strain. This may be caused by extra out-of-pocket costs for medicine or travel expenses, or from loss of income. These extra costs can cause people and their families a lot of stress. Applying for new insurance (life, income protection or travel) may be harder.
- Returning to work — Work is an important part of life for many people. Aside from income, work can provide satisfaction, a sense of normality, a means of maintaining self-esteem, and a chance to socialise. For some people, returning to the same job may not be possible due to changes in ability and length of time away. The desire to reduce work-related stress or seek more meaningful work may also motivate people to change jobs. If cancer or its treatment has made it impossible for a person to return their previous work, then rehabilitation and retraining programs can prepare these people for another job. Some people also experience discrimination and need support to respond.

There is help available, but without clear referral pathways for survivors many people risk falling through the cracks. Clearer and more consistent referrals to post-treatment care can improve the wellbeing of patients and support a better quality of life as a survivor.

Source: Based on information from Cancer Council Victoria, 2018, *Living Well After Cancer* accessed at: https://www.cancervic.org.au/downloads/resources/booklets/Living-Well-After-Cancer.pdf

Make systematic genomic and genetic testing part of the standard of care

Looking forward, more precise and less invasive diagnostics have the potential to improve patient outcomes and health system efficiencies, such as liquid biopsies (Box 4.4) and the increased use of genetic and genomic testing.

Box 4.4: Liquid Biopsies – an emerging opportunity for less invasive, more precise and less costly diagnosis

The liquid biopsy for blood cancers offers the promise of a new era of less invasive, more precise and effective management of blood cancers, in place of painful bone marrow or lymph node biopsies.

In 2017, researchers from Peter MacCallum reported in *Nature Communications and Blood*, liquid biopsies can be applied in clinical cases of CLL and MDS. The test monitors tiny fragments of DNA emitted from cancer cells into the blood stream, called circulating tumour DNA (ctDNA). Unlike traditional biopsies, ctDNA tests track

disease status throughout the body; can be used at any time over the course of cancer treatment; and enables rapid adjustments if a patient relapses or fails to respond to a particular therapy.

Current diagnosis from a single tissue biopsy from the bone marrow or lymph node does not accurately reflect the composition of the whole tumour as there is significant variation – so called intra-tumour heterogeneity – that exists between the individual cells that make up any cancer. ctDNA collected from a routine blood sample more accurately mirrors the disease across all parts of the body.

The emergence of liquid biopsies as precision cancer trackers has the potential to significantly reduce costs to our health system. For example, Peter Mac currently conducts some more than 800 bone marrow biopsies each year at around $2,500 per procedure, and patients undergoing the procedure are required to stay in hospital for up to six hours each time.

The ctDNA tests are expected to become a standard clinical tool in the near future.

Source: Peter MacCallum, 2017, *World-first liquid biopsy for blood cancers promises less invasive, more precise and effective treatments*, March 17, accessed at: https://www.petermac.org/news/world-first-liquid-biopsy-blood-cancers-promises-less-invasive-more-precise-and-effective

Over time, applications of Artificial Intelligence (AI) to scans will also be a more commonly used tool to improve the precision of diagnosis and support treatment decisions.

More systematic use of new diagnostic tests, including in particular genetic and genomic tests that already available today, represent a very substantial opportunity to improve survival outcomes and quality of life for people living with blood cancer. As shown in Chapter 3, a third or less of patients reported the use of genetic or genomic testing to guide diagnosis and treatment (Figure 3.14).

To understand the potential benefits of more systematic testing, it is worthwhile to use a real-world example of a test which is only philanthropically funded at the Christine and Bruce Wilson Centre for Lymphoma Genomics at Peter MacCallum. It is not funded through the MBS or by public hospitals.

As discussed in Chapter 3, Figure 3.26, the test provided clinically important information in 61 per cent of patients tested — changing their diagnosis, understanding of prognosis and treatment plan.

Consider the benefits of more widespread applications of this test. In 2019, it was expected that 12,570 people are likely to be diagnosed with a lymphoid malignancy.[63] Given the potential error rates suggested by the pilot data for lymphoid malignancy, these data suggest that in the absence of a genetic or genomic testing in 2019 alone:

- 3,900 people may be mis-diagnosed and inappropriately treated
- 5,500 people may be over- or under-treated
- 1,500 people could benefit from the selection of the best therapy for their specific tumour and genetic profile.

Some scenario analysis (presented in Table 4.1) can help show the rationale for regulatory reform to support the more rapid systematic update of tests to guide treatment. For example, the current cost of the next generation test is $600 per patient. To systematically test each patient with a lymphoid malignancy would bring the cost of the test to roughly $7.5 million per annum. On the benefits side there is the potential to extend life, improve the quality of life (from avoided side-effects) and avoid health

[63] The test is also used for myeloid malignancy but data was not available in the timeframes for this report.

system waste. Only very small changes in the health outcome need to be realised to justify the test. For example:

- *Extensions of life through better treatment selection* — If only 10 per cent of patients identified to have a directly targetable lesion saw an improvement in survival of one additional year (150 people gaining one more year of life), applying a value of $50,000 to these year of life gained would see the investment in the test break even. If a higher cost per QALY were assumed, or if more people received the right treatment compared to a counterfactual where no test was available, the benefit cost ratio would exceed 1.0.

- *Improved health system efficiencies* — A better understanding of prognosis allows for treatment choice that spares patients from interventions for potentially little gain. In particular the potential to avoid stem cell transplant could deliver an improvement to the health care system and patients. A 2009 study of the cost of allogenic and autologous bone marrow transplants estimated the cost per transplant in NSW ranged from $62,812 per autologous adult stem cell transplant to $227,286 per allogenic transplant in a paediatric hospital, with a weighted average of approximately $106,500 in $2009 (or $127,000 in $2018).[64] If only 1.1% of patients that might have been provided a stem cell transplant are spared this treatment, the test would break even holding all else constant. Because the cost of transplant is so high, the benefit cost ratio is very sensitive to the assumptions for the percentage of people who might avoid transplants.

Currently, however, this test is not funded, and so even though more than 12,000 patients could benefit in a year, only patients who happen to be in the right State, at the right treatment location, get access to this test. In the time to develop evidence to the required hurdles for wider listing between 25,000 and 69,000 people will be diagnosed with a blood cancer that could have potentially benefitted from the more precise understanding of their disease. Section 4.4 considers options for new approaches to evidence development to support systematic and equitable access to therapies while also having a strong focus on scientific rigour and evidence development.

As part of implementing more systematic care using genetics and genomic testing, as well as potentially other diagnostic therapies, the Leukaemia Foundation could also partner with groups like the Australian Genomics Health Alliance which are championing the issues related to ethics, legal and social issues of more systematic testing, including issues of consent for research, a moratorium on the use of genetic tests by the life insurance industry and continuing professional development for GPs in the use of genetic and genomic testing in routine clinical practice.[65]

[64] Gordon R, Thompson C, Carolan JG, Eckstein G, Rostron C, 2009, *A Costing Study of Blood and Marrow Transplantation Services in NSW: Final Report*. University of Wollongong Australia: Centre for Health Service Development, p 3
[65] See Australian Genomics Health Alliance, 2018, *Position Statement: use of information in life insurance and related-policies*, November.

Table 4.1 Scenario analysis of the value of Next Generation Sequencing using data from the Christine and Bruce Wilson Centre for Lymphoma Genomics

Population assumptions					
Number of people diagnosed with lymphoid cancer				12,571	
Diagnosis clarified for 31% of patients compared to no test				3,897	
Prognosis clarified for 44% of patients compared to no test				5,531	
Targeted therapy identified for 12% of patients				1,509	
Costs					
Cost per person		$600			
Total cost of systematic testing		$7,542,600			
Potential benefits					
Improvement in survival outcomes through better treatment selection					
	Number of people	Valued at $50,000/year gained	BCR	Valued at $70,000/year gained	BCR
Life extended by 1 year for 10% of patients through use of targeted therapy or earlier use	151	$7,542,600	1.0	$10,559,640	1.4
Life extended by 1 year for 15% of patients through use of targeted therapy or earlier use	226	$11,313,900	1.5	$15,839,460	2.1
Life extended by 1 year for 20% of patients through use of targeted therapy or earlier use	302	$15,085,200	2.0	$21,119,280	2.8
Health system efficiencies					
	Number of people	Valued at $127,000 per transplant	BCR		
Avoidance of transplants in 1% of population where prognosis clarified	55	$7,024,675	0.9		
Avoidance of transplants in 2% of population where prognosis clarified	11	$14,049,350	1.9		
Combinations of benefit					
		Value	BCR		
Life extended 1 Year for 10% and 1% avoidance in transplants		$14,567,275	1.9		
Life extended 1 Year for 15% and 1% avoidance in transplants		$18,338,575	2.4		

Source: Scenario analysis on data provided by Christine and Bruce Wilson Centre for Lymphoma Genomics at Peter MacCallum. Note BCR means Benefit Cost Ratio. A BCR > 1.0 indicates the benefits of an action exceed the costs. A BCR of 1.0 exactly indicate the benefits and the costs are equivalent. A BCR of less than 1.0 indicates the costs exceed the benefits.

Make consistent screening and referral to supportive care part of the standard of care

As discussed in Chapter 3, outside of the optimal care pathways developed by Cancer Council Victoria for AML and Lymphoma, supportive care tends to be defined narrowly as physical care needs, including in particular infection control. This is not to diminish the importance of these care needs, but a broader definition of supportive care is important to patients and has been shown to improve survival outcomes for some patient cohorts.

In particular, stakeholder consultations and the survey indicated that while more could be done across a range of areas, there are two major gaps in referrals and access to supportive care:

- Rehabilitation (physiotherapy), which helps patients to manage fatigue
- Psychosocial services.

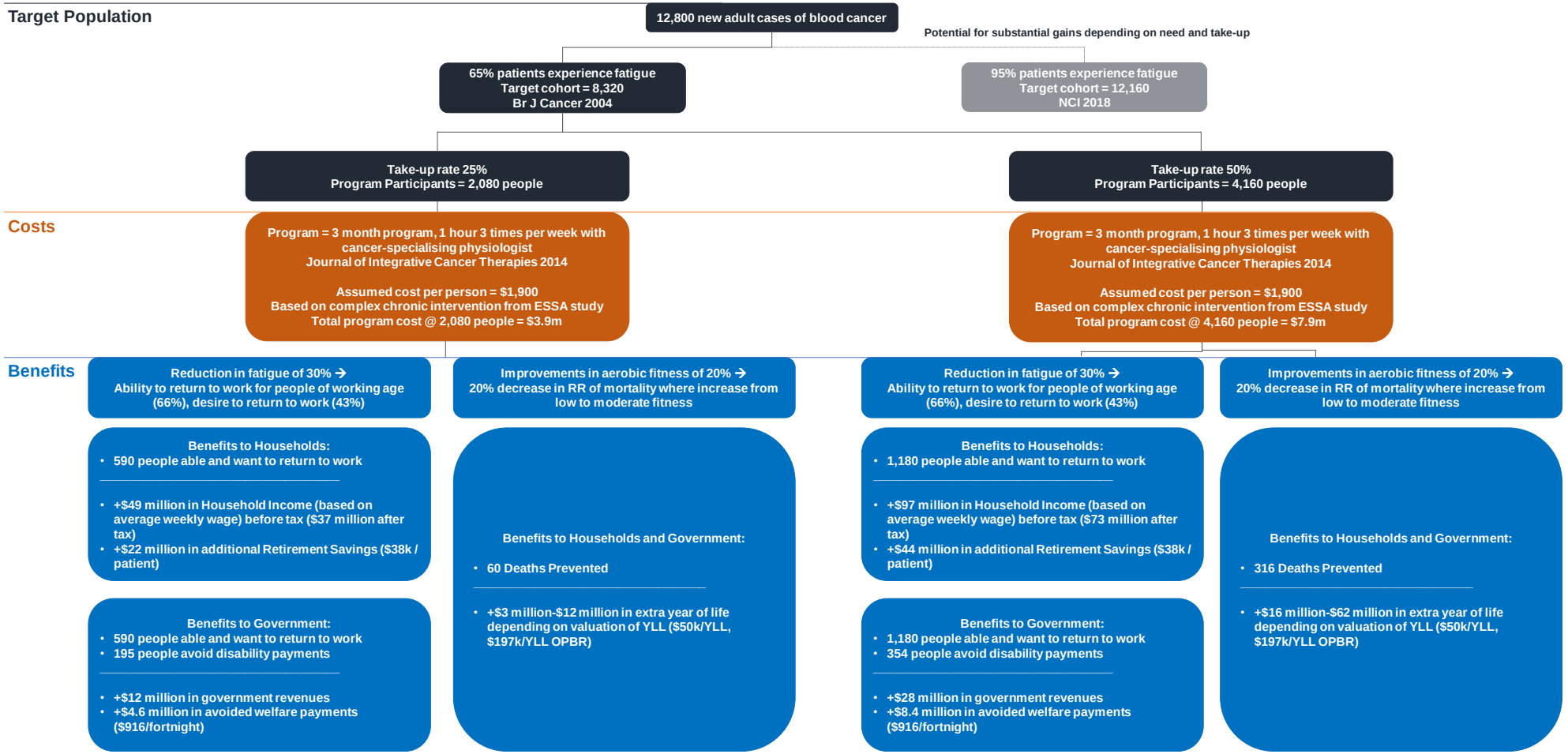
These were the issues where there was likely to be the biggest gaps between discussions about supportive care, and what patients had wished had been discussed. It was also likely that patients would 'fall through the cracks' in referral to both types of care.

For example, with respect to rehabilitation, clinicians acknowledged there is a 'hole' in the care model, where even if patients are referred to a program they may be rejected because they are immunocompromised and assessed to be too sick. A cancer-friendly rehabilitation program was seen as a major opportunity to improve quality of life through reduced fatigue and survival outcomes through improved aerobic fitness.

Using a conservative study of an exercise program for blood cancer patients in 2014, and conservative estimates of the cost per patient to deliver the program (a 2015 report into the benefits of exercise physiology for the Exercise & Sports Science Australia estimated the costs per person could range from $580 for a diabetes intervention program to $1,900 per person for complex chronic disease management)[66] the costs and benefits of a potential program are explored in Figure 4.5 below.

[66] Exercise & Sports Science Australia, 2015, *Value of Accredited Exercise Physiologists in Australia*, p75.

Figure 4.5: Potential benefits and costs of cancer-friendly rehabilitation program



Sources: Schmid D, and Leitzmann MF, 2015, 'Cardiorespiratory fitness as a predictor of cancer mortality', *Annals of Oncology*, Volume 26, Issue 2, 1 February 2015, Pages 272–278; National Cancer Institute, 2013, *Information from PDQ for patients*; Wagner LA, Cella D, 2004, 'Fatigue and cancer: causes, prevalence and treatment approaches', *Br J Cancer*, 2004;91:822-828; Repka CP, Peterson BM, Brown JM, et al, 2014, 'Cancer type Does Not Affect Exercise Mediated Improvements in Cardiorespiratory Function and Fatigue', *Journal of Integrative Cancer Therapies*, Volume 13 issue: 6, p 473-481; Exercise & Sports Science Australia, 2015, *Value of Accredited Exercise Physiologists in Australia*, p75; McKell Institute, 2018, *Our Health Our Wealth: The Impact of Ill Health on Retirement Savings in Australia*, August 2018; ABS Cat. No. 6302; Department of Human Services, *Disability Payment rates for Disability Support Pension*.

The scenario analysis in Figure 4.5 shows that even at high per person rates a cancer-friendly exercise physiology program offers the potential to improve survival outcomes, with between 90 and 190 people expected to survive compared to no intervention, depending on take-up rates. In addition, to the extent that a reduction in fatigue helps people return to work – in addition to the quality of life improvements associated with reduced fatigue which were not valued – this creates a range of tangible economic benefits to households (in the form of increased income and retirement savings) and the wider community through reduced demand for disability support compared to what would otherwise have been the case, which allows government to redirect these scarce funds to other uses, thereby improving the productivity of government services. Working with both governments and private health insurers to expand access to programs has the potential to deliver very significant gains to the community.

Similarly, more consistent referral to psychosocial support also offers the potential for improvements in survival outcomes and quality of life. As explained in Chapter 3, a 2015 study into depression in cancer patients found the rate of depression to be likely more than 10 per cent of patients. [67] This accords with the patient reported outcomes in the WhiMSICAL database. A 2009 meta-analysis found that minor or major depression increases mortality rates by up to 39 per cent, and that patients displaying even few depressive symptoms may be a 25 per cent increased risk of mortality.[68]

If 1 in 10 of the survivors at the end of year-1 display some form of depressive symptoms this equates to potentially 850 people each year that require screening for psychological services. For patients with chronic or community-based treatments stakeholders indicated that the likelihood of these patients 'falling through the cracks' are far higher. While the balance of chronic blood cancer is higher than acute sub-types, if only half of patients were at high risk this would identify 425 people each year that, if not screened are at a higher risk of mortality. Because referral rates are not known, it is not possible to identify the additional patients that could be more systematically captured to reduce the risk of mortality. With the current Office of Best Practice Regulation guidance indicated the value of a statistical life year is $4.2 million, only a few people would need a successful intervention to break even on a more systematic screening and referral of high-risk patients.

Make clinical trials part of the standard of care

As discussed in Chapter 3, current rates of referral to clinical trials are low. The reasons for this are complex, including lack of clinician time, lack of funding, and sometimes limited incentives for industry to open a trial site due to inability to recruit patients, high costs relative to total patient recruitment numbers and reimbursement frameworks (offsetting Australian advantages in quality). As a consequence, the most common reason for non-participation in a clinical trial was because the specialist did not discuss it. While other policies are required at the research end to address the above issues (See Section 4.5 below), making clinical trial participation a standard of care and measuring outcomes through KPIs for clinical trial participation represent a major opportunity to overcome inertia and other hurdles to increase patient participation in trials.

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[67] Smith H, 2015, 'Depression in cancer patients: Pathogenesis, implications and treatment (Review)', *Oncology Letters*, 2015 Apr; 9(4): 1509–1514.
[68] Satin JR, Linden W, Phillips MJ., 2009, 'Depression as a predictor of disease progression and mortality in cancer patients: a meta-analysis'. *Cancer*. 2009;115:5349–5361. doi: 10.1002/cncr.24561.

Support the expansion of community-based care and telehealth

The potential for the expanded use of community-based care and telehealth also represents a major opportunity to improve treatment and care of patients. Research by the Clinical Oncological Society of Australia (COSA) has indicated that tele-oncology models of care have been shown to satisfy many specialist health care needs of rural and regional patients in countries with large rural populations and has developed in partnership with the Cancer Council clinical guidelines for using telehealth in the delivery of supportive care.[69] In addition, cancer services can be delivered to patients closer to home in a timely manner. Emerging tools such as chemo@home, real-time remote monitoring of patients, tele-consults for routine consults, and other options offered the possibility of improving outcomes for people in remote areas (Box 4.5). Looking forward, these models will increasingly be expanded to patients nationally.

Box 4.5: Tele-oncology models in development

Case study: Tele-oncology in public settings

The Townsville tele-oncology model enables medical oncologists from Townsville, Australia to provide their services to rural sites, using traditional video-conferencing technology or web-based systems. At larger rural centres, rurally based doctors, chemotherapy competent nurses and allied health workers accompany patients during tele-consultations. At other rural sites, patients are accompanied by either a doctor or a nurse for post-treatment reviews, toxicity reviews or follow-up visit(s) tele-consultations.

Case study: Tele-oncology for private patients: chemo@home

BUPA and Medibank patients are able to access a range of cancer treatments at home, including chemotherapy, targeted cancer therapies, bone strengthening medications, infusions for chronic conditions, and antibiotics. The cost of the treatment at home is met without a gap payment.

Chemo@home is owned, managed and staffed by nurses and pharmacists and supported by a 24 hour a day telephone service.

Case study: Monitoring and improving adherence to therapy in clinical trials

Adherence to therapy ensures that the effect of an investigational drug is fully reflected in the data. However, high adherence rates can be hard to achieve and verify using traditional methods. A senior scientific director at a midsize biopharma company describes the problem: "We found that based on blood samples on the pharmacokinetic monitoring, 35–40 percent of patients had no drug on board. This drug had a half-life of 5.5 days. This meant those patients didn't skip just one dose, they hadn't taken the drug for up to two weeks." Adherence tools such as AiCure use facial recognition to confirm that the medicine has been ingested and generate non-adherence alerts to investigators.

Sources: COSA, 2016, *The COSA Tele-oncology Guidelines: Evidence-based guidelines for using telehealth in the supportive care of oncology patients*, accessed at: https://www.worldcancercongress.org/sites/congress/files/atoms/files/Pre0138-Ward%20Liz.pdf; COSA, 2018, Clinical Practice Guidelines for Tele-oncology accessed at: https://wiki.cancer.org.au/australia/COSA:Teleoncology'; BUPA, 2018, chemo@home research papers, http://chemoathome.com.au/research/publications/.

