VISION 20-30

Building an Australian Cancer Futures Framework

NOA | NATIONAL ONCOLOGY ALLIANCE

IN PARTNERSHIP WITH

rare cancers AUSTRALIA

MINDEROO FOUNDATION

A VISION BUILT ON **COLLABORATION**

Our heartfelt gratitude goes to the families of the patients who are tragically no longer with us, who so generously shared their stories to help others.

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rare cancers AUSTRALIA

MINDEROO FOUNDATION

AUTHOR

DR AMANDA RUTH

HEAD OF POLICY
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RARE CANCERS AUSTRALIA

“Change in cancer care is emerging at a rapid rate. We need to look openly and honestly at the system, how it fits within the global context and how it copes with the new world of cell therapy, genomics, and personalised treatment.

RICHARD VINES, CHIEF EXECUTIVE
RARE CANCERS AUSTRALIA FOUNDER, NOA

“Innovation is providing an unprecedented opportunity to rethink how we use data and technology to improve outcomes for cancer patients. Minderoo Foundation is pleased to be a partner in the NOA and the Vision 20-30 framework, both of which are intended to drive greater collaboration across philanthropy, government, industry, research and clinical care. Together we can make cancer non-lethal.

DR. STEVE BURNELL, CEO OF MINDEROO FOUNDATION’S
COLLABORATE AGAINST CANCER

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FOREWORD
VISION 20-30

In 2020, 50,000 Australians will die from cancer. It is a breathtaking and heartbreaking number. Even more so when you consider that this number will include children, teenagers, young adults, and parents of growing families. In fact, cancer is the biggest cause of death in most of these groups. And of course, cancer will exact a huge toll on boomers in 2020 and beyond.

For these Australians, neither their death nor the path towards it will be pleasant. Their journey from diagnosis to death will most likely be filled with a succession of treatments and interventions, including surgery, radio oncology and chemotherapy. They will struggle with pain, side effects, financial ruin, fear, and uncertainty until they finally reach the point of "no further treatment" and spend their final days in an opioid-induced haze.

Their fate will not be to pass peacefully in their sleep at a ripe old age, but rather to end their days in confusion and uncertainty as the world simply moves on. Our projections tell us that by 2030, this number will increase to around 63,000 each year if we do nothing. That cannot be an option for Australia.

So how did we get here, what can we do to make things better and why do we urgently need an Australian Cancer Futures Framework?

The Australian health system is shaped by contributions from the federal and state governments, public and private hospital sectors, research institutions and private medical practitioners. It is a complex beast that has evolved over the years to broadly reflect advances in our understanding of health and medicine.

But the system is under pressure, and nowhere does that pressure manifest more than in cancer. Therapies and technologies that patients need are supplied by mega corporations for whom Australia is a small, although not insignificant, market. The priority for the release of new treatments by these companies is inevitably the USA, where a completely different health system operates. Long delays in the availability of new therapies in Australia are already occurring and may potentially increase.

We need to recognise that any delays to the availability of new treatments in Australia are not metrics to boast about or manipulate but rather they result in Australians dying without the opportunity to extend or save their lives. Celebrating the registration and reimbursement of a new therapy should always be tempered by the reality of all those patients who missed out whilst the negotiations between government and industry dragged on.

We need to look openly and honestly at the system, how it fits within the global context and how it copes with the new world of cell therapy, genomics, and personalised treatment.

Finally and most importantly, before I let you jump into this outstanding document – I would like to thank the whole team at RCA, especially Amanda Ruth for her herculean effort in writing and producing the Vision. Thanks to Christine Cockburn and her team for sensitively building the patient stories and to Mike Parker, Natalie Clancy and the rest of team for their amazing efforts in putting together the workshops, digital production, speakers, logistics and endless proofreading and research. And of course, Kate Vines, our founder and inspiration, without whom we would never have had the courage and vision to try.

Richard Vines
Founder, NOA
Chief Executive, Rare Cancers Australia

A UNITED VISION FOR CANCER CARE – 10 YEARS

Australia has a fully patient centred health system.