Stakeholders reported a strongly positive response to these service innovations, but these perspectives were also weighed against equal parts of caution for how they are implemented. In particular, chemotherapy for people with blood cancer can result in distressing and potentially life-threatening toxicities and side-effects,[70] and without appropriate specialist support in the region this can put patient safety at risk. (Figure 4.6). These challenges are not insurmountable, and COSA research has identified

[69] COSA, 2016, The COSA Tele-oncology Guidelines: Evidence-based guidelines for using telehealth in the supportive care of oncology patients, accessed at: https://www.worldcancercongress.org/sites/congress/files/atoms/files/Pre0138-Ward%20Liz.pdf; COSA, 2018, *Clinical Practice Guidelines for Tele-oncology* accessed at: https://wiki.cancer.org.au/australia/COSA:Teleoncology

[70] Breen, S, Kofoed, Ritchie, Dryden, Maguire R, et al, 2017, *Remote real-time monitoring for chemotherapy side-effects in patients with blood cancers*.

international examples that have implemented safe tele-oncology models that have been acceptable to patients, families and health professionals and can enhance the capabilities of rural health systems in oncology services to provide cancer care. There was a consensus that the effective roll-out of tele-oncology over time will depend on the full implementation of a 'hub and spoke' model for cancer care, with a regional cancer care centre able to support patients if community-based care resulted in complications.

Figure 4.6: Stakeholder perspectives on ideas for increasing community-based care and tele-oncology

In addition, as more and more care is delivered in community-based settings, there will be increasing opportunities for the private sector to play a role. Government will need to establish minimum standards of care for the provision of these services to ensure consistency and quality in care delivery.

Invest in Australia's health workforce

Fundamental to improvements in the consistent use of clinical best practice is continuing professional development of GPs and investment in the required computational biologists to support haematologists in expanded genetic and genomic data analysis. Partnering with the Department of Health and Ageing, Haematological Society of Australia and New Zealand (HSANZ), the Australian Medical Association (AMA) and Australian Genomic Health Alliance to support collaborative efforts for increasing the supply and capabilities of the workforce in the context of increasing use of precision medicines will support the more consistent implementation of clinical care guidelines.

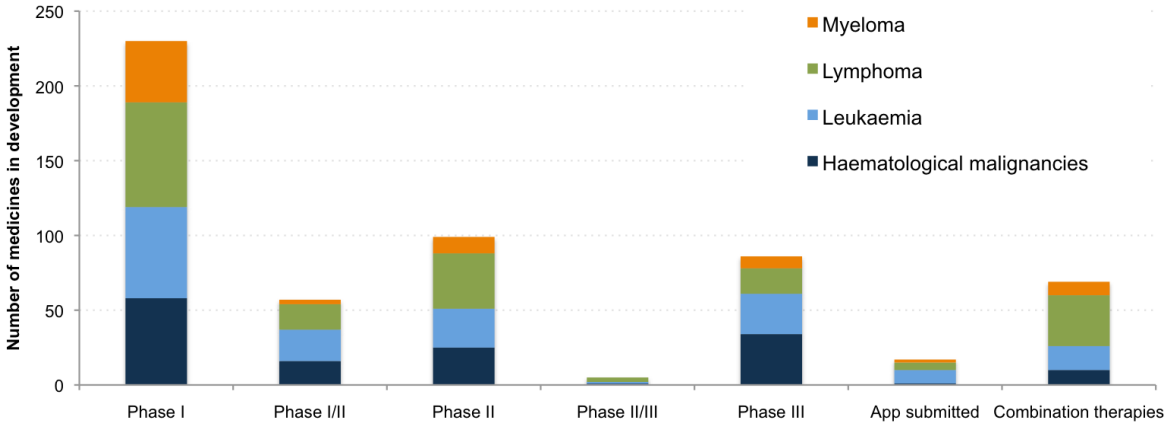
Moreover, there are also opportunities to improve the delivery of community-based palliation to blood cancer patients at the end of life, including in particular children; several stakeholders indicated further sub-specialty training would improve the delivery of these service.

4.4 Reform Regulatory Systems to Support Evidence Development and Timely Access

Significant new advances in less toxic, curative therapies and precision medicine are emerging and the pipeline for new therapies is significant.

In a May 2018 report on the pipeline of cancer medicines in the US, PhRMA reported that more than 490 new medicines are in development for blood cancers, including 145 new medicines for leukaemias, 149 for lymphoma, 135 for other haematological malignancies, and 65 for myeloma. Of these, approximately 14 per cent were developed to be used in combination with other therapies. Moreover in 2017, the FDA approved 18 novel therapies and in 2018 more than 6 have also been approved (Figure 4.7).

Figure 4.7: More than 490 new blood cancer medicines currently in development



Source: PhRMA 2018 Pipeline of New Cancer Medicines

Noting that FDA approval is not equivalent to public subsidy for therapies and there are significant differences in the healthcare systems, enabling access to these therapies as they become available holds the potential to substantially improve survival outcomes and quality of life for people living with blood cancer.

As shown in Chapter 3, issues of access are commonly discussed as if there were a single 'access' issue, when in fact different products are at different stages of clinical development with varying maturity of evidence. These variable issues require a differentiated policy response (Figure 4.8).

For example, for medicines that are in use for other conditions that perhaps target a similar genetic mutation (such as BCL-2 or PD1 inhibitors) but for which there is very little evidence (pre-clinical or Phase I) to support usage or 'repurposing' for a different blood cancer sub-type, there are opportunities to evaluate these therapies through a research program, such as the International Blood Cancer Research Mission (see Section 4.5).

At the other end of the spectrum, barriers to access to high cost combination therapies will likely require a range of policy responses, including enhanced patient engagement on the costs relative to the potential value in order to engage in an informed discussion of the trade-offs. This could be ideally supported by patient reported outcome data to support more rigour in the analysis of the benefits and costs. Ultimately, there may be very high cost therapies which do not meet government tests for cost-effectiveness which is a function of a rationed, universal healthcare system. There could be some policy options for a partial subsidy, such as a capitated payment, but this would require evaluation of the potential equity implications and any risks for distortions in the PBS and MBS reimbursement systems.

Figure 4.8: Potential policy responses to different access and evidence challenges

Access consideration	Therapy in use for other indications but very little evidence (Pre-clinical or Phase I) for blood cancer indication	Therapy approved and/or in use for other indications or overseas for blood cancer indication, but limited evidence (Phase II)	Novel therapy is standard of care overseas but no submission to Australian market due to market failures and/or does not meet Australian cost-effectiveness thresholds (Phase II or Phase III data)	Combination therapies are standard of care overseas but does not meet Australian cost-effectiveness thresholds and/or no sponsor submission due to market failures or submission risks (Phase II or Phase III data)
Current state-of-play for Australian patients	Access dependent on: 1) Pharma opening a clinical trial site, or 2) Funding for investigator led trial While Australian research quality consistently cited, pharma not always willing to bring trials to Australia and funding for investigator-led trials limited - Complicated and long lead times for ethics and governance - Inconsistent testing, siloed data slows patient recruitment - Contributes to cost Safety issues limit options for 'tele-trial' innovations	Where market incentives are inadequate to develop evidence and/or seek listing, clinicians and/or patient organisations must prepare submission. But this relies on access to data, so patients can be caught in catch-22. No formal mechanisms for capturing real world data (e.g., of off-label use) and potentially heroic 'gladiator' type model assumptions for clinicians to champion products through regulatory processes. If medicine/service not listed, cost is generally unobtainable for most Australians. This creates risk of a two-tiered system where patients with means access therapies in Australia or by travelling overseas and other patients do not.	Where market incentives are inadequate to develop evidence and/or seek listing, clinicians and/or patient organisations must prepare submission. But this relies on access to data, so patients can be caught in catch-22. No formal mechanisms for capturing real world data (e.g., of off-label use) and potentially heroic 'gladiator' type model assumptions for clinicians to champion products through regulatory processes. If medicine/service not listed, cost is generally unobtainable for most Australians. This creates risk of a two-tiered system where patients with means access therapies in Australia or by travelling overseas and other patients do not.	Where market incentives are inadequate to develop evidence and/or seek listing, clinicians and/or patient organisations must prepare submission. If medicine/service not listed, cost is generally unobtainable for most Australians. This creates risk of a two-tiered system where patients with means access therapies in Australia or by travelling overseas and other patients do not. Low level of understanding among patients and community regarding benefit cost trade-offs being made by government.
Examples	Venetoclax for CML in blast crisis; currently no therapy for these patients. RAH sought participation in trial running at MD Anderson but pharma reluctant to open site with only single patient likely to present at RAH over year	Off-label medicines & compassionate access • Venetoclax for Ph+ALL, AML • TKIs for ALL(dasatinib and ponatinib just listed at Nov meeting after long delay) • CAR-T for AML • PD-1 checkpoint inhibitors for AML	Off-label medicines & compassionate access • Ibrutinib for 1st line CLL, Waldenstrom's • Venetoclax for 1st line CLL indications • Daratumumab for multiple myeloma • Blinotumumab 1st line for ALL	Off-label medicines & compassionate access Combination therapies for multiple myeloma (lenolidomide, daratumumab, carfilzomib), leukaemias, lymphomas
Government & clinician concerns	• Patient safety • Need for a clear signal of benefit (e.g., MRD outcomes, safety in at least 5 patients)	• Does not meet PBS/MBS evidence requirements • Equity concerns • Patient safety • How to advance science and not pursue 'scattergun' approach	• Equity concerns • PBAC/MSAC are submission driven • May exceed PBS cost-effectiveness thresholds • Co-dependent diagnostic challenges • Evidence for cellular therapies as services • Risk of high costs, particularly for targeted therapies which patients must take for the rest of their lives	• Risk of astoundingly high costs, particularly for targeted therapies which patients must take for the rest of their lives, which exceed PBS cost-effectiveness thresholds • Co-dependent diagnostic challenges • Evidence for cellular therapies as services • Equity concerns • PBAC/MSAC are submission driven • Challenges when multiple companies involved
Potential Policy Options	**International Blood Cancer Research Mission** focused around pre-accredited centres of excellence linked into international clinical trial research programs, especially targeted at emerging curative therapies	Systematise off-label prescribing to support evidence development through **"Right to Trial"** program for therapies meeting key eligibility criteria (esp for curative therapies which may have different cost projections over time) **linked to International Blood Cancer Research Mission** - Supported by **Real World Evidence collection and reporting**, captured through new billing codes **International Blood Cancer Research Mission** could **include FTE for submission support** to at trial sites	Patient education and engagement Systematise off-label prescribing to support evidence development through **Real World Evidence pilot** to support patient and clinician listings, linked to **Fundamental and Translational Research Program** **Right to Trial program** linked to International Blood Cancer Research Mission PBS/MBS Coverage with Evidence Development / Managed Entry Scheme / Pan-tumour indications	Patient education & engagement around cost issues Systematise off-label prescribing to support evidence development through **Real World Evidence pilot** to support patient and clinician listings, linked to **Fundamental and Translational Research Program** **Right to Trial program** linked to International Blood Cancer Research Mission PBS/MBS Coverage with Evidence Development / Managed Entry Scheme

In between these two extremes are examples of where a medicine is in use overseas but there is either:

- Good evidence of a potential benefit but which does not meet PBS or MBS evidence requirements
- Strong evidence but a lack of market incentives to make a submission for listing and/or issues related to sponsor listing strategies to maintain a global benchmark prices.

During consultations and the review of international variation, there were a number of medicines where there were early signals of evidence for benefit, but there had been substantial delays between these signals and PBS listing. Box 4.6 shows an example of a therapy where there was evidence of benefit in 2013 with publications in the *Journal of Clinical Oncology* and others, but Australian patients did not see a listing until 2018.

Box 4.6: Case study of therapies that could benefit from new approaches to evidence development: TKIs in ALL with ABL1

Tyrosine Kinase Inhibitors for all newly diagnosed ALL patients with ABL1/ABL2 and CSFR1 associated gene fusions

Although more than 80 per cent of children who are diagnosed with ALL experience favourable clinical outcomes, a substantial number of children have high risk disease with an increased probability of relapse and poor prognosis. Genetic alterations, including chromosomal rearrangements and deletions are important determinants of leukemogenesis and responsiveness to therapy. The ability to identify high risk patients at the time of diagnosis would enable clinicians to select more targeted therapies and improve survival.

For example, patients with BCR-ABL1 positive ALL generally respond poorly to conventional chemotherapy, but research in 2013 indicated that outcomes could be improved with the addition of Tyrosine Kinase Inhibitors (TKIs) such as imatinib, nilotinib, dasatinib, ponatinib that target the myristate inhibitor ABL001.

Research in 2013 showed that for patients with this genetic profile they were unlikely to survive, but the use of TKIs holds the potential to functionally cure these patients. A case study was published in 2013 *Journal of Clinical Oncology* of a 10-year-old boy that had presented with a 3-week history of low-grade fever and fatigue. The patient was diagnosed with B-cell ALL and treated with a four-drug induction chemotherapy of intrathecal cytarabine, intravenous vincristine, daunorbicin, PEG asparaginase and oral prednisone.

By day 11, the boy developed slurred speech, visual hallucinations, seizures, and unresponsiveness.

Reverse transcriptase PCR (a genetic test) identified genetic mutations with the potential for aberrant tyrosine kinase activation with the involvement of a growth factor receptor called PDGFRB. On day 29, the boy was prescribed imatinib in combination with chemotherapy.

After only 14 days, the boy's bone marrow aspirate showed complete remission, with minimal residual disease in the marrow reduced to 0.059%.

High dose chemotherapy which has significant off-target effects for patients including cardiovascular issues, infections due to immunosuppression, developmental delays in children, among others.

Even with these positive signals for use of TKIs as far back as 2013, listing for this medicine was not made until 2018. In that time just under 500 people have been diagnosed each year with ALL in the past five years, and LLS reports prevalence of AB1 mutations of 25 per cent in adult cohorts and 3 per cent in paediatric. While a substantial proportion have good survival outcomes overall, people with these genetic mutations did not, and were prescribed with chemotherapy even as alternatives were emerging because there was no real mechanism for listing outside of the PBS. A policy that targets this risk by enabling access to accelerate evidence development could help to prevent deaths. A Right to Trial program as proposed below could support evidence development for the test (PCR) and therapy.

Source: Weston BW, Hayden MA, Roberts KG, et al, 2013, 'Tyrosine Kinase Therapy Induces Remission in a Patient with Refractory EBF1-PDFRB-Positive Acute Lymphoblastic Leukaemia', *Journal of Clinical Oncology*, 31, no 25 (September 2013), e413,e416

It would be easy to dismiss this example, by saying: 'Well it's listed now, so what's the issue?'

However, this is just one of a number of examples. While the use of TKIs for ALL sub-types were recently listed, today other unsubsidized examples exist, where evidence is available to support re-purposing, or a therapy is in use overseas as the standard of care overseas, but fails to meet PBS evidence hurdles or there are a lack of market incentives to list such that there may be substantial delays between use overseas and Australia. As shown in the international benchmarking reported in Appendix A, which was based on Optimal Care Pathways by the Cancer Council, eviQ and PBS listing information, ESMO clinical guidelines and NICE clinical guidelines in the UK, and supported by Australian clinical review, current examples include:

- PD1 checkpoint inhibitors for AML
- Ibrutinib for first line CLL and small lymphocytic leukaemia
- Daratumumab and combination therapies for myeloma
- CAR-T therapies for AML and Follicular Lymphoma
- Brentuximab, nivolumab and pembrolizumab for relapsed Hodgkin lymphoma
- Brentuximab T-Cell Lymphoma
- Romidepsin for Peripheral T-Cell Lymphoma
- Rituximab for post-transplant Mantle Cell Lymphoma
- Venetoclax as a first-line treatment or treatment for relapsed/refractory treatment for a number of sub-types (at the time of writing there was a recommendation for a PBS Authority listing for limited CLL cohorts only)
- A range of therapies used for the treatment of cytopenias in Myelodysplastic Syndrome
- Next generation genomic sequencing to inform diagnosis and treatment for lymphoid and myeloid malignancies.

Taken together, one can see that the challenge of access to novel therapies which are in routine use globally affects almost every blood cancer sub-type today.

Interviews with government indicated that there was an increasing understanding of this issue and blood cancers that had once been "invisible in the system". Moreover, as one government stakeholder noted: "A malignancy is different to other conditions; they don't have the time that say people with high blood pressure have, where they can wait for the system to sort itself out."

As noted by the Senate Inquiry into access to new cancer medicines, if these therapies are not publicly subsidised they are out of reach for most Australians which creates concerns for equity. Ideally, these patients would be able to join a clinical trial, but less than 1 in five or potentially less than 1 in 10 patients participate in clinical trials and four out of five patients report it is not even discussed.

Importantly, there was a consistent concern among stakeholders not to dilute the rigour of the PBS, but rather to support it through an enhanced

R&D process targeted at repurposing medicines where there were signals of clinical benefit and where there may not be a commercial incentive to bring a submission by industry.

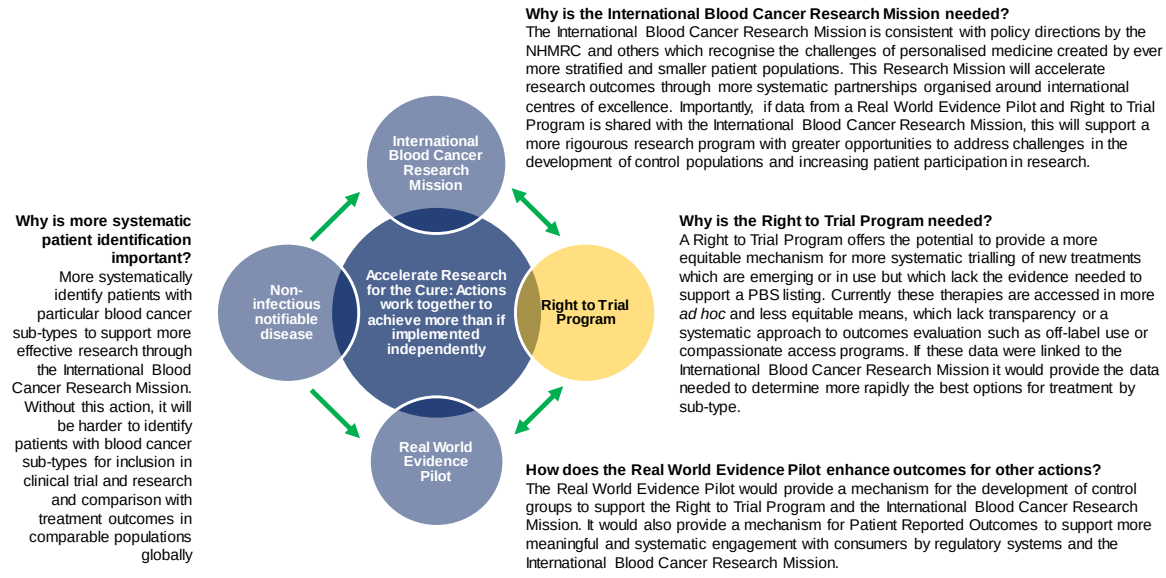
To this end, a Right to Trial program could support more systematic evidence development and clinician-led or patient-led submissions for new therapies. This would provide a mechanism for the more regular and systematic use and evaluation of off-label medicines, and could reduce dependence on industry to conduct the research needed to advance potentially curative therapies.

The Right to Trial Program would need to be developed to ensure that therapies accessed through the program met required eligibility criteria, such as the criteria used to determine off-label use, or applications for compassionate access, where safety criteria can be prescribed and met, and are in routine use already today. In addition, there would need to be clear entry and exit timelines to limit potential unintended consequences vis-a-vis the PBS. This would provide a more systematic and scientific mechanism for the evaluation of medicines that are used off-label and more equitable access to emerging therapies.

Such a program, properly designed, would reduce inequities of access to therapies where evidence is in development. Moreover, while the program could be piloted for blood cancers it could easily be extended to a wider range of conditions over time; it need not be blood cancer specific.

Importantly, the data from the program could ideally be connected to an International Blood Cancer Research Mission (Section 4.5) and build upon the work of the MRFF (Box 4.6), which could accelerate advances in diagnosis and treatment. Similarly, a Real World Evidence pilot in the MyHealthRecord, which could demonstrate the benefits of the health record for its users and support the science through the development of control groups for the Right to Trial Program. Ideally the programs could be developed with reference to each other in order to enhance the outcomes from each.

Figure 4.9: A Right To Trial Program Supported by a Real World Evidence Pilot in the MyHealthRecord and an International Blood Cancer Research Mission could accelerate research for a cure



4.5 Accelerate Research for Curative Therapies through an International Blood Cancer Research Mission

Since the completed mapping of the genome in 2003 and the identification of the Philadelphia chromosome in patients with CML in 2001, there has been a rapid advance in the understanding of blood cancers at a molecular level and the increasing development of novel therapies that are changing the prognosis for many blood cancers from a likely less-than-five year survival outcome following a brutal cytotoxic chemotherapy regimen, to a chronic disorder that can be managed with a targeted oral therapy with fewer off-target effects.

Figure 4.10: Stakeholder perspectives on the prospect of significant advances in blood cancer

Where disease can be well managed through drug therapies or cell engineering this also holds the potential for the avoidance of transplant.

Further advances have been made in the development of immunotherapies and other curative therapies, such as CAR-T therapies, which hold the promise of a limited number of services rather than a lifetime of drug therapy, and even fewer side-effects. For example, PhRMA in 2018 summarised the next generation of major scientific advances in blood cancers to include:

- *CAR-T therapies* — Following approval in Europe in August, NHS England has announced it will fund the routine use of CAR-T immunotherapy for patients under the age of 25 with refractory ALL. CD19-targeted CAR-T cells have produced strong results in patients with lymphomas. For example, in a small NCI-led trial of CAR-T cells primarily in patients with advanced diffuse large B-cell lymphoma, more than half had complete responses to the treatment. Similarly, LLS in 2018 announced funding for 'off the shelf' CAR-T cell therapies AML that promises to stave off rejection of donor cells. LLS has also funded

myeloma researchers to test treatments combining CAR-T and bi-specific antibodies (those that target two proteins at once).

- *Oncolytic viral therapies* — Myeloma has been especially targeted by oncolytic viral therapy because the standard of care repeatedly failed to prevent relapse in the long term. At the Mayo Clinic in the US, a Phase I clinical trial of a viral therapy showed efficacy and disease regression among the patients treated. At the same clinic, US virotherapy company Vyriad is currently undertaking a Phase I trial on NCT03017820 for previously treated or recurrent myeloma, as well as patients with T cell lymphoma and AML.

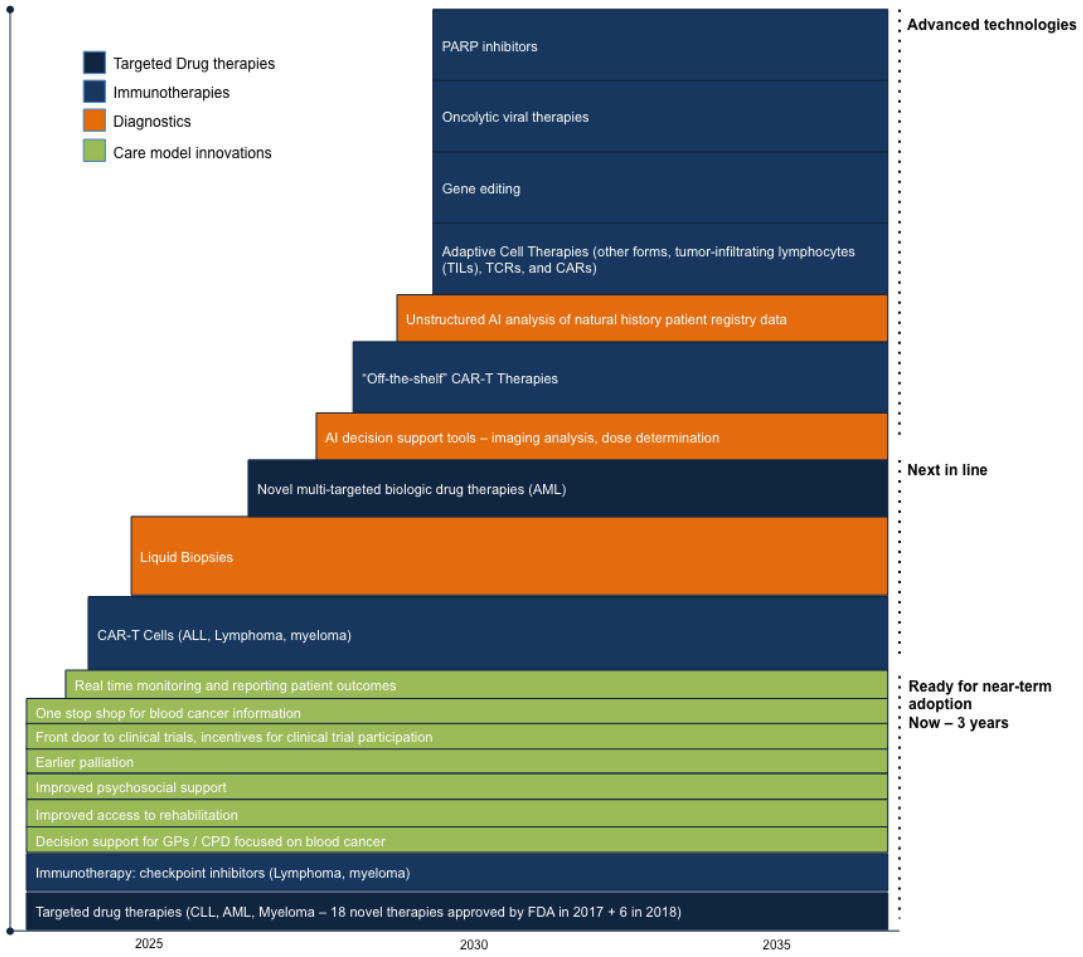
- *CRISPR gene editing* — Human trials are underway for myeloma in the US. The US trial conducted by the University of Pennsylvania involved deleting two genes in patient's NYCE T-cells to make them more effective at targeting and killing cancer cells. The LLS has also funded trials to identify how a mutation called DNMT3A contributes to the development of AML as well as another study that uses genetic profiling to detect leukaemic stem cells in AML.

- *PARP inhibitors* — For example, one PARP inhibitor approved for women with ovarian, fallopian tube and peritoneal cancer, olaparib, is being investigated in a Phase I/II trial for blood cancer patients with CLL, T-prolymphocytic leukaemia and mantle cell lymphoma. HMRI has shown that leukaemia cells with high levels of BAALC are sensitive to PARP inhibitors. Clinical trials are planned for high BAALC-expressing childhood leukaemias

- *Preventative therapies* — LLS-supported researchers are using immuno-positron emission tomography to detect myeloma cells in patients with pre-myeloma conditions, or in post-therapy cells.

Accelerating advances in these therapies has the potential to further reduce the mortality, health and economic costs of cancer, which are projected to claim more than 186,000 lives between now and 2035 and more than 1.4 million years of life lost.

Figure 4.11: Accelerating a pipeline of new advances through International Blood Cancer Research Mission



The pursuit of a cure for blood cancers will require greater collaboration in research than ever before, and is arguably more important for Australians than other, larger markets (See Section 3.2).

While it would be unrealistic to expect Australia to lead the way in the cures for all sub-types given its relative market size, it would also be untrue to assume that Australia has no role to play in the path towards the cure. For example, Australia offers important capabilities in:

- Centres of excellence in a number of blood cancer sub-types, with local research institutes ranked among the top centres internationally for a number of blood cancers, including (but not limited to):
  - The Alfred Hospital for technologies for the treatment of Myeloma
  - The Queensland Institute for Medical Research and QIMR Berghofer in stem cell transplant and other technologies
  - South Australia Health and Medical Research Institute in therapies for the treatment of CML and ALL and fundamental research in blood cancer genomics
  - University of Sydney and Westmead Hospital in CAR-T cell therapies and novel gene therapies

  - Walter and Eliza Hall Institute for clinical translational in advanced and aggressive leukaemias and lymphomas
  - Queensland University and Queensland Diamatina Institute in immunotherapies for lymphomas
  - Translational Research Institute Australia in Queensland in genomics and novel immunotherapies, with a specialisation in CLL
  - Harry Perkins Institute of Medical Research in Western Australia in a range of cellular therapies
  - The Children's Medical Research Institute in Sydney in childhood cancers
  - Peter MacCallum Cancer Centre for translational research in blood cancer genomics and treatment.
- Patient recruitment for meaningful sample sizes as part of international research in blood cancer sub-types
- The potential for national data development and analysis leveraging the MyHealthRecord.

There are a number of models at a domestic level that could be evolved into a global model for international research collaboration. For example:

- The benefits of organising around a common goal have been demonstrated through the NIH's Rare Diseases Clinical Research Network in the US, which has been designed to accelerate medical research for rare diseases by supporting fundamental and clinical studies and facilitating collaboration, patient enrolment and data sharing across network nodes. Critically, NORD reported in 2018 that the NDCRN had developed three new therapies for rare diseases as a result of the collaboration.
- Similarly, Trials Acceleration Program in the UK uses a hub and spoke model with 13 hubs nationally to conduct shared research. All trials work through the hub to get the right number of patients and there is a dedicated local clinical trial unit (CTU) at each site who develop local relationships and support the trials. This reduces the time to trial and supports their participation in global clinical trial research.

Reflecting the challenges and opportunities of blood cancer, an International Blood Cancer Research Mission could be developed in partnership with major Australian research funders, such as the Leukaemia Foundation, Snowdome and the Lions Club, as well as international research partners such as the LLS in the US and Bloodwise in the UK, with the potential to seek matched funding from government as a public private partnership.

The International Blood Cancer Research Mission would facilitate more formal links as between domestic and international nodes of research excellence by blood cancer sub-type.

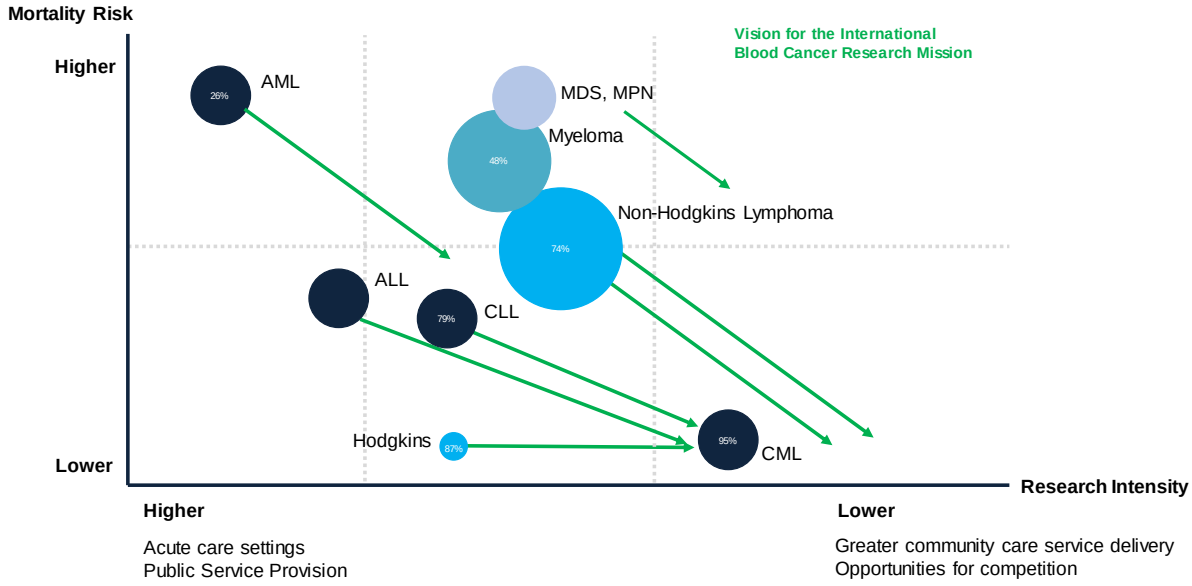
Ensuring Australian patients and researchers are integrated into the International Blood Cancer Research Mission will require targeted investments in fundamental research and translational research collaboration, and new approaches to clinical trials for blood

cancers covered by the Research Mission. In particular, the Research Mission could provide for:

- Pre-accredited trial locations backed by a common layer of insurance to reduce the time to trial
- Patient recruitment through the non-infectious disease notification status for blood cancer patients
- Use of tele-trial models to support regional patient participation.

For example, by 2035 there will be more than 4,500 and 3,000 deaths from lymphoma and myeloma, respectively, based on current survival rates. Bringing forward a breakthrough, similar to CML, where there is now the potential for functional cure rate in 95 per cent of the population, has the potential to deliver significant health and economic benefits.

Figure 4.12: Accelerating a pipeline of new advances through International Blood Cancer Research Mission



Importantly, the Research Mission should be focused not only on treatment but also prevention of blood cancers. While the prevention of blood cancers is not possible today, ultimately a breakthrough in prevention will deliver the greatest gains to the community. The design of the Research Mission would need to be developed to ensure this balance, and to maximise returns on research investment over time.

Funding for this could be provided through a public private partnership, with public funds being contributed by Australian and international governments and private funding contributed from industry, philanthropists and blood cancer research charities. Australian Government funding could come from the NHMRC, Cancer Australia and the Medical Research Future Fund for the various fundamental, translational and clinical trial components of the research strategy. Box 4.7 provides a background on the MRFF Program.

Box 4.7: Medical Research Future Fund & Alignment of the International Blood Cancer Research Mission

The MRFF is an integral component in the Australian Medical Research and Innovation Strategy for 2016-2021. Specifically, it is a $20 billion vehicle for investment in health and medical research. It represents the single largest boost to research funding in Australia's history. The vision for the MRFF is a health system fully informed by quality health and medical research and the aim of the MRFF is to transform health and medical research and innovation through strategic investment, to improve lives, build the economy and contribute to the health system sustainability.

The objectives of the MRFF are to:

- Create health and economic benefits from research discoveries and innovations
- Embed research evidence in healthcare policy and in practice improvement
- Drive collaboration and innovation across the research pipeline and healthcare system
- Strengthen transdisciplinary research collaboration
- Provide better access to research infrastructure
- Maximise opportunities for research translation by engaging with consumers
- Position the research sector and health system to tackle future challenges
- Facilitate the commercialisation of great Australian research
- Demonstrate the value and impact of research investment

The MRFF will invest in strategic platforms, including: Strategic and international horizons; Data and infrastructure; Health services and systems; Capacity and collaboration; Trials and translation; and Commercialisation. It will measure its impact through:

- Better patient outcomes
- Beneficial change to health practices
- Evidence of increased efficiency in the health system
- Commercialisation of health research outcomes
- Community support for the use of and outcomes for funding.

The International Blood Cancer Research Mission are strongly aligned to the objectives of the MRFF, proposing synergistic investment in a number of strategic platforms for international collaboration, better use of data and infrastructure, improvements in health service and systems, trials and translation and potentially commercialisation:

- By investment in strategic international research collaborations, the projected number of deaths from blood cancer (186,000 people) can be demonstrably reduced, with advances able to be realised over the short and medium terms health and economic benefits from research discoveries and innovations
- Data shows that more consistent implementation of evidence-based care and practice improvement could reduce the number of deaths by 15 per cent, and potentially up to 30 per cent based on stakeholder interviews, just through consistent use of already demonstrated best practice
- Through data sharing from the Right to Trial Program into the fundamental, translational and clinical trials programs the Mission will drive collaboration and innovation across the research pipeline and healthcare system
- The Real World Evidence Pilot in MyHealthRecord or other platform will provide better access to research infrastructure and collaboration with international natural history and patient data including HARMONY, LLS, HMRN, and other platforms, and will maximise opportunities for research translation by engaging with consumers and supporting consumer input to PBS, MBS and Right to Trial Programs
- The Mission will demonstrate a new approach to research in an era of precision medicine, helping to position the research sector and health system to tackle the emerging challenges around precision medicine
- Facilitate the commercialisation of great Australian research, building on the legacy of investment in venetoclax
- Demonstrate the value and impact of research investment through investment in clear programs for the acceleration of research building on the very substantial research advances that have been made in the last five years in Australia and overseas.

Working in partnership with researchers and clinicians, and leveraging the projections for survival, the Zero by 2035 Strategy and International Blood Cancer Research Mission will be able to identify expected improvements in health outcomes, improvements to health practice (benchmarked against baseline data from the survey), increased efficiency in the health system (e.g., reduced inappropriate referrals), commercialisation of products for blood cancer patients globally in the context of rising incidence, and community support for the use of and research outcomes, with Blood Cancer of a similar magnitude of impact to the community as other 'big' cancers.

Source: Descriptions of the MRFF program based on Australian Government, 2016, *Medical Research Future Fund*, and *Australian Medical Research and Innovation Strategy: 2016-2021.*

4.6 Review Hospital, Insurance and Welfare Financing and Support

The other major opportunity, which is more difficult to achieve, is advocating for a review of hospital and healthcare funding arrangements to address extant issues related to cost shifting and out of pocket costs for patients. This is a complex and significant agenda, which has been recognised and recommended by a range of groups, including the Productivity Commission, the National Hospital Reform Commission, the Australian Centre for Health Research, Consumer Health Forum, Private Healthcare Australia and Medicines Australia.

In the short run, a detailed review of in-patient and out-patient funding arrangements for blood cancer designed to identify any adverse incentives that have the potential to distort treatment planning could be undertaken as an adjunct to the development of clinical care standards (See Section 4.3). The review should include variation in service provision and financing in public and private hospital settings nationally.

Another further opportunity exists to collaborate with the Australian Genomic Health Alliance to seek regulatory reform related to life insurance, to ensure there are no unnecessary deterrents to genetic and genomic testing that could improve survival outcomes for people living with blood cancer specifically, and other diseases more generally. An opportunity potentially exists to form a Roundtable of Cancer Support Organisations to advocate for regulatory reform to government.

Opportunities also exist to better support patients experiencing financial hardship as a result of their cancer. The Cancer Council and Oncology Social Work Australia have identified a number of opportunities to better support patients through a case management approach to welfare programs across government and fast-tracking applications, including in particular for low income earners, services to better support CALD communities, and a full review of Centrelink protocols, processes and intent-to-claim reforms.

4.7 Conclusions

Very substantial opportunities exist to improve survival outcomes, with the potential to address the metro-regional divide and improve the consistent use of evidence based best-practice.

In particular, significant opportunities to change outcomes for blood cancer patients include:

- Make cancer a non-infectious notifiable disease that supports referrals to patient support
- Develop clinical standards of care with clear referral pathways for supportive care and survivorship
- Develop a one-stop shop for information on Blood Cancers backed by a broader digital strategy for supporting people living with blood cancer
- Develop a cancer-friendly rehabilitation program, and ensure consistent screening and referral to psychosocial support
- Support the development of a Right to Trial Pilot Program to support evidence development for new therapies and tests

- Support the development of an International Blood Cancer Research Mission, linked to the Right to Trial Program and a Real World Evidence Pilot
- Support the development of Patient Reported Outcomes through either a Real World Evidence Pilot in the MyHealthRecord or a Patient-Entered Data Registry.

Chapter 5

Getting to Zero: The Leukaemia Foundation's Plan and Partnerships

Realising the objective of zero deaths from blood cancer will require not a single policy reform, but many policies and actions across the blood cancer ecosystem, implemented in partnership with people living with blood cancer, their families, clinicians, researchers, industry and governments at the State and Federal level.

Since 2016, the Leukaemia Foundation has reformed its operations and now operates a stakeholder-centric engagement model. This State of the Nation: Blood Cancer in Australia *report aligns with and builds upon the previous assessments of stakeholder needs.*

This chapter outlines the Leukaemia Foundation's vision for 2035, its plan and priorities to get there, and the key partners it will work with on the journey.

5.1 The Leukaemia Foundation's Vision for 2035

The Leukaemia Foundation was originally founded in 1975 with a vision to cure blood cancer, and a mission to care for people living with blood cancer.

Since its founding the Leukaemia Foundation has supported countless people living with blood cancer, their families and the wider community through accommodation support for patients requiring acute care, transportation services, psychosocial support and other supportive care.

The *State of the Nation: Blood Cancer in Australia* report renews its vision and mission, and calls on governments and blood cancer partners to build on recent advances in treatments to accelerate research for a cure and ensure all Australians have access to life-saving and life-enhancing therapies regardless of means. To this end, the goal of the Leukaemia Foundation is zero lives lost to blood cancer by 2035. This includes:

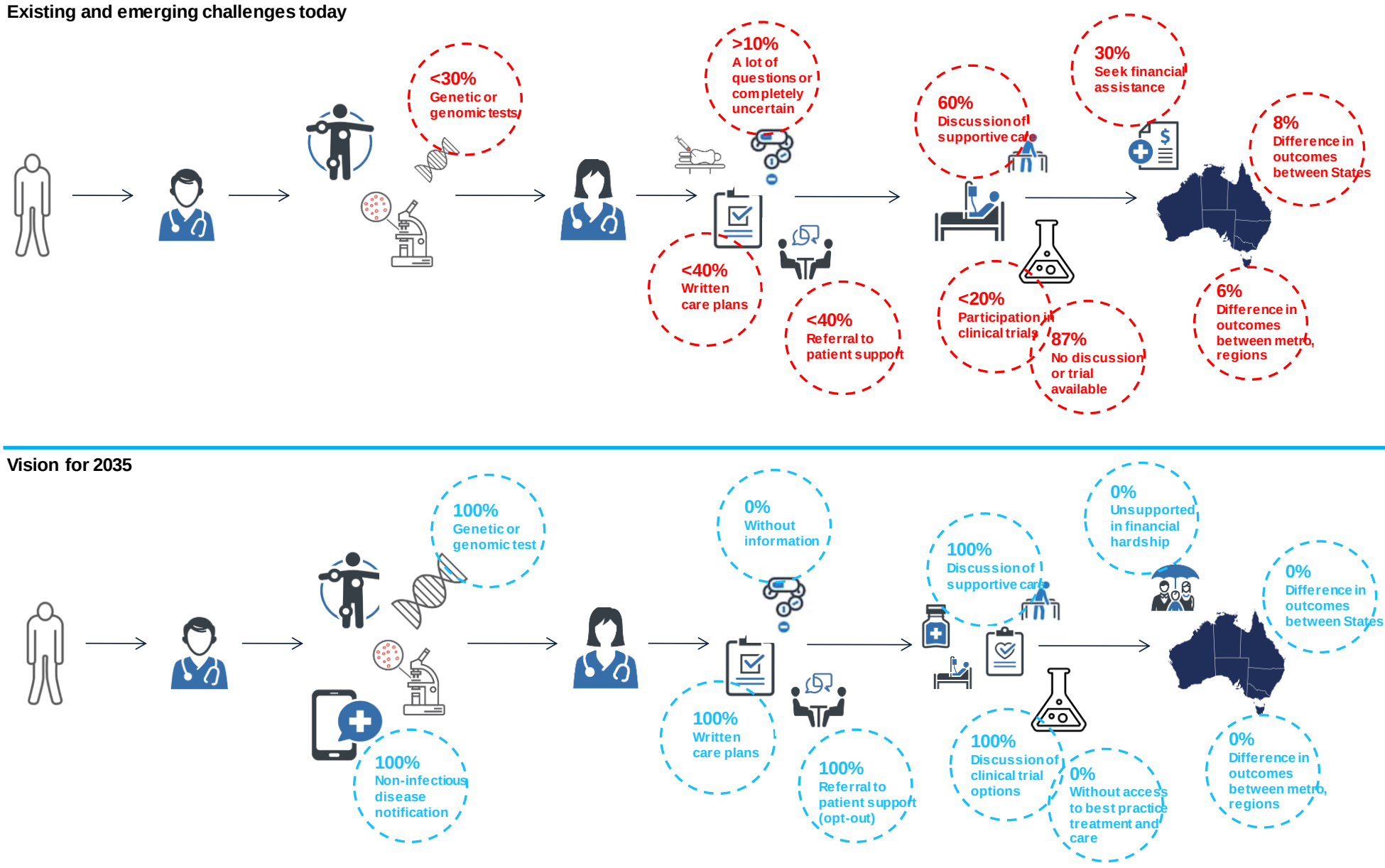
Vision to Cure: Zero preventable deaths from blood cancers by removing barriers to access and addressing inequality in survival outcomes

Mission to Care: Zero people without access to information

Mission to Care: Zero people without access to best practice treatment and care

Figure 5.1 shows how the realisation of this vision will change the care pathways for people living with blood cancer.

Figure 5.1: Addressing challenges in care and seizing new opportunities: Leukaemia Foundation's Vision for 2035



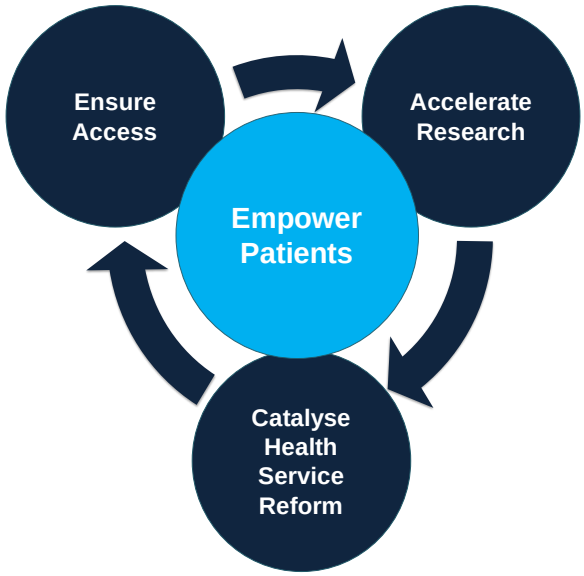
5.2 Getting to Zero: A Plan for Action

To reach this goal, the Leukaemia Foundation wants to work in partnership with government and the key participants in the blood cancer science and clinical community to coordinate effort that will enable the achievement of this goal. Each of these priorities contribute towards the overall vision for Zero by 2035.

The four priorities are:

- Empower Patients
- Enable Access
- Catalyse Health Reform
- Accelerate Research for the Cure.

Figure 5.2: Getting to Zero - Priorities for change



Actions to Empower Patients
- Make blood cancer a notifiable disease
- Opt-out model for referrals to patient support organisations
- Create a one-stop shop for blood cancers
- Create a complex referral MBS item and referral support tools
- Support the development of Patient Reported Outcomes
- KPIs for written care plans

Actions to Accelerate Research
- Establish an International Blood Cancer Research Mission
- Develop a Real World Evidence Pilot for the MyHealthRecord - Including Patient Reported Outcomes

Actions to Ensure Access
- Make systematic genetic and genomic testing part of the standard of care
- Develop a Right to Trial Pilot Program
- Implement KPIs for clinical trial participation

Actions to Catalyse Health Service Reform
- Address care pathway and clinical guideline gaps
- Develop KPIs for sub-type specialist input to treatment plans
- Develop KPIs for supportive care screening and referrals
- Review of in-patient and out-patient funding arrangements
- Roll-out GP education and decision support tools
- Develop and roll-out a cancer-friendly rehabilitation program
- Support the expansion of community-based care
- Advocate for insurance reform
- Advocate for welfare support, including Centrelink payments reform
- Advocate for patient assisted travel scheme reform

The priorities are synergistic, and the implementation of progress against each will deliver outcomes that are greater than the sum of the individual parts.

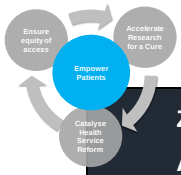
The implementation of actions have been prioritised to ensure that key enabling infrastructure is in place to drive more effective engagement with stakeholders. For example, to empower patients to engage with providers in relation to treatment options, there first needs to be nationally endorsed clinical guidelines for all blood cancer sub-types; consequently, the development of care pathways and clinical guidelines for blood cancer are a 'Phase 1 – Enabling priority'. These are the first actions to be implemented, followed by other Phase 1 actions and to be reviewed over time.

Priority 1: Empower Patients

The actions to improve survival and wellness under the Empower Patients priority are:

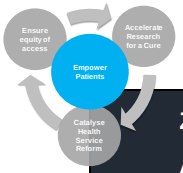
- Make blood cancer a non-infectious notifiable disease (Action 1.1)
- Opt-out model for referrals to patient support organisation (Action 1.2)
- Create a one-stop shop for blood cancers (Action 1.3) backed by:
  - A comprehensive digital health and information strategy to support people living with blood cancer and their families
- Complex referral MBS item with digital solution for transparency in patient mix and expected gap fees to support patient choice (Action 1.4)
- Support the development of Patient Reported Outcomes through either the MyHealthRecord or a Patient-Entered Data Registry (Action 1.5)
- KPIs for written care plans (Action 1.6).

These actions are detailed in turn.

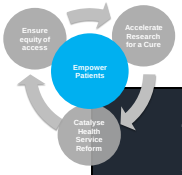


Zero by 2035 Priority: Empower patients Action 1.1: Make cancer a non-infectious notifiable disease	
What will be different?	As a non-infectious notifiable disease, the diagnosis of a blood cancer will trigger an alert in the form of a letter or email from the MyHealthRecord or other authority that will empower the patient to: • Engage with their GP in the selection of the best specialist for them based on their sub-type and expected fees • Receive personalised information about their sub-type • Ensure they receive treatment based on their specific sub-type diagnosis • Automatically refer the patient to patient support service • Seek consent from patients to enroll in clinical trials
Key dependencies	• Support from Federal and State Governments
Key partners for implementation	State and Federal Governments Blood cancer patient support organisations Clinician Research
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: 100% of patients with a blood cancer diagnosis listed in a registry

Zero by 2035 Priority: Empower patients Action 1.2: Opt-out model for referrals to patient support organisations	
What will be different?	Under the opt-out model for referral to patient support organisations, the diagnosis of a blood cancer will trigger an alert in the form of a letter or email from the MyHealthRecord or other authority an automatic referral to a patient support organisaton. This will ensure that patients are immediately empowered with information to ensure their treatment is in line with clinical care standards.
Key dependencies	• Support from Federal and State Governments
Key partners for implementation	State and Federal Governments Blood cancer patient support organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero patients without referral to patient support organisations

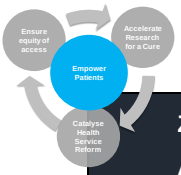


Zero by 2035 Priority: Empower patients Action 1.3: Create a One-Stop Shop for Blood Cancer, backed by a comprehensive digital health and information strategy	
What will be different?	Patients and Clinicians will be empowered to more easily navigate Australia's healthcare system and engage with up-to-date information on their disease sub-type through the creation of a 'One-Stop Shop' Blood Cancer Information Portal which acts as an aggregator of information from Australian and international sites. The One Stop Shop should be developed as part of a wider, comprehensive digital health and information strategy which considers new opportunities to better link blood cancer survivors, technologies to support medication management and adherence, remote monitoring of symptoms, capturing patient reported outcomes of side-effects and other measures of wellness, and participation in research.
Key dependencies	• Support from Federal and State Governments
Key partners for implementation	State and Federal Governments Other blood cancer patient support organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero patients without access to information through the One-Stop Shop Development of a digital health and information strategy for blood cancer

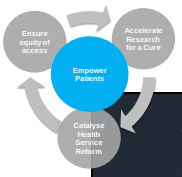


Zero by 2035 Priority: Empower patients Action 1.4: Complex MBS item referral and transparency of specialist patient mix and fees	
What will be different?	The diagnosis of a blood cancer will trigger an alert in the form of a letter or email from the MyHealthRecord or other authority that will empower the patient to engage with their GP in the selection of the best specialist for them based on their sub-type and expected fees. At the consultation the GP and patients will be able to review de-identified specialist options with simple statistics on average patient mix, and then a shortlist of identified specialist options with expected wait times to appointment and fees.
Key dependencies	• Support from Federal and State Governments

Zero by 2035 Priority: Empower patients Action 1.4: Complex MBS item referral and transparency of specialist patient mix and fees	
Key partners for implementation	State and Federal Governments Clinicians Blood cancer patient support organisations Cancer support organisations for other conditions
Timeline for implementation	Phase 1
How will we measure our success?	KPI: Zero patients without support to select specialist in their sub-type



Zero by 2035 Priority: Empower patients Action 1.5: Capture Patient Reported Outcomes through the MyHealthRecord or other platform	
What will be different?	Patients will be empowered to report day-to-day information about the lived experience of their disease to support engagement with regulators on the value of new drug therapies and post-market surveillance, and to provide information to industry and researchers for the development of new therapies. The MyHealthRecord provides an obvious platform for the entry of these data, and could support the realisation of benefits from foundational investment in this capability. If the MyHealthRecord is too difficult, a platform such as CART-Wheel or NORD in the US could be leveraged and extended.
Key dependencies	• Support from Federal Government
Key partners for implementation	Federal Governments Clinicians Blood cancer patient support organisations
Timeline for implementation	Phase 1
How will we measure our success?	KPI: Zero patients without ability to report their lived experience



Zero by 2035 Priority: Empower patients Action 1.6: KPIs for written care plans	
What will be different?	Patients will be empowered through the consistent receipt of written records of: • Diagnosis • Treatment planning • Post-treatment care
Key dependencies	• Reform of KPIs for hospitals to include confirmation of written care plans at each stage
Key partners for implementation	State and Federal Governments Hospitals administrators and clinicians Blood Cancer Support Organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority

Zero by 2035 Priority: Empower patients Action 1.6: KPIs for written care plans	
How will we measure our success?	KPI: Zero patients without written care plans at diagnosis, treatment planning and active treatment completion

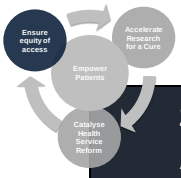
Priority 2: Enable Access

The actions to improve survival and wellness under the Enable Access priority are:

- Make systematic genetic and genomic testing part of the standard of care (Action 2.1)
- Develop a Right to Trial Program (Action 2.2)
- Implement KPIs for clinical trial participation (Action 2.3).

These actions are detailed in turn.

Zero by 2035 Priority: Enable access to novel therapies Action 2.1: Make systematic genetic and genomic testing part of the standard of care	
What will be different?	The diagnosis and treatment of every patient will be informed by an understanding of the disease at a molecular level. Whole Genome Testing for selected patient groups identified in the International Blood Cancer Research Mission will be systematically collected.
Key dependencies	• Reforms to support fast-tracked MBS item listing for genetic and genomic tests • Regulatory reform to address ethics, legal and social issues for whole genome testing • Investment in the supply of computational bioinformatics skills • Continuing professional development to support the ordering and interpretation of genetic and genomic testing
Key partners for implementation	State and Federal Governments Blood Cancer Support Organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero patients without genomic or genetic test to inform diagnosis, treatment and research where clinically valid test is available



Zero by 2035 Priority: Enable access to novel therapies Action 2.2: Develop a Right to Trial Program	
What will be different?	The regulatory system will have in place a mechanism for investigator-led evidence development to support clinician and patient-led submissions to the PBS where there are market barriers to evidence development and listing.
Key dependencies	• Support from the Federal and State governments for program design, funding and implementation

Zero by 2035 Priority: Enable access to novel therapies Action 2.2: Develop a Right to Trial Program	
	• Engagement with industry in design, funding and implementation
Key partners for implementation	State and Federal Governments Blood Cancer Support Organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero gaps in access to therapies that are agreed clinical standards of care

Zero by 2035 Priority: Enable access to novel therapies Action 2.3: Develop KPIs for clinical trial participation	
What will be different?	The treatment plans for each patient will have considered options for clinical trial participation, including through the Right to Trial program or the International Blood Cancer Research Mission.
Key dependencies	• Inclusion of KPIs of clinical trials for hospital management • Funding of clinical trial unit resource to support administration • Pre-accreditation for all blood cancer trial sites supported by single layer of insurance for Right to Trial program and International Blood Cancer Research Program • Non-infectious disease notification for blood cancers to support patient recruitment
Key partners for implementation	State and Federal Governments Hospitals and clinicians Blood Cancer Support Organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero patients without discussion of potential clinical trial options

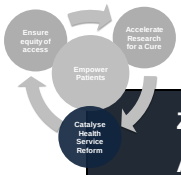
Priority 3: Catalyse Health Care Reform

The actions to improve survival and wellness under the Catalyse Health Care Reform priority are:

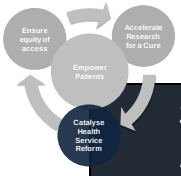
- Address care pathway and clinical guideline gaps (Action 3.1), including:
  - Complete care pathways and guidelines for all sub-types
  - Ensure all clinical guidelines and optimal care pathways to include supportive care
  - Develop quality indicators as part of clinical standards development
  - Encourage take-up of care pathways and guidelines
  - Develop post-treatment care pathways and guidelines

- Develop KPIs for sub-type specialist input to treatment plan (Action 3.2)
- Develop KPIs for supportive care screening and referral (Action 3.3)
- Review of in-patient and out-patient funding arrangements and incentives (Action 3.4)
- Roll-out GP education and decision support tools (Action 3.5)
- Develop and roll-out a cancer friendly rehab program (Action 3.6)
- Support the expansion of community-based care (Action 3.7)
- Advocate for insurance reform (Action 3.8)
- Advocate for welfare payment reform (Action 3.9)
- Advocate for patient assisted travel scheme reform (Action 3.10).

These actions are detailed in turn.

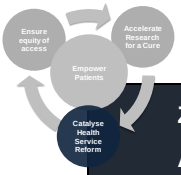


Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.1: Address care pathway and clinical care guidelines**	
What will be different?	Each treatment plan will be informed by care pathways, clinical care standards and quality indicators for each sub-type. These pathways and standards will be available at the One-Stop Shop for Blood Cancer (Blood Cancer Information Portal) and will support more consistent delivery of written care plans and referral to supportive care, as well as evidence-based recommendations for first-line treatment (leveraging eviQ). For each patient that completes treatment there will be a post-treatment care pathway that supports them in a survivorship phase.
Key dependencies	• Support and engagement by clinicians • Publication through HealthPathways or other services to promote take-up
Key partners for implementation	Clinicians State and Federal Governments Blood Cancer Support Organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero gaps in care pathways and clinical care guidelines for active treatment KPI: Zero gaps in care pathways and clinical care guidelines for survivorship

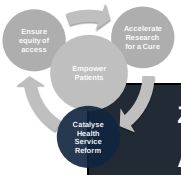


Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.2: Develop KPIs for sub-type specialist input to treatment plans for patients treated by general oncologists or in rural and regional areas where patient numbers may be lower**	
What will be different?	Treatment planning will have input by a sub-type specialist to ensure current best practice is implemented, even if patients are not treated by a sub-type specialist
Key dependencies	• Knowledge network for sub-type specialisation

Zero by 2035 Priority: Catalyse Health Care Reform Action 3.2: Develop KPIs for sub-type specialist input to treatment plans for patients treated by general oncologists or in rural and regional areas where patient numbers may be lower	
Key partners for implementation	Clinicians State and Federal Governments Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero treatment plans without sub-type specialist input by treating clinician or through multi-disciplinary team (MDT) review



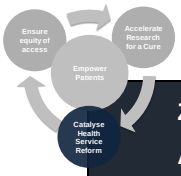
Zero by 2035 Priority: Catalyse Health Care Reform Action 3.3: Develop KPIs for consistent referral to supportive care	
What will be different?	Every patient will be consistently screened and referred to supportive care throughout diagnosis, treatment and survivorship. Supportive care will include traditional definitions of supportive care, including infection control and pain management, as well as information needs and referral to pre-habilitation, rehabilitation, psychosocial support, practical and social support, financial and employment support, and spiritual support.
Key dependencies	• Review of a resource model for consistent supportive care screening and referral including potentially the use of nurse practitioners or other staff in hospital settings • Development of a combination of continuing professional development for GPs and health service triggered by Patient Reported Outcomes and/or MyHealthRecord in line with patient treatment plan
Key partners for implementation	Clinicians State and Federal Governments Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	KPI: Zero patients without access to supportive care



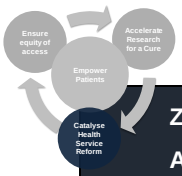
Zero by 2035 Priority: Catalyse Health Care Reform Action 3.4: Review of in-patient and out-patient funding arrangements and incentives	
What will be different?	There will be transparency in financing arrangements and the impact of these reimbursement arrangements on treatment planning. This will support engagement with State and Federal Government governments as well as private health insurers to ensure financial incentives do not distort treatment planning or create inequities for people treated in different care settings.
Key dependencies	• Care pathway and clinical care guidelines
Key partners for implementation	State and Federal Governments Hospital administrators

Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.4: Review of in-patient and out-patient funding arrangements and incentives**	
	Private health insurance Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	Completion of the in-patient and out-patient funding arrangements and incentives

Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.5: Roll-out continuing professional development and decision support tools for GPs**	
What will be different?	GPs will have a better understanding of the tests to order to more quickly diagnose and refer patients to a specialist, reducing time to see a haematologist. GPs will be supported through knowledge at the One-Stop Shop for Blood Cancer with information by sub-types and access to a complex MBS referral item so they can support patients to find the right specialist for them.
Key dependencies	• One-stop shop for Blood Cancer • Care pathway and clinical care guidelines • MBS item for complex referrals • Decision support tool to enable transparency in specialist patient mix, time to appointment and expected fees.
Key partners for implementation	AMA State and Federal Governments Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1
How will we measure our success?	Development and roll-out of CPD and decision support in partnership with AMA and Governments.

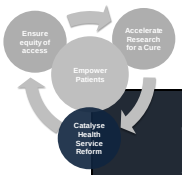


Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.6: Develop and roll-out a cancer-friendly rehabilitation program**	
What will be different?	All patients will have access to a community-based cancer-friendly rehabilitation program with an accredited cancer-specialist exercise physiologist.
Key dependencies	• Develop cancer friendly-rehabilitation program leveraging published results from successful pilot programs in the US • Care pathway and clinical care guidelines • One-stop shop for Blood Cancer
Key partners for implementation	Exercise & Sports Science Australia State and Federal Governments Blood Cancer Support Organisations Cancer Support Organisations for other cancers



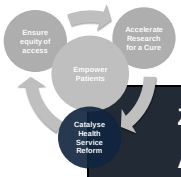
Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.6: Develop and roll-out a cancer-friendly rehabilitation program**	
Timeline for implementation	Phase 1
How will we measure our success?	Development of a cancer friendly rehabilitation program KPIs: Zero patients without access to rehabilitation

Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.7: Support the expansion of community-based service delivery**	
What will be different?	Patients will have increasingly greater access to treatment either at-home or in their local area, while being supported through a proven model for safe cancer care.
Key dependencies	• Care pathway and clinical care guidelines • Review of in-patient and out-patient funding arrangements and incentives • One-stop shop for Blood Cancer
Key partners for implementation	State and Federal Governments Hospital administrators Private health insurance Industry Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1
How will we measure our success?	KPIs: Number of patients utilising community-based services



Zero by 2035 Priority: Catalyse Health Care Reform **Action 3.8: Advocate for life insurance reform**	
What will be different?	Working in partnership with the Australian Genomics Health Alliance and other partners, the Leukaemia Foundation will advocate for regulation to require a moratorium on discrimination of consumers for genetic and genomic testing.
Key dependencies	• Support from State and Federal governments to tackle barriers to testing that can improve the health and wellbeing of patients
Key partners for implementation	Australian Genomics Health Alliance State and Federal Governments Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1
How will we measure our success?	Development of a position statement on ethical, legal and social issues

Zero by 2035 Priority: Catalyse Health Care Reform Action 3.9: Advocate for welfare payments reform	
What will be different?	Working in partnership with the Cancer Council and other partners, the Leukaemia Foundation will advocate for reforms to Australia's complex welfare payments system to ensure vulnerable patients are appropriately supported based on their financial circumstances and needs.
Key dependencies	• Support from Federal governments to support a range of reforms and policies to enable better support to Australian patients at risk of experiencing financial hardship.
Key partners for implementation	Cancer Council Oncology Social Work Australia Federal Governments Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1
How will we measure our success?	Development of a position statement on welfare reform



Zero by 2035 Priority: Catalyse Health Care Reform Action 3.10: Advocate for reform to the patient assisted travel scheme	
What will be different?	Patients will receive a nationally uniform rate of financial support that limits or eliminates the financial impact of travel and accommodation for cancer care treatment depending on means.
Key dependencies	• Support from State and Federal governments
Key partners for implementation	State and Federal Governments Blood Cancer Support Organisations Cancer Support Organisations for other cancers
Timeline for implementation	Phase 1
How will we measure our success?	KPI: Zero patients below national standard for transport and accommodation support KPI: Zero clinical trial participants without access to transport and accommodation support

Priority 4: Accelerate Research for the Cure

The actions to improve survival and wellness under the Accelerate Research for the Cure priority are:

- Establish an International Blood Cancer Research Mission (Action 4.1)
- Develop a Real World Evidence Pilot for the MyHealthRecord including Patient Reported Outcomes (Action 4.2).

These actions are detailed in turn.

Zero by 2035 Priority: Accelerate Research for the Cure Action 4.1: Establish an International Blood Cancer Research Mission	
What will be different?	The Leukaemia Foundation will work in partnership with Australian and international researchers, donors and governments to develop a program that establishes international centres of excellence by blood cancer sub-type and identifies priorities for investigator-led fundamental and translational research to accelerate advances by sub-type. The Mission will improve research outcomes by increasing patient population and data through cross-border research collaboration. The Mission will be accelerated by access to data from the Right to Trial program which will capture outcomes from off-label medicines use and use of novel therapies. Australian research centres of excellence will be pre-accredited trial sites supported by a single layer of insurance and clinical trial administrative support units that will reduce costs and time to establish research under the program. The Mission would be a public private partnership for the cure of blood cancer.
Key dependencies	• Make blood cancer a non-infectious notifiable disease • KPIs for clinical trial participation • Systematic genomic and genetic testing • MBS item for complex referrals • Patient Reported Outcomes in the MyHealthRecord or other platform
Key partners for implementation	State and Federal Governments Australian and International Research Institutes and Hospitals Australian and International Blood Cancer Research Donors Blood Cancer Support Organisations
Timeline for implementation	Phase 1 – enabling infrastructure priority
How will we measure our success?	Development of a Roadmap for Investment in the International Blood Cancer Research Mission Funding for Australian nodes of International Blood Cancer Research Mission by Australian Government Research advances in disease definition and treatment

Zero by 2035 Priority: Accelerate Research for the Cure Action 4.2: Capture Real World Evidence and Patient Reported Outcomes through the MyHealthRecord	
What will be different?	Data for the natural history, comorbidities, treatments and outcomes of every patient is captured and potentially available on a de-identified basis for research purposes with consent. Patients will be empowered to report day-to-day information about the lived experience of their disease to support engagement with regulators on the value of new drug therapies and post-market surveillance, and to provide information to industry and researchers for the development of new therapies. There may be cost efficiencies realised from the centralisation of data capture that can be redirected to research purposes.
Key dependencies	• Support from Federal Government
Key partners for implementation	Federal Governments Clinicians

Zero by 2035 Priority: Accelerate Research for the Cure Action 4.2: Capture Real World Evidence and Patient Reported Outcomes through the MyHealthRecord	
	Blood cancer patient support organisations
Timeline for implementation	Phase 1 – Phase 2
How will we measure our success?	KPI: Zero patients where real world outcomes not captured and available for research with consent KPI: Number of blood cancer patients providing consent for research KPI: Zero patients without ability to report their lived experience

5.3 Partnerships in Getting to Zero

Since its establishment in 1975 the Leukaemia Foundation has been a long-term partner with Government and the blood cancer community in the support of people living with blood cancer and their families, and investment in research that has supported advances in therapies that have delivered improvements in both survival and quality of life. The Leukaemia Foundation has been a major provider of accommodation, transport, psychosocial, nutritional and other support services to people living with blood cancer, in addition to being a major funder of blood cancer research. This support continues today:

- The Leukaemia Foundation currently provides funding for 170 apartments, which enabled more than 11,790 patients to stay with their families during treatment in 2016-17. The Foundation's accommodation services deliver very substantial efficiencies and savings to government while also providing patients and their families with a higher quality service. If these 170 beds were provided by government the capital costs of their construction would be between $34 million and $80 million alone.[71] In addition government is able to avoid operating costs associated with patients that would have been admitted to hospital, and patients that would have otherwise been discharged to a motel receive better care and treatment support than would otherwise have been the case.

- The Leukaemia Foundation delivers more than 175,000 passenger trips each year, covering more than 4.8 million kilometres in patient transport services. Valued at $0.21 per km, this delivers savings of more than $1 million each year to government and households, as well as achieving the primary goals of reducing patient and family anxiety and improving patient survival outcomes and wellness.

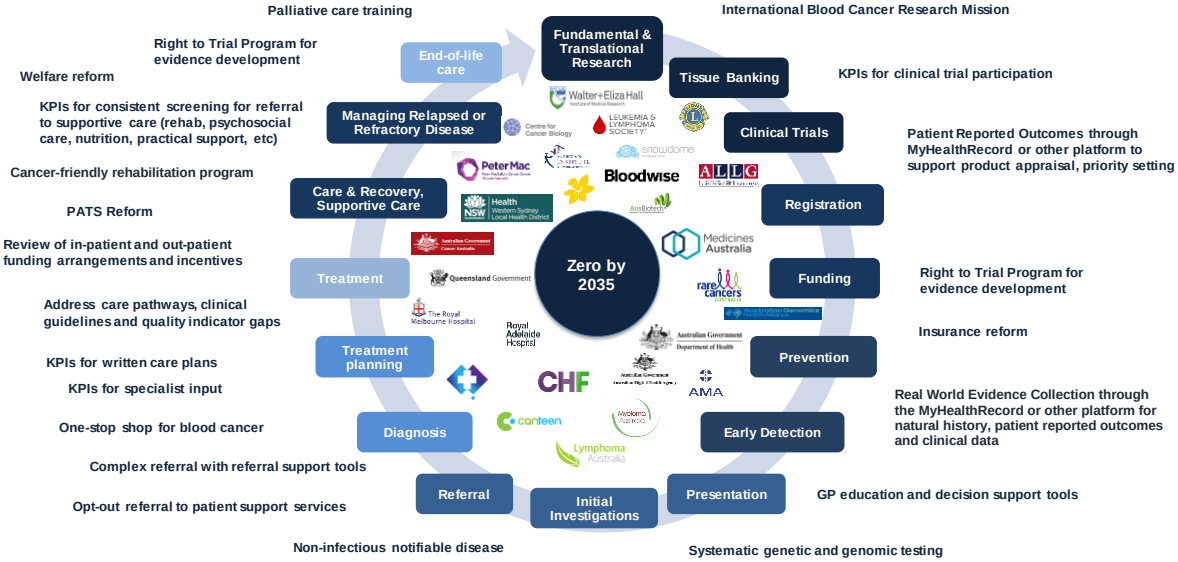
- Through patient support services the Leukaemia Foundation delivers psychosocial services to more than 1,600 people each year, helping to reduce patient and family anxiety and improving patient survival outcomes and wellness.

- The Foundation has also been a major investor in blood cancer research, funding more than $47 million in fundamental and clinical research since 2002 alone.

[71] Victorian Department of Health Infrastructure Planning and Delivery, 2016, *Hospital Capital Planning Module*, accessed at: http://www.capital.dhs.vic.gov.au/Project_proposals/Benchmarking/Hospital_capital_planning_module/ which estimates that the average cost per bed is between $200,000 and $500,000 in $2016 depending on requirements.

Continuing this journey, and realising the vision of zero deaths from blood cancer will require new, innovative, and meaningful partnerships with both Government and our blood cancer community, as well as international research partners.

Figure 5.3: Partnerships in Getting to Zero



The Leukaemia Foundation will act in partnership with Governments and the Blood Cancer community to successfully implement change and realise the goal of zero preventable deaths from blood cancer. It will also report against progress against each goal in an Annual *State of the Nation* Report.

Appendix A

Care Pathways & International Benchmarking

A.1 Overview and sources

This appendix presents care pathways for the following sub-types:

- Section A.2: Acute Myeloid Leukaemia
- Section A.3: Acute Lymphoblastic Leukaemia
- Section A.4: Chronic Myeloid Leukaemia
- Section A.5: Chronic Lymphocytic Leukaemia
- Section A.6: Lymphomas
- Section A.7: Myeloma
- Section A.8: Myelodysplastic Syndrome
- Section A.9: Myeloproliferative Neoplasms.

The care pathways and international benchmarking reviews have been developed in an iterative process which included clinician review of draft pathways based on:

- Optimal Care Pathways by the Cancer Council for AML and Hodgkin/Non-Hodgkin Lymphoma (DLBCL)
- eviQ reporting as at December 2018
- PBS outcomes as at December 2018
- NICE Clinical Guidelines in the UK for blood and bone marrow malignancies
- Latest published ESMO clinical guidelines as at December 2018.

Importantly, the pathways and benchmarking analysis are continually evolving and are intended to be used to support a discussion around current practice challenges and potential opportunities to address real or perceived gaps in the availability of therapies in Australia. Variations by State or hospital may exist which have not been captured here and this may not represent every patient's experience.

A.2 Care pathway analysis: Acute Myeloid Leukaemia

Figure A.1: Optimal care pathway and current practice challenges in AML

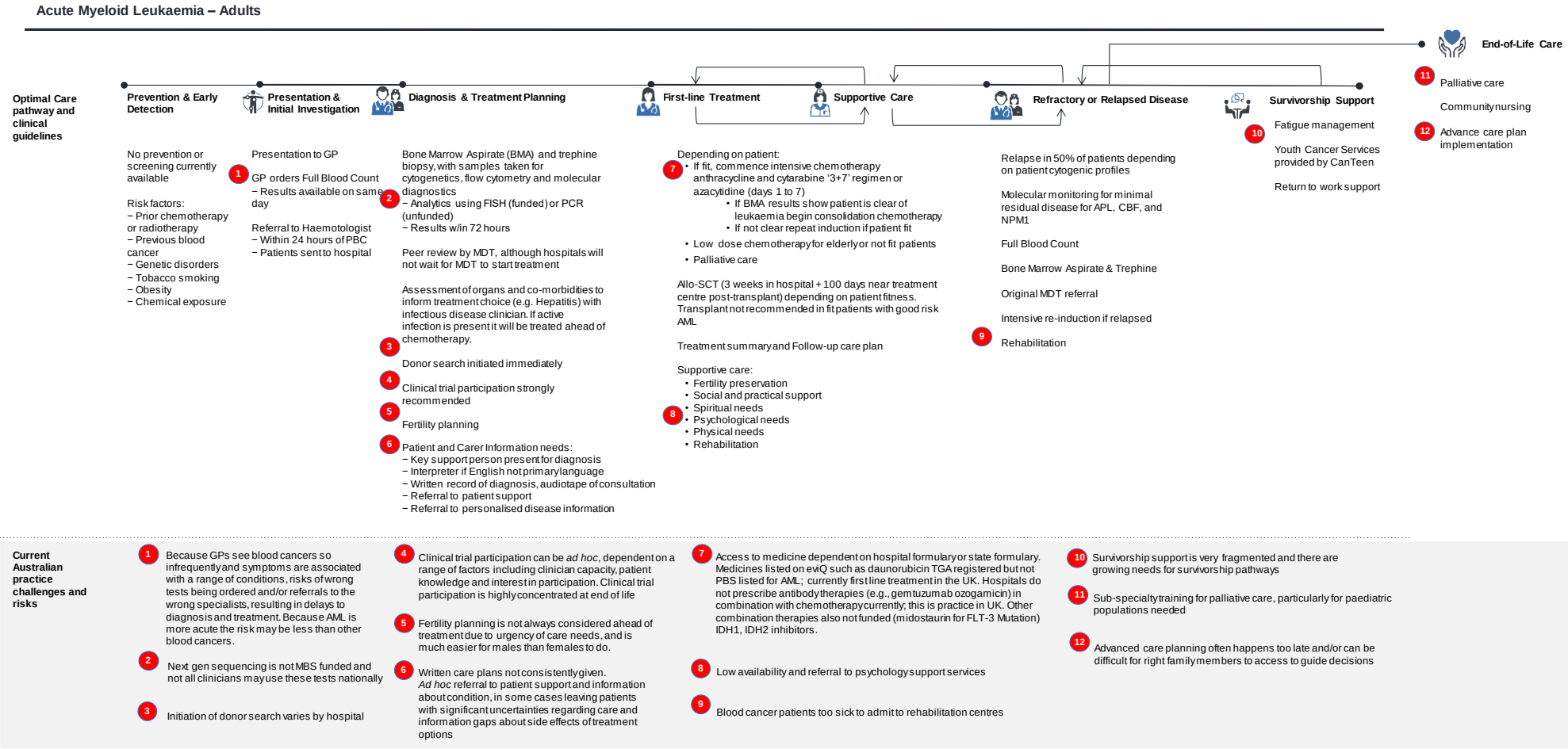


Figure A.2: International Benchmarking in AML

What's different? In the UK, genomic testing is publicly funded and used to diagnose and guide treatment planning. In addition, the standard of care includes combination chemotherapy and drug therapy for gemtuzumab for some cohorts and midostaurin for untreated AML in patients with FLT3. The EU and Australian standards follow long-standing treatment regimens for AML.

Diagnosis & Treatment Planning

Bone Marrow Aspirate (BMA) and trephine biopsy, with samples taken for cytogenetics, flow cytometry and molecular diagnostics
− Analytics using FISH (funded) or PCR (unfunded)
− Results w/in 72 hours

Peer review by MDT, although hospitals will not wait for MDT to start treatment

Assessment of organs and co-morbidities to inform treatment choice (e.g. Hepatitis) with infectious disease clinician. If active infection is present it will be treated ahead of chemotherapy.
Donor search initiated immediately
Clinical trial participation strongly recommended
Fertility planning

First-Line Treatment

Depending on patient:

- If fit, commence intensive chemotherapy anthracycline and cytarabine '3+7' regimen or azacitidine (days 1 to 7)
  - If BMA results show patient is clear of leukaemia begin consolidation chemotherapy
  - If not clear repeat induction if patient fit
- Low dose chemotherapy for elderly or not fit patients
- Palliative care

Allo-SCT (3 weeks in hospital + 100 days near treatment centre post-transplant) depending on patient fitness. Transplant not recommended in fit patients with good risk AML

Diagnosis & Treatment Planning

Bone Marrow Aspirate (BMA) and trephine biopsy, with samples taken for cytogenetics, flow cytometry and molecular diagnostics
− Analytics using FISH (funded) or PCR – Funded by government
− Results w/in 72 hours

Peer review by MDT, although hospitals will not wait for MDT to start treatment

Assessment of organs and co-morbidities to inform treatment choice (e.g. Hepatitis) with infectious disease clinician. If active infection is present it will be treated ahead of chemotherapy.
Donor search initiated immediately
Clinical trial participation strongly recommended
Fertility planning

First-line Treatment

Depending on patient:

- If fit, commence intensive chemotherapy of daunorubicin and cytarabine in combination with gemtuzumab ozogamicin for treatment naïve AML for CD33 positive AML excluding APL
- Midostaurin for untreated AML in patients with FLT3 mutation+ in combination with daunorubicin and cytarabine, and alone after complete response if company provides discount in patient access scheme
- Arsenic trioxide for APL with t[15;17]
- Low dose chemotherapy for elderly or not fit patients
- Palliative care

Allo-SCT (3 weeks in hospital + 100 days near treatment centre post-transplant) depending on patient fitness. Transplant not recommended in fit patients with good risk AML

A.3 Care pathway analysis: Acute Lymphoblastic Leukaemia

Figure A.3: Optimal care pathway and current practice challenges in ALL

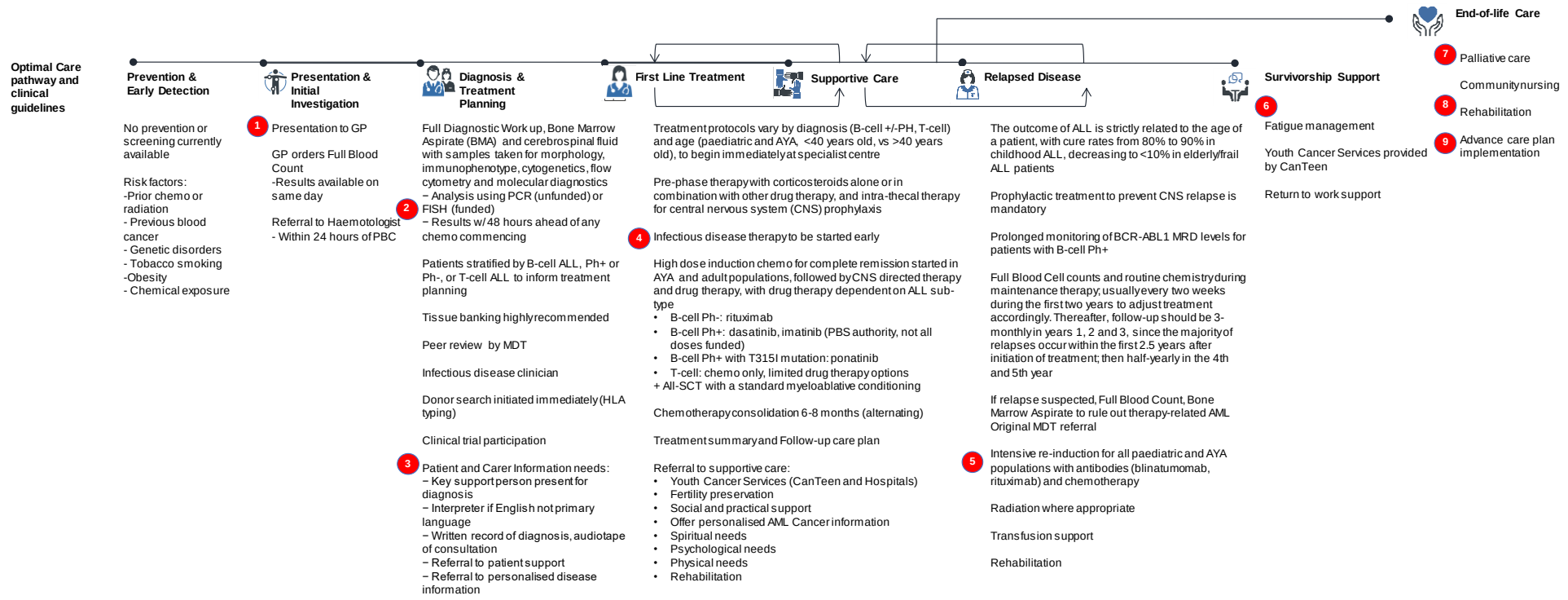


Figure A.4: International Benchmarking in ALL

What's different? In the EU more options are recommended to be used in front line therapies for B-cell lineage ALL patients, and additional drug therapies are recommended as the standard of care compared to Australia where effectively only chemotherapy is funded to T-cell lineage patients. The UK also makes a wholly different recommendation for first line therapy for children, AYA and adults that are treatment naïve (pegaspargase). Consultations also indicated that although blinatumomab is funded as a second line therapy it may not be available at each hospital due to in-patient funding components that must be met by hospital budgets. In addition, in the UK, patients aged up to 25 years old with B-cell refractory or relapsed post-transplant, and in >2nd line relapse are able to trial a CAR-T therapy, tisagenlecleucel.

Diagnosis & Treatment Planning

Full Diagnostic Work up, Bone Marrow Aspirate (BMA) and cerebrospinal fluid with samples taken for morphology, immunophenotype, cytogenetics, flow cytometry and molecular diagnostics
− Analysis using PCR (unfunded) or FISH (funded)
− Results w/ 48 hours ahead of any chemo commencing

Patients stratified by B-cell ALL, Ph+ or Ph-, or T-cell ALL to inform treatment planning

Tissue banking highly recommended

Peer review by MDT

Infectious disease clinician

Donor search initiated immediately (HLA typing)

Clinical trial participation

First-Line Treatment

Treatment protocols vary by diagnosis (B-cell +/-PH, T-cell) and age (paediatric and AYA, <40 years old, vs >40 years old), to begin immediately at specialist centre

Pre-phase therapy with corticosteroids alone or in combination with other drug therapy, and intra-thecal therapy for central nervous system (CNS) prophylaxis

Infectious disease therapy to be started early

High dose induction chemo for complete remission started in AYA and adult populations, followed by CNS directed therapy and drug therapy, with drug therapy dependent on ALL sub-type
- B-cell Ph-: rituximab
- B-cell Ph+: dasatinib, imatinib (PBS authority)
- B-cell Ph+ with T315I mutation: ponatinib
- T-cell: chemo

+ All-SCT with a standard myeloablative conditioning

Chemotherapy consolidation 6-8 months (alternating)

Relapsed Disease Treatment

The outcome of ALL is strictly related to the age of a patient, with cure rates from 80% to 90% in childhood ALL, decreasing to <10% in elderly/frail ALL patients

Prophylactic treatment to prevent CNS relapse is mandatory

Prolonged monitoring of BCR-ABL1 MRD levels for patients with ALL Ph+

Full Blood Cell counts and routine chemistry during maintenance therapy; usually every two weeks during the first two years to adjust treatment accordingly. Thereafter, follow-up should be 3-monthly in years 1, 2 and 3, since the majority of relapses occur within the first 2.5 years after initiation of treatment; then half-yearly in the 4th and 5th year

If relapse suspected, Full Blood Count, Bone Marrow Aspirate to rule out therapy-related AML
Original MDT referral

Intensive re-induction for all paediatric and AYA populations with antibodies (blinatumomab, rituximab) and chemotherapy

Radiation where appropriate
Transfusion support
Rehabilitation

Diagnosis & Treatment Planning

Full Diagnostic Work up, Bone Marrow Aspirate (BMA) and cerebrospinal fluid with samples taken for morphology, immunophenotype, cytogenetics, flow cytometry and molecular diagnostics
− Analysis using PCR or FISH
− Results w/ 48 hours ahead of any chemo commencing

Patients stratified by B-cell ALL, Ph+ or Ph-, or T-cell ALL to inform treatment planning

Tissue banking highly recommended

Peer review by MDT

Infectious disease clinician

Donor search initiated immediately (HLA typing)

Clinical trial participation

First-line Treatment

Treatment protocols vary by diagnosis and age, to begin immediately at specialist centre

Pre-phase therapy with corticosteroids alone or in combination with other drug therapy, and intra-thecal therapy for central nervous system (CNS) prophylaxis

Infectious disease therapy to be started early

High dose induction chemo for complete remission started in AYA and adult populations, followed by CNS directed therapy and drug therapy, with drug therapy dependent on ALL sub-type
Antibodies for B-lineage ALL patients: rituximab, blinatumomab, inotuzumab ozogamicin, epratuzumab, CAR T-cells
Antibodies for T-ALL patients: nelarabine or γ-secretase inhibitors
Tyrosine kinase inhibitors for Ph+ ALL: imatinib first line, nilotinib and dasatinib, ponatinib for T315I mutation
Tyrosine kinase inhibitors for Ph-like: imatinib, dasatinib, ruxolitinib
+ All-SCT with a standard myeloablative conditioning

Chemotherapy consolidation 6-8 months (alternating)

Relapsed Disease Treatment

The outcome of ALL is strictly related to the age of a patient, with cure rates from 80% to 90% in childhood ALL, decreasing to <10% in elderly/frail ALL patients

Prophylactic treatment to prevent CNS relapse is mandatory

Post- Allo-SCT prophylactic imatinib maintenance for Ph+ patients for 1-two years
+ Prolonged monitoring of BCR-ABL1 MRD levels

Full Blood Cell counts and routine chemistry during maintenance therapy; usually every two weeks during the first two years to adjust treatment accordingly. Thereafter, follow-up should be 3-monthly in years 1, 2 and 3, since the majority of relapses occur within the first 2.5 years after initiation of treatment; then half-yearly in the 4th and 5th year

If relapse suspected, Full Blood Count, Bone Marrow Aspirate to rule out therapy-related AML
Original MDT referral

Intensive re-induction with chemotherapy and drug therapy

Radiation where appropriate
Transfusion support
Rehabilitation

Diagnosis & Treatment Planning

Full Diagnostic Work up, Bone Marrow Aspirate (BMA) and cerebrospinal fluid with samples taken for morphology, immunophenotype, cytogenetics, flow cytometry and molecular diagnostics
− Analysis using PCR or FISH – genomic testing funded by government
− Results w/ 48 hours ahead of any chemo commencing

Patients stratified by B-cell ALL, Ph+ or Ph-, or T-cell ALL to inform treatment planning

Tissue banking highly recommended

Peer review by MDT

Infectious disease clinician

Donor search initiated immediately (HLA typing)

Clinical trial participation

First–line Treatment

Treatment protocols vary by diagnosis and age, to begin immediately at specialist centre

Pre-phase therapy with corticosteroids alone or in combination with other drug therapy, and intra-thecal therapy for central nervous system (CNS) prophylaxis

Infectious disease therapy to be started early

High dose induction chemo for complete remission started in AYA and adult populations, followed by CNS directed therapy and drug therapy, with pegapargase
+ All-SCT with a standard myeloablative conditioning

Chemotherapy consolidation 6-8 months (alternating)

Relapsed Disease Treatment

The outcome of ALL is strictly related to the age of a patient, with cure rates from 80% to 90% in childhood ALL, decreasing to <10% in elderly/frail ALL patients

Prophylactic treatment to prevent CNS relapse is mandatory

Post- Allo-SCT prophylactic imatinib maintenance for Ph+ patients for 1-two years
+ Prolonged monitoring of BCR-ABL1 MRD levels

Full Blood Cell counts and routine chemistry during maintenance therapy; usually every two weeks during the first two years to adjust treatment accordingly. Thereafter, follow-up should be 3-monthly in years 1, 2 and 3, since the majority of relapses occur within the first 2.5 years after initiation of treatment; then half-yearly in the 4th and 5th year

If relapse suspected, Full Blood Count, Bone Marrow Aspirate to rule out therapy-related AML
Original MDT referral

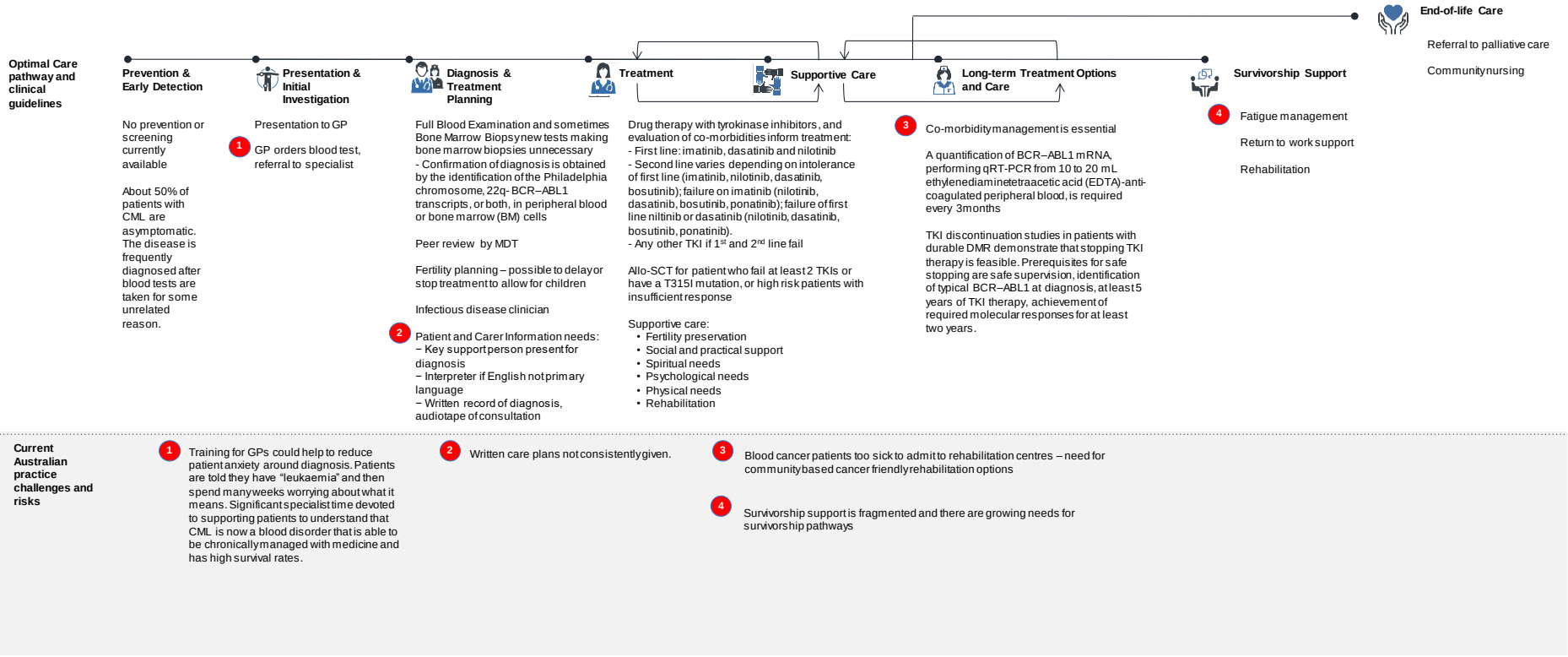
CAR-T cell therapy (tisagenlecleucel) for patients up to 25 years old

Intensive re-induction with chemotherapy and drug therapy (inotuzumab ozogamicin for relapsed refractory B-cell Precursor, blinatumomab for Ph- precursor B-cell ALL, ponatinib in Ph+ ALL if disease resistant to dasatinib, and T315I mutation present

Radiation where appropriate
Transfusion support
Rehabilitation

A.4 Care pathway analysis: Chronic Myeloid Leukaemia

Figure A.5: Optimal care pathway and current practice challenges in CML



A.5 Care pathway analysis: Chronic Lymphocytic Leukaemia

Figure A.6: Optimal care pathway and current practice challenges in CLL

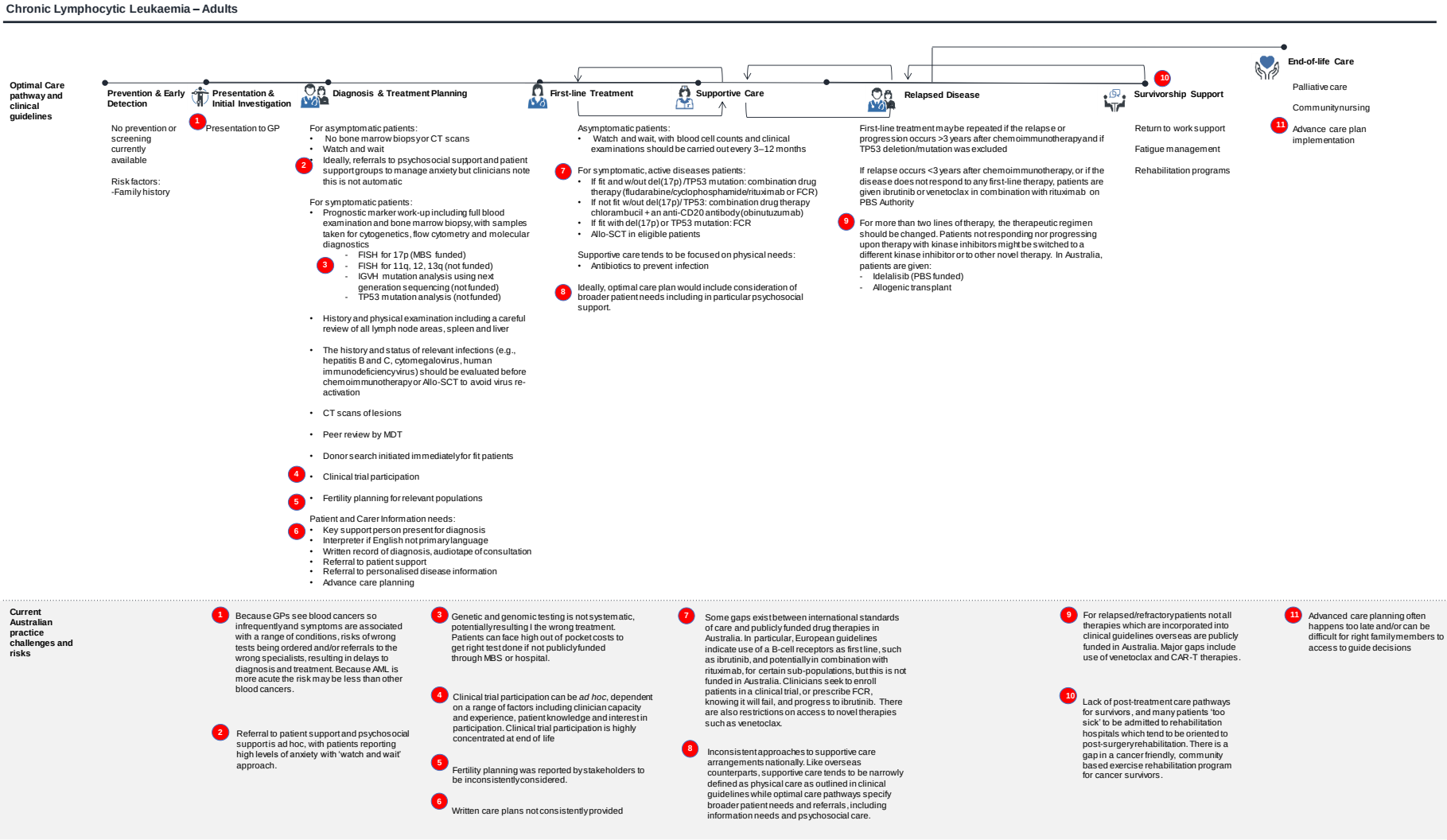


Figure A.7: International Benchmarking in CLL

What's different? In the UK, genomic testing is publicly funded and used to diagnose and guide treatment planning. In addition, patients with a del(17p)/Tp53 mutation are provided venetoclax first line, or ibrutinib if venetoclax is unsuitable. In the EU, this patient cohort also has combination therapy options that include rituximab as a first line therapy. Venetoclax is TGA registered but not PBS listed in Australia, and patients are prescribed ibrutinib expecting they will fail (two cycles) before being able to access ibrutinib as a second line therapy. In the EU and UK, venetoclax is provided as a standard second line therapy.

Diagnosis & Treatment Planning

For asymptomatic patients:
- No bone marrow biopsy or CT scans
- Watch and wait

For symptomatic patients:
- Prognostic marker work-up including full blood examination and bone marrow biopsy, with samples taken for cytogenetics, flow cytometry and molecular diagnostics
- History and physical examination including a careful review of all lymph node areas, spleen and liver
- The history and status of relevant infections (e.g., hepatitis B and C, cytomegalovirus, human immunodeficiency virus) should be evaluated before chemoimmunotherapy or Allo-SCT to avoid virus re-activation
- CT scans of lesions
- Peer review by MDT (although treatment will be initiated ahead of MDT), including consultation with Infectious disease clinician
- Donor search initiated immediately for fit patients
- Clinical trial participation

First-Line Treatment

Asymptomatic patients:
- Watch and wait, with blood cell counts and clinical examinations should be carried out every 3–12 months

For symptomatic, active diseases patients:
- If fit and w/out del(17p) /TP53 mutation: combination drug therapy (fludarabine/cyclophosphamide/rituximab or FCR)
- If not fit w/out del(17p)/ TP53: combination drug therapy chlorambucil + an anti-CD20 antibody (obinutuzumab)
- If fit with a del(17p) / TP53 mutation: FCR

Supportive care tends to be focused on physical needs:
- Antibiotics to prevent infection

Relapsed Disease Treatment

First-line treatment may be repeated if the relapse or progression occurs >3 years after chemoimmunotherapy and if TP53 deletion/mutation was excluded

If relapse occurs <3 years after chemoimmunotherapy, or if the disease does not respond to any first-line therapy, patients are given ibrutinib or venetoclax in combination with rituximab (PBS authority restricted)

For more than two lines of therapy, the therapeutic regimen should be changed. Patients not responding nor progressing upon therapy with kinase inhibitors might be switched to a different kinase inhibitor or to other novel therapy. In Australia, patients are given Idelalisib (PBS funded).

Diagnosis & Treatment Planning

For asymptomatic patients:
- No bone marrow biopsy or CT scans
- Watch and wait

For symptomatic patients:
- Prognostic marker work-up including full blood examination and bone marrow biopsy, with samples taken for cytogenetics, flow cytometry and molecular diagnostics
- History and physical examination including a careful review of all lymph node areas, spleen and liver
- The history and status of relevant infections (e.g., hepatitis B and C, cytomegalovirus, human immunodeficiency virus) should be evaluated before chemoimmunotherapy or Allo-SCT to avoid virus re-activation
- CT scans of lesions
- Peer review by MDT (although treatment will be initiated ahead of MDT), including consultation with Infectious disease clinician
- Donor search initiated immediately for fit patients
- Clinical trial participation

First-line Treatment

Asymptomatic patients:
- Watch and wait, with blood cell counts and clinical examinations should be carried out every 3–12 months

For symptomatic, active diseases patients:
- If fit and w/out del(17p) /TP53 mutation: combination drug therapy (fludarabine/cyclophosphamide/rituximab or FCR)
- If elderly w/out del(17p)/ TP53: combination drug therapy chlorambucil + an anti-CD20 antibody (rituximab, obinutuzumab)
- If fit with a del(17p)/TP53 mutation: combo drug therapy BCR +/- rituximab, with Allo-SCT in remission
- If elderly w/ dep 17 /TP53: Combo BCR =/- rituximab

Relapsed Disease Treatment

First-line treatment may be repeated if the relapse or progression occurs at least 24–36 months after chemoimmunotherapy and if TP53 deletion/mutation was excluded

If relapse occurs within 24–36 months after chemoimmunotherapy, or if the disease does not respond to any first-line therapy, the therapeutic regimen should be changed, to trial novel therapies include BCR =/- rituximab.

Patients not responding nor progressing upon therapy with kinase inhibitors might be switched to a different kinase inhibitor or to BCL2 antagonists when available (according to clinical trials)

Diagnosis & Treatment Planning

For asymptomatic patients:
- No bone marrow biopsy or CT scans
- Watch and wait

For symptomatic patients:
- Prognostic marker work-up including full blood examination and bone marrow biopsy, with samples taken for cytogenetics, flow cytometry and molecular diagnostics
- Genomic testing funded by government
- History and physical examination including a careful review of all lymph node areas, spleen and liver
- The history and status of relevant infections (e.g., hepatitis B and C, cytomegalovirus, human immunodeficiency virus) should be evaluated before chemoimmunotherapy or Allo-SCT to avoid virus re-activation
- CT scans of lesions
- Peer review by MDT (although treatment will be initiated ahead of MDT), including consultation with Infectious disease clinician
- Donor search initiated immediately for fit patients
- Clinical trial participation

First-line Treatment

Asymptomatic patients:
- Watch and wait, with blood cell counts and clinical examinations should be carried out every 3–12 months

For symptomatic, active diseases patients:
- If fit and w/out del(17p) /TP53 mutation: combination drug therapy idelalisib and rituximab
- If w/out del(17p)/ TP53: combination drug elderly g therapy chlorambucil + an anti-CD20 antibody (rituximab, obinutuzumab)
- If fit with a del(17p)/TP53 mutation and BCR is unsuitable: venetoclax
- If fit with a del(17p)/TP53 mutation and BCR is suitable: ibrutinib

Relapsed Disease Treatment

If relapse occurs with del(17p) or TP53 mutation, second line therapy is venetoclax.

For patients without dep(17p) or TP53 mutation, venetoclax can be given after chemotherapy and BCR

A.6 Care pathway analysis: Lymphomas

Figure A.8: Optimal care pathway and current practice challenges in Lymphomas

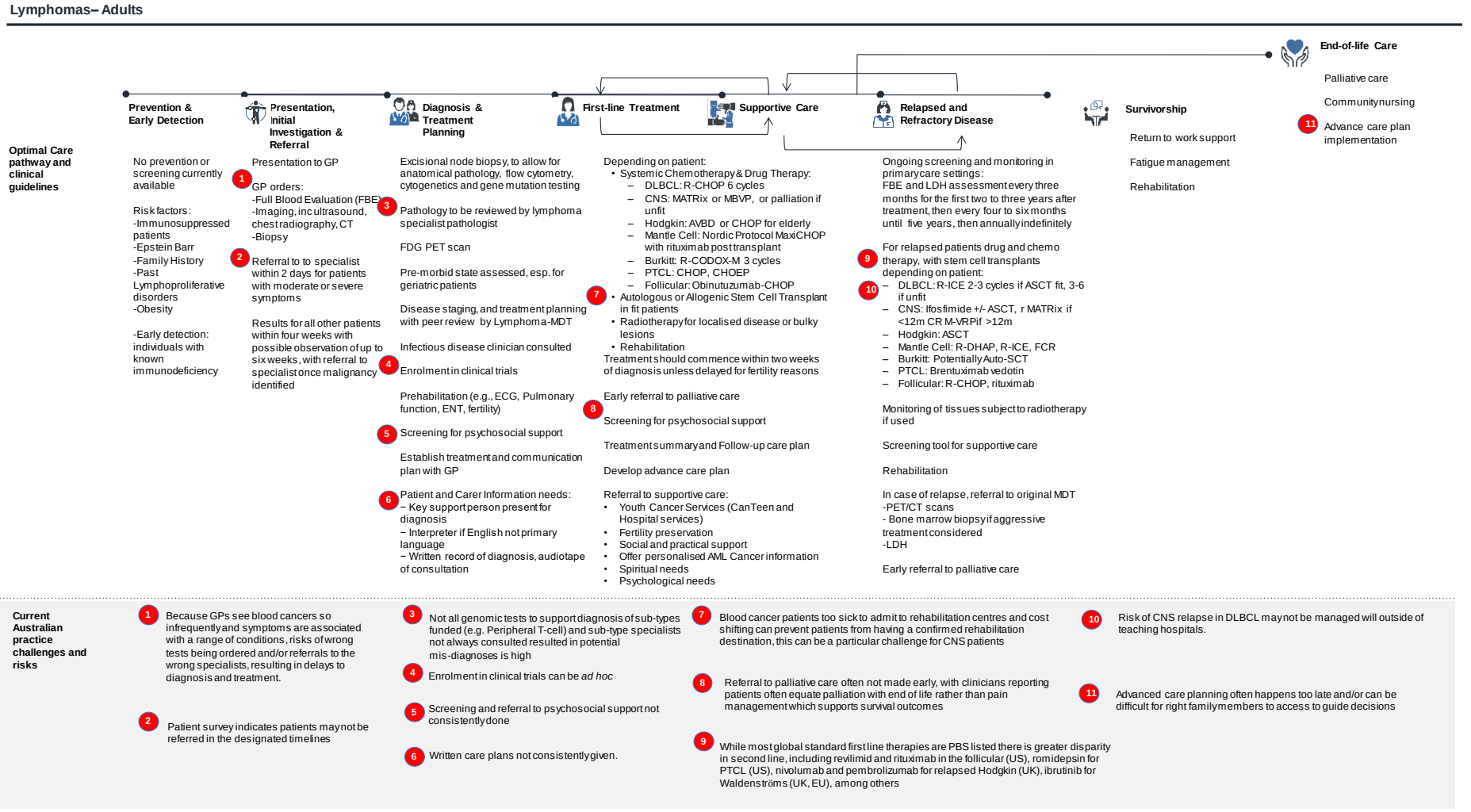


Figure A.9: International Benchmarking in Lymphomas

What's different? Many first line therapies for lymphomas in Australia are in line with global standards for treatment, with differences identified in Waldenström, Hodgkin and Follicular Lymphoma first line treatments. More variation can be observed in second line treatments for relapsed disease with both the UK and EU recommending variations in treatment for Hodgkin, Mantle Cell, Waldenström, and DLBCL.

First-Line Treatment

Depending on patient:
- Systemic Chemotherapy & Drug Therapy:
  - DLBCL: R-CHOP 6 cycles
  - CNS: MATRix or MBVP, or palliation if unfit
  - Hodgkin: AVBD ,or CHOP for elderly
  - Mantle Cell: Nordic Protocol MaxiCHOP with rituximab post transplant
  - Burkitt: R-CODOX-M 3 cycles
  - PTCL: CHOP, CHOEP
  - Follicular: Obinutuzumab-CHOP
  - Waldenström: DRC
- Autologous or Allogenic Stem Cell Transplant in fit patients
- Radiotherapy for localised disease or bulky lesions
- Rehabilitation

Treatment should commence within two weeks of diagnosis unless delayed for fertility reasons

Relapsed Disease Treatment

Ongoing screening and monitoring in primary care settings:
FBE and LDH assessment every three months for the first two to three years after treatment, then every four to six months until five years, then annually indefinitely

For relapsed patients drug and chemo therapy, with stem cell transplants depending on patient:
- DLBCL: R-ICE 2-3 cycles if ASCT fit, 3-6 if unfit
- CNS: Ifosfimide +/- ASCT, r MATRix if <12m CR M-VRPif >12m
- Hodgkin: ASCT
- Mantle Cell: R-DHAP, R-ICE, FCR
- Burkitt: Potentially Auto-SCT
- PTCL: Brentuximab vedotin
- Follicular: R-CHOP, rituximab
- Waldenström: DRC

First-line Treatment

Depending on patient:
- Systemic Chemotherapy & Drug Therapy:
  - DLBCL: R-CHOP 6-8 cycles depending on staging, fitness
  - CNS: MATRix or MBVP, or palliation if unfit
  - Hodgkin: AVBD, or BEACOPP depending on staging
  - Mantle Cell: R-CHOP with rituximab post transplant
  - Burkitt: R-CODOX-M 3 cycles
  - PTCL: CHOP, CHOEP
  - Follicular: Rituximab (mild symptoms), R-CHOP, R-CVP, BR
  - Waldenström: DR, BR, BDR, VR, Ibrutinib, Rituximab or Chlorambucil depending on fitness and symptoms
- Autologous or Allogenic Stem Cell Transplant in fit patients
- Radiotherapy for localised disease or bulky lesions
- Rehabilitation

Treatment should commence within two weeks of diagnosis unless delayed for fertility reasons

Relapsed Disease Treatment

Ongoing screening and monitoring in primary care settings:
FBE and LDH assessment every three months for the first two to three years after treatment, then every four to six months until five years, then annually indefinitely

For relapsed patients drug and chemo therapy, with stem cell transplants depending on patient:
- DLBCL: R-ICE 2-3 cycles if ASCT fit, 3-6 if unfit
- CNS: Ifosfimide +/- ASCT, r MATRix if <12m CR M-VRPif >12m
- Hodgkin: Chemo+ASCT, DHAP, ICE, Brentuximab vedotin if fail ASCT
- Mantle Cell: R-BAC, R-CHOP, rituximab maintenance, ibrutinib, lenalidomide where ibrutinib contraindicated
- Burkitt: Potentially Auto-SCT
- PTCL: Brentuximab vedotin
- Follicular: Rituximab ,idelalisib, or chemo BR, R-CHOP, R-CVP
- Waldenström: Ibrutinib

First-line Treatment

Depending on patient:
- Systemic Chemotherapy & Drug Therapy:
  - DLBCL: Rituximab (for advanced) and in combination CVP, CHOP
  - CNS: MATRix or MBVP, or palliation if unfit
  - Hodgkin: Brentuximab vedotin (CD30)
  - Mantle Cell: Rituximab+chemo, Bortezomib where SCT unfit
  - Burkitt: R-CODOX-M 3 cycles
  - PCTL: CHOP
  - Follicular: Rituximab, R-CHOP, Obinutuzumab-CHOP
  - Waldenström: Ibrutinib
- Autologous or Allogenic Stem Cell Transplant in fit patients
- Radiotherapy for localised disease or bulky lesions
- Rehabilitation

Treatment should commence within two weeks of diagnosis unless delayed for fertility reasons

Relapsed Disease Treatment

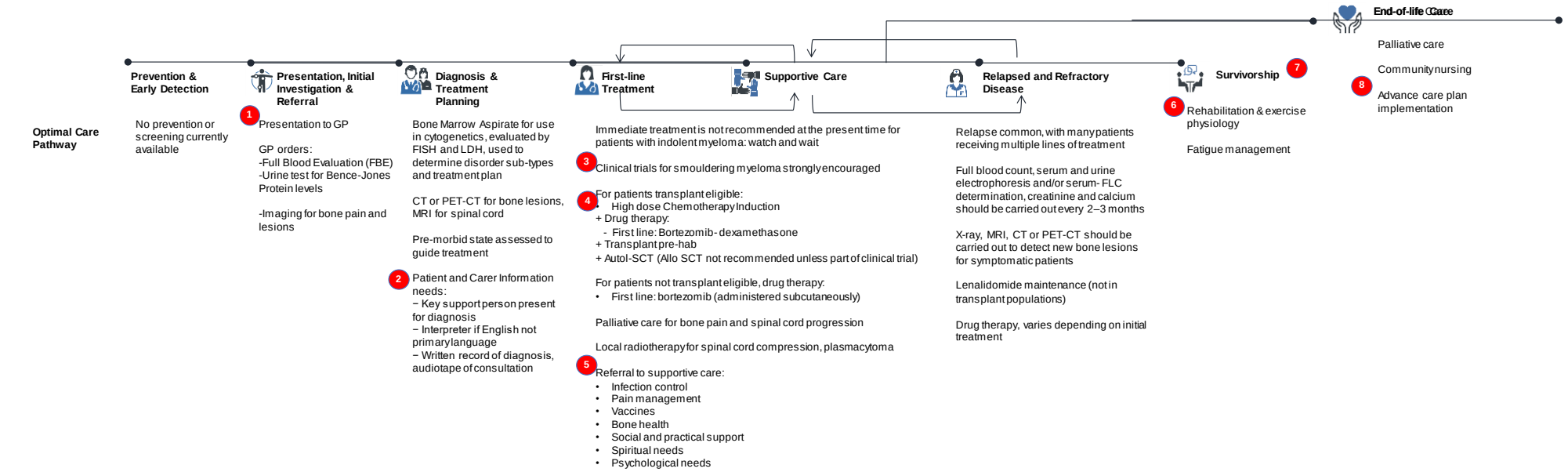
Ongoing screening and monitoring in primary care settings:
FBE and LDH assessment every three months for the first two to three years after treatment, then every four to six months until five years, then annually indefinitely

For relapsed patients drug and chemo therapy, with stem cell transplants depending on patient:
- DLBCL: Pixantrone
- CNS: Ifosfimide +/- ASCT, r MATRix if <12m CR M-VRPif >12m
- Hodgkin: Nivolumab, Pembrolizumab
- Mantle Cell: Ibrutinib, temsirolimus
- Burkitt: Potentially Auto-SCT
- Follicular: R-CHOP, rituximab
- Waldenström: Ibrutinib

A.7 Care pathway analysis: Myeloma

Figure A.10: Optimal care pathway and current practice challenges in Myeloma

Myeloma – Adults



Current Australian practice challenges and risks

1. Because GPs see blood cancers so infrequently and symptoms are associated with a range of conditions, risks of wrong tests being ordered and/or referrals to the wrong specialists, resulting in delays to diagnosis and treatment.
2. Written care plans not consistently given.
3. Enrolment in clinical trials can be *ad hoc*
4. A number of medicines in use in EU and UK not PBS funded in Australia, including revlimid for transplant eligible patients, combination therapies sch as revlimid and antibodies such as daratumumab and ecotuzumab, carfilzomib for first line treatment, prembrolidomide for 1st line or 2nd line. For transplant ineligible patients combination bortezomib and thalidomide not funded.
5. *Ad hoc* referral to patient support and information about condition
6. Blood cancer patients too sick to admit to rehabilitation centres
7. Survivorship support is very fragmented and there are growing needs for survivorship pathways
8. Advanced care planning often happens too late and/or can be difficult for right family members to access to guide decisions

Figure A.11: International Benchmarking in Myeloma

What's different? In the UK, genomic testing is publicly funded and used to diagnose and guide treatment planning. In addition, the standard of care for first line treatment for fit patients is a combination therapy. In the EU and UK lenalidomide maintenance is also a standard of care for relapsed disease for all patient cohorts, while daratumumab, ixazomib and other combination therapies are recommended for some patient cohorts. In Australia lenalidomide maintenance is not funded for transplant populations and daratumumab is TGA registered but not PBS listed.

Diagnosis & Treatment Planning

Bone Marrow Aspirate for use in cytogenetics, evaluated by FISH and LDH, used to determine disorder sub-types and treatment plan

CT or PET-CT for bone lesions, MRI for spinal cord

Pre-morbid state assessed to guide treatment

Patient and Carer Information needs:
– Key support person present for diagnosis
– Interpreter if English not primary language
– Written record of diagnosis, audiotape of consultation

First-Line Treatment

Immediate treatment is not recommended at the present time for patients with indolent myeloma: watch and wait

Clinical trials for smouldering myeloma strongly encouraged

For patients transplant eligible:
• High dose Chemotherapy Induction
+ Drug therapy:
- First line: Bortezomib- dexamethasone
+ Transplant pre-hab
+ Autol-SCT (Allo SCT not recommended unless part of clinical trial)

For patients not transplant eligible, drug therapy:
• First line: bortezomib (administered subcutaneously)

Palliative care for bone pain and spinal cord progression

Local radiotherapy for spinal cord compression, plasmacytoma

Relapsed Disease Treatment

Relapse common, with many patients receiving multiple lines of treatment

Full blood count, serum and urine electrophoresis and/or serum- FLC determination, creatinine and calcium should be carried out every 2–3 months

X-ray, MRI, CT or PET-CT should be carried out to detect new bone lesions for symptomatic patients

Lenalidomide maintenance (not in transplant populations)

Drug therapy, varies depending on initial treatment
• Carfilzomib-dexamethasone
• Thalidomide- dexamethasone

Diagnosis & Treatment Planning

Bone Marrow Aspirate for use in cytogenetics, evaluated by FISH and LDH, used to determine disorder sub-types and treatment plan

CT or PET-CT for bone lesions, MRI for spinal cord

Pre-morbid state assessed to guide treatment

First-Line Treatment

Immediate treatment is not recommended at the present time for patients with indolent myeloma: watch and wait

Clinical trials for smouldering myeloma strongly encouraged

For patients <70y:
-High dose Chemotherapy Induction (4-6 doses)
+ Drug therapy:
- First line: Bortezomib- dexamethasone
- Off-label bortezomib- dexamethasone + third agent, either thalidomide (VTD), doxorubicin (PAD), lenalidomide (RVD) or cyclophosphamide (VCD)
+ Autol-SCT (Allo SCT not recommended unless part of clinical trial)

For patients >70y, drug therapy:
• First line: bortezomib (administered subcutaneously)/melphalan/prednisone (VMP) or lenalidomide plus low-dose dexamethasone (Rd)

Palliative care for bone pain and spinal cord progression

Local radiotherapy for spinal cord compression, plasmacytoma

Relapsed Disease Treatment

Relapse common, with many patients receiving multiple lines of treatment

Full blood count, serum and urine electrophoresis and/or serum- FLC determination, creatinine and calcium should be carried out every 2–3 months

X-ray, MRI, CT or PET-CT should be carried out to detect new bone lesions for symptomatic patients

Lenalidomide maintenance

Drug therapy, varies depending on initial treatment

Diagnosis & Treatment Planning

Bone Marrow Aspirate for use in cytogenetics, evaluated by FISH and LDH, used to determine disorder sub-types and treatment plan

CT or PET-CT for bone lesions, MRI for spinal cord

Pre-morbid state assessed to guide treatment

First-Line Treatment

Immediate treatment is not recommended at the present time for patients with indolent myeloma: watch and wait

Clinical trials for smouldering myeloma strongly encouraged

For patients transplant eligible:
-High dose Chemotherapy Induction (4-6 doses)
+ Drug therapy:
- First line: Bortezomib- dexamethasone
+ Autol-SCT (Allo SCT not recommended unless part of clinical trial)

For patients transplant ineligible, drug therapy:
• First line: combination bortezomib and thalidomide

Palliative care for bone pain and spinal cord progression

Local radiotherapy for spinal cord compression, plasmacytoma

Relapsed Disease Treatment

Relapse common, with many patients receiving multiple lines of treatment

Full blood count, serum and urine electrophoresis and/or serum- FLC determination, creatinine and calcium should be carried out every 2–3 months

X-ray, MRI, CT or PET-CT should be carried out to detect new bone lesions for symptomatic patients

Lenalidomide maintenance

Drug therapy, varies depending on initial treatment
- Ixazomib
- Carfilzomib
- Panobiostat in combo with Bortezomib- dexamethasone
- Daratumumab monotherapy

A.8 Care pathway analysis: Myelodysplastic Syndrome

Figure A.12: Optimal care pathway and current practice challenges in MDS

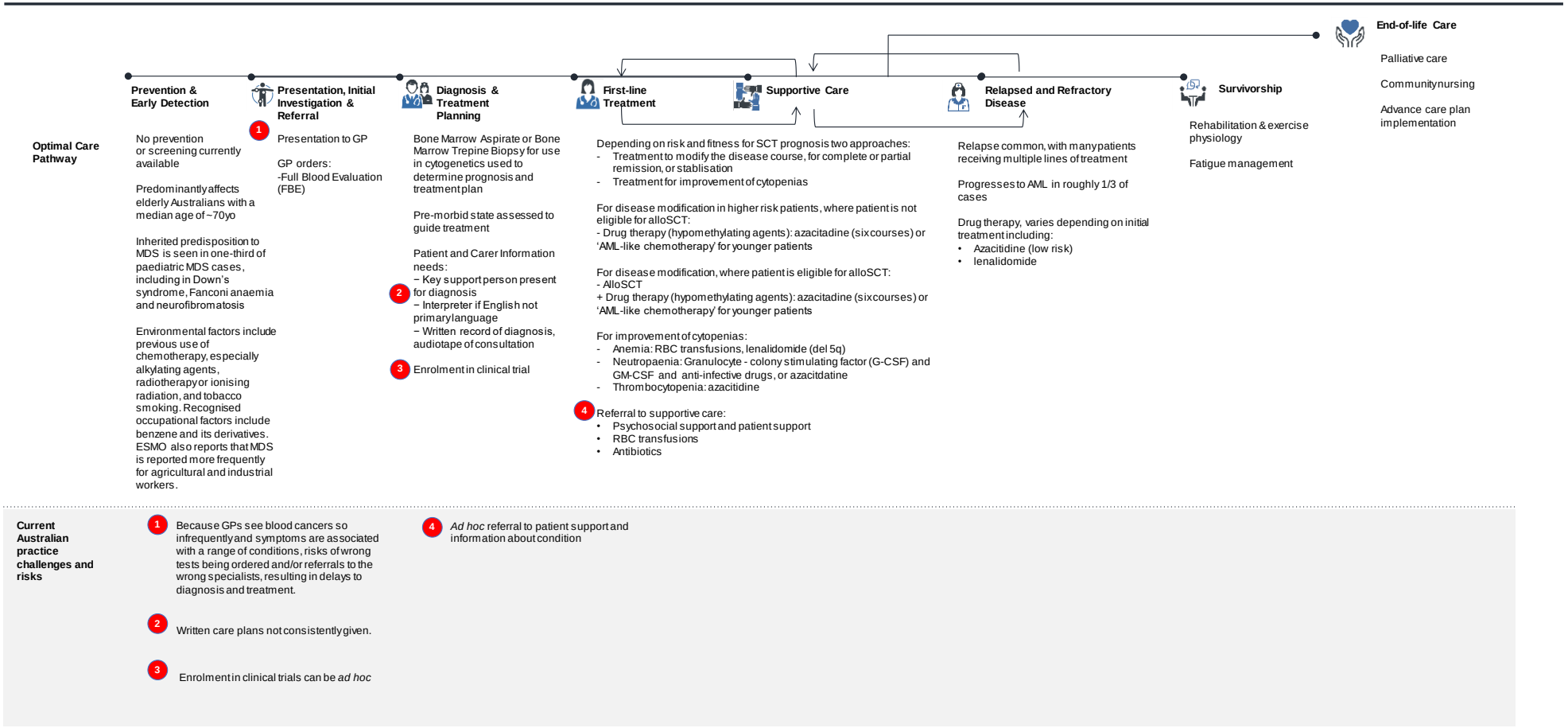


Figure A.13: International Benchmarking in MDS

What's different? In the EU more drug therapies are recommended for the treatment of cytopenias, decitabine is included as a first line option in addition to azacitadine.

First-Line Treatment

Depending on risk and fitness for SCT prognosis two approaches:
- Treatment to modify the disease course, for complete or partial remission, or stablisation
- Treatment for improvement of cytopenias

For disease modification in higher risk patients, where patient is not eligible for alloSCT:
- Drug therapy (hypomethylating agents): azacitadine (six courses) or 'AML-like chemotherapy' for younger patients

For disease modification, where patient is eligible for alloSCT:
- AlloSCT
+ Drug therapy (hypomethylating agents): azacitadine (six courses) or 'AML-like chemotherapy' for younger patients

For improvement of cytopenias in lower risk patients:
- Anemia: RBC transfusions, lenalidomide (del 5q)
- Neutropaenia: Granulocyte - colony stimulating factor (G-CSF) and GM-CSF and anti-infective drugs, or azacitdatine depending on risk
- Thrombocytopenia: azacitidine

Relapsed Disease Treatment

Relapse common, with many patients receiving multiple lines of treatment

Progresses to AML in roughly 1/3 of cases

Drug therapy, varies depending on initial treatment including:
- Azacitidine
- Lenalidomide

First-Line Treatment

Depending on risk and fitness for SCT prognosis two approaches:
- Treatment to modify the disease course, for complete or partial remission, or stablisation
- Treatment for improvement of cytopenias

For disease modification in higher risk patients, where patient is not eligible for alloSCT:
- Drug therapy (hypomethylating agents): azacitadine (six courses) or decitabine or 'AML-like chemotherapy' for younger patients

For disease modification, where patient is eligible for alloSCT:
- AlloSCT
+ Drug therapy (hypomethylating agents): azacitadine (six courses) or decitabine or 'AML-like chemotherapy' for younger patients

For improvement of cytopenias in lower risk patients:
- Anemia: RBC transfusions, lenalidomide (del 5q), Erythropoetine (EPO) (no del 5q), ESAs depending on genetics (del5q)
- Neutropaenia: Granulocyte - colony stimulating factor (G-CSF) and GM-CSF and anti-infective drugs, or high dose androgens ,azacitdatine
- Thrombocytopenia: Thrombopoietin(TPO) receptor agonist, Anti-thymocyte globulin (ATG), azacitidine

Relapsed Disease Treatment

Relapse common, with many patients receiving multiple lines of treatment

Progresses to AML in roughly 1/3 of cases

Drug therapy, varies depending on initial treatment including:
- Azacitidine
- Lenalidomide

First-Line Treatment

For disease modification in higher risk patients, where patient is not eligible for alloSCT:
- Drug therapy (hypomethylating agents): azacitadine

Relapsed Disease Treatment

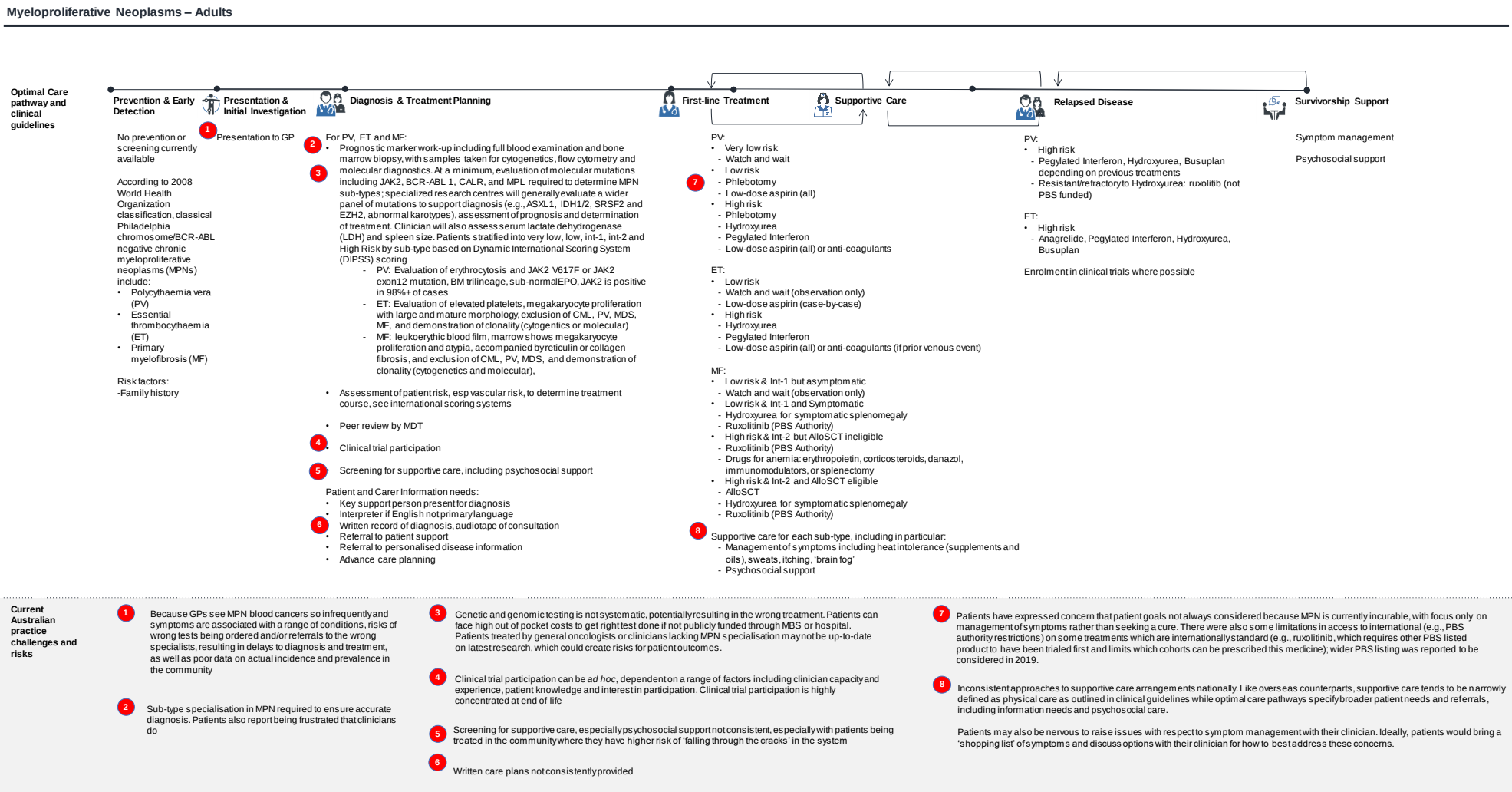
Relapse common, with many patients receiving multiple lines of treatment

Progresses to AML in roughly 1/3 of cases

Drug therapy, varies depending on initial treatment including:
- Azacitidine
- Lenalidomide

A.9 Care pathway analysis: Myeloproliferative Neoplasms

Figure A.14: International Benchmarking in MPN



Appendix B

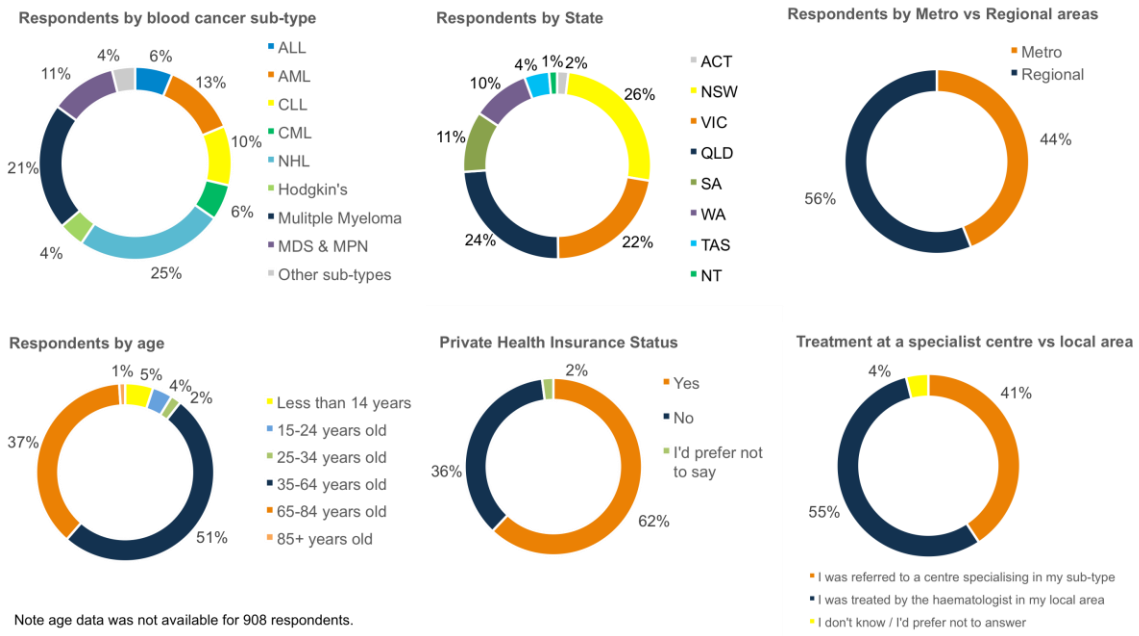
Survey of People Living with Blood Cancer: Key Response Statistics

In total, 3,227 people responded to the survey.

The survey delivered a good representation of sub-types, States, regional status, age and private health insurance status.

The sample sizes were statistically significant with a confidence level of 95% or greater at confidence intervals of +/-5% across sub-types overall, with a slightly wider confidence interval for Hodgkin Lymphoma of +/-8%, CML of +/-6% and CLL of +/-6%.

Figure B1: Summary of respondents



The length of the survey varied depending on the responses to some questions, with page logic built in so that people did not see irrelevant questions. In total the survey was between 25 and 35 questions depending on the respondent's answers.

Appendix C

Technical Appendix of Blood Cancer Incidence, Prevalence and Mortality Projections

C.1. Method Overview

The Blood Cancer Projections to 2035 were developed using a bottom-up cohort-component method.

ABS Population Projections for Series A and B were aggregated into 5-year age groups to match AIWH Australian Cancer Database, State Cancer Registry data and PHN data. Prevalence was based on public and custom requested data from Victoria and Queensland Cancer Registries.

Rates of incidence and incidence growth rates based on AIHW data by sex and blood cancer sub-type were applied to ABS projections by five-year age-group from 2018 to 2035 and then stratified into PHN using ABS data.

Mortality was projected based on the application of age-based survival curves at 1-year, 5-year and long run conditional survival age-based survival data was obtained from the State Cancer Registries through a customised data request to the incidence and prevalence cohorts. Using long run conditional survival data from the AIHW only a proportion of the deaths of long run survivors were attributed to blood cancer.

Years of life lost were determined by taking the difference between the year of death and the life expectancy by gender reported by the AIWH (78 for males, 84 for females).

The model was built to allow for sensitivity analysis in:

- Higher Population Growth (Series A Projections, as opposed to Series B which are reported)
- Under incidence in reporting to State Cancer registries (the report assumes no under-reporting occurs)
- Alternative incidence growth rates (the report presents five-year average growth from 2009-2014 (latest data) and zero growth, with 10-year or 20-year averages producing astoundingly high expectations for the incidence and prevalence of blood cancer)
- Variation in incidence by PHN
- Variation in survival outcomes by State, by age group by sex by blood cancer sub-type.

C.2 Key Outputs

The results from the Blood Cancer Projection Model include:

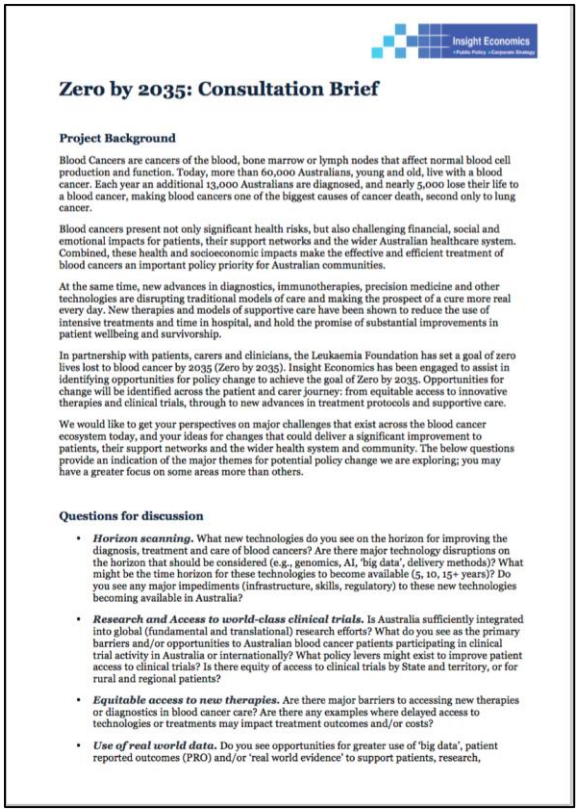
- Incidence by cancer sub-type, age and sex by PHN, State and nationally for the years 2018-2035
- Prevalence by cancer sub-type, age and sex by PHN, State and nationally for the years 2018-2035
- Mortality by cancer sub-type, age and sex by PHN, State and nationally for the years 2018-2035
- YLL by cancer sub-type, age and sex by PHN, State and nationally for the years 2018-2035
- YLD by cancer sub-type, age and sex by PHN, State and nationally for the years 2018-2035.

C.3 List of Data

Variable	Data source
Population projections	ABS Cat. No. 3222
Incidence	AIHW Australian Cancer Database, including Australian Cancer Incidence and Mortality Books for each sub-type ABS Cancer Incidence and Mortality by PHN
Prevalence	Victorian Cancer Registry Queensland OASys
Survival and mortality	Victorian Cancer Registry, Cancer Institute NSW, Queensland OASys, Tasmanian Cancer Registry, AIHW Cancer in Australia 2017. Data for WA and SA were not able to be made available in the time to write the report.

Appendix D

Consultation Brief



Insight Economics

Zero by 2035: Consultation Brief

Project Background

Blood Cancers are cancers of the blood, bone marrow or lymph nodes that affect normal blood cell production and function. Today, more than 60,000 Australians, young and old, live with a blood cancer. Each year an additional 13,000 Australians are diagnosed, and nearly 5,000 lose their life to a blood cancer, making blood cancers one of the biggest causes of cancer death, second only to lung cancer.

Blood cancers present not only significant health risks, but also challenging financial, social and emotional impacts for patients, their support networks and the wider Australian healthcare system. Combined, these health and socioeconomic impacts make the effective and efficient treatment of blood cancers an important policy priority for Australian communities.

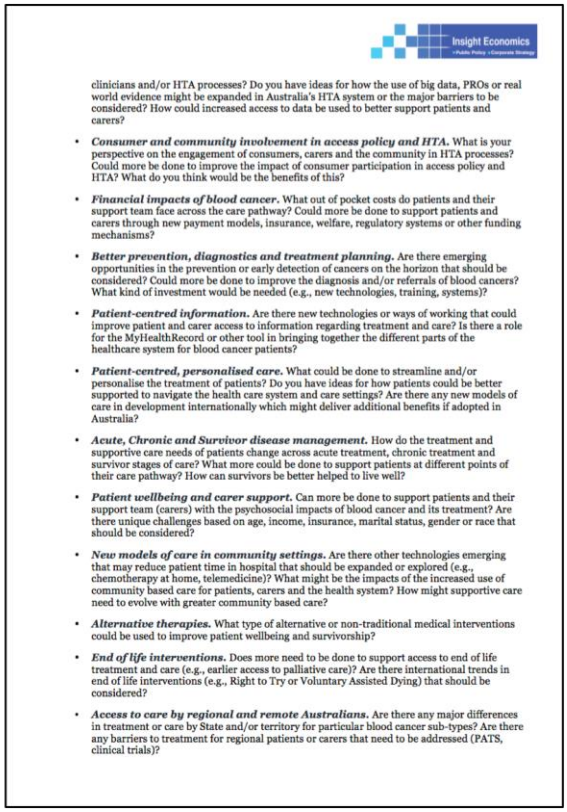
At the same time, new advances in diagnostics, immunotherapies, precision medicine and other technologies are disrupting traditional models of care and making the prospect of a cure more real every day. New therapies and models of supportive care have been shown to reduce the use of intensive treatments and time in hospital, and hold the promise of substantial improvements in patient wellbeing and survivorship.

In partnership with patients, carers and clinicians, the Leukaemia Foundation has set a goal of zero lives lost to blood cancer by 2035 (Zero by 2035). Insight Economics has been engaged to assist in identifying opportunities for policy change to achieve the goal of Zero by 2035. Opportunities for change will be identified across the patient and carer journey: from equitable access to innovative therapies and clinical trials, through to new advances in treatment protocols and supportive care.

We would like to get your perspectives on major challenges that exist across the blood cancer ecosystem today, and your ideas for changes that could deliver a significant improvement to patients, their support networks and the wider health system and community. The below questions provide an indication of the major themes for potential policy change we are exploring; you may have a greater focus on some areas more than others.

Questions for discussion

- ***Horizon scanning.*** What new technologies do you see on the horizon for improving the diagnosis, treatment and care of blood cancers? Are there major technology disruptions on the horizon that should be considered (e.g., genomics, AI, 'big data', delivery methods)? What might be the time horizon for these technologies to become available (5, 10, 15+ years)? Do you see any major impediments (infrastructure, skills, regulatory) to these new technologies becoming available in Australia?
- ***Research and Access to world-class clinical trials.*** Is Australia sufficiently integrated into global (fundamental and translational) research efforts? What do you see as the primary barriers and/or opportunities to Australian blood cancer patients participating in clinical trial activity in Australia or internationally? What policy levers might exist to improve patient access to clinical trials? Is there equity of access to clinical trials by State and territory, or for rural and regional patients?
- ***Equitable access to new therapies.*** Are there major barriers to accessing new therapies or diagnostics in blood cancer care? Are there any examples where delayed access to technologies or treatments may impact treatment outcomes and/or costs?
- ***Use of real world data.*** Do you see opportunities for greater use of 'big data', patient reported outcomes (PRO) and/or 'real world evidence' to support patients, research,



Insight Economics

clinicians and/or HTA processes? Do you have ideas for how the use of big data, PROs or real world evidence might be expanded in Australia's HTA system or the major barriers to be considered? How could increased access to data be used to better support patients and carers?

- ***Consumer and community involvement in access policy and HTA.*** What is your perspective on the engagement of consumers, carers and the community in HTA processes? Could more be done to improve the impact of consumer participation in access policy and HTA? What do you think would be the benefits of this?
- ***Financial impacts of blood cancer.*** What out of pocket costs do patients and their support team face across the care pathway? Could more be done to support patients and carers through new payment models, insurance, welfare, regulatory systems or other funding mechanisms?
- ***Better prevention, diagnostics and treatment planning.*** Are there emerging opportunities in the prevention or early detection of cancers on the horizon that should be considered? Could more be done to improve the diagnosis and/or referrals of blood cancers? What kind of investment would be needed (e.g., new technologies, training, systems)?
- ***Patient-centred information.*** Are there new technologies or ways of working that could improve patient and carer access to information regarding treatment and care? Is there a role for the MyHealthRecord or other tool in bringing together the different parts of the healthcare system for blood cancer patients?
- ***Patient-centred, personalised care.*** What could be done to streamline and/or personalise the treatment of patients? Do you have ideas for how patients could be better supported to navigate the health care system and care settings? Are there any new models of care in development internationally which might deliver additional benefits if adopted in Australia?
- ***Acute, Chronic and Survivor disease management.*** How do the treatment and supportive care needs of patients change across acute treatment, chronic treatment and survivor stages of care? What more could be done to support patients at different points of their care pathway? How can survivors be better helped to live well?
- ***Patient wellbeing and carer support.*** Can more be done to support patients and their support team (carers) with the psychosocial impacts of blood cancer and its treatment? Are there unique challenges based on age, income, insurance, marital status, gender or race that should be considered?
- ***New models of care in community settings.*** Are there other technologies emerging that may reduce patient time in hospital that should be expanded or explored (e.g., chemotherapy at home, telemedicine)? What might be the impacts of the increased use of community based care for patients, carers and the health system? How might supportive care need to evolve with greater community based care?
- ***Alternative therapies.*** What type of alternative or non-traditional medical interventions could be used to improve patient wellbeing and survivorship?
- ***End of life interventions.*** Does more need to be done to support access to end of life treatment and care (e.g., earlier access to palliative care)? Are there international trends in end of life interventions (e.g., Right to Try or Voluntary Assisted Dying) that should be considered?
- ***Access to care by regional and remote Australians.*** Are there any major differences in treatment or care by State and/or territory for particular blood cancer sub-types? Are there any barriers to treatment for regional patients or carers that need to be addressed (PATS, clinical trials)?

Appendix E

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Acronyms

ABS	Australian Bureau of Statistics
AI	Artificial Intelligence
AIDS	Acquired Immune Deficiency Syndrome
AIHW	Australian Institute for Health and Welfare
ALL	Acute Lymphoblastic Leukaemia
ALLG	Australasian Leukaemia and Lymphoma Group
AMA	Australian Medical Association
AML	Acute Myeloid Leukaemia
ANZCHOG	Australian and New Zealand Children's Haematology and Oncology Group
AYA	Adolescents and Young Adults
BCL-2	B-cell lymphoma 2
BCR	Benefit Cost Ratio
CAR-T	Chimeric Antigen Receptor Therapy
CART-Wheel	Centre for Analysis of Rare Tumours
CDC	Centers for Disease Control and Prevention
CLL	Chronic Lymphocytic Leukaemia
CML	Chronic Myeloid Leukaemia
CNS	Central Nervous System
COSA	Clinical Oncological Society of Australia
CRO	Contract Research Organisation
CTCLs	Cutaneous T-cell lymphomas
ctDNA	Circulating tumour DNA
CTU	Clinical Trial Unit
DALY	Disability Adjusted Life Year
DLBCL	Diffuse large B-cell lymphoma
DNA	Deoxyribonucleic acid
EMA	European Medicines Agency
ESMO	European Society for Medical Oncology
EU	European Union
FDA	Food and Drug Administration
FL	Follicular lymphoma
GP	General Practitioner
HIV	Human Immunodeficiency Virus

HSANZ	Haematological Society of Australia and New Zealand
ICD	International Classification of Diseases
KPI	Key Performance Indicator
LaRDR	Lymphoma and Related Diseases Registry
LLS	Leukaemia & Lymphoma Society
MALT	Mucosa-Associated Lymphoid Tissue
MBS	Medicare Benefits Scheme
MCL	Mantle cell lymphoma
MDS	Myelodysplastic Syndrome
MDT	Multi-Disciplinary Team
MOGA	Medical Oncology Group of Australia
MPN	Myeloproliferative neoplasms
MSAC	Medical Services Advisory Committee
NAS	National Aggregate Statistics
NCI	National Cancer Institute
NFC	Nationally Funded Centres
NHL	Non-Hodgkin Lymphoma
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NICE	National Institute for Clinical Excellence
NIH	National Institutes of Health
NNDSS	National Notifiable Disease Surveillance System
NOA	National Oncology Alliance
NORD	National Organisation for Rare Disorders
NPV	Net Present Value
NZ	New Zealand
OBPR	Office of Best Practice Regulation
PARP	Poly ADP Ribose Polymerase
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PD-1	Programmed T cell death 1
PHN	Primary Health Network
PRO	Patient Reported Outcome
PTCL	Peripheral T-cell lymphoma
QALY	Quality Adjusted Life Year
SEER	Surveillance, Epidemiology and End Results

TGA	Therapeutic Goods Administration
TKI	Tyrosine Kinase Inhibitor
UK	United Kingdom
WhIMSICAL	Waldenström's Macroglobulinemia Study In CART-WheeL
YLD	Years Lived with a Disability
YLL	Years of Potential Life Lost


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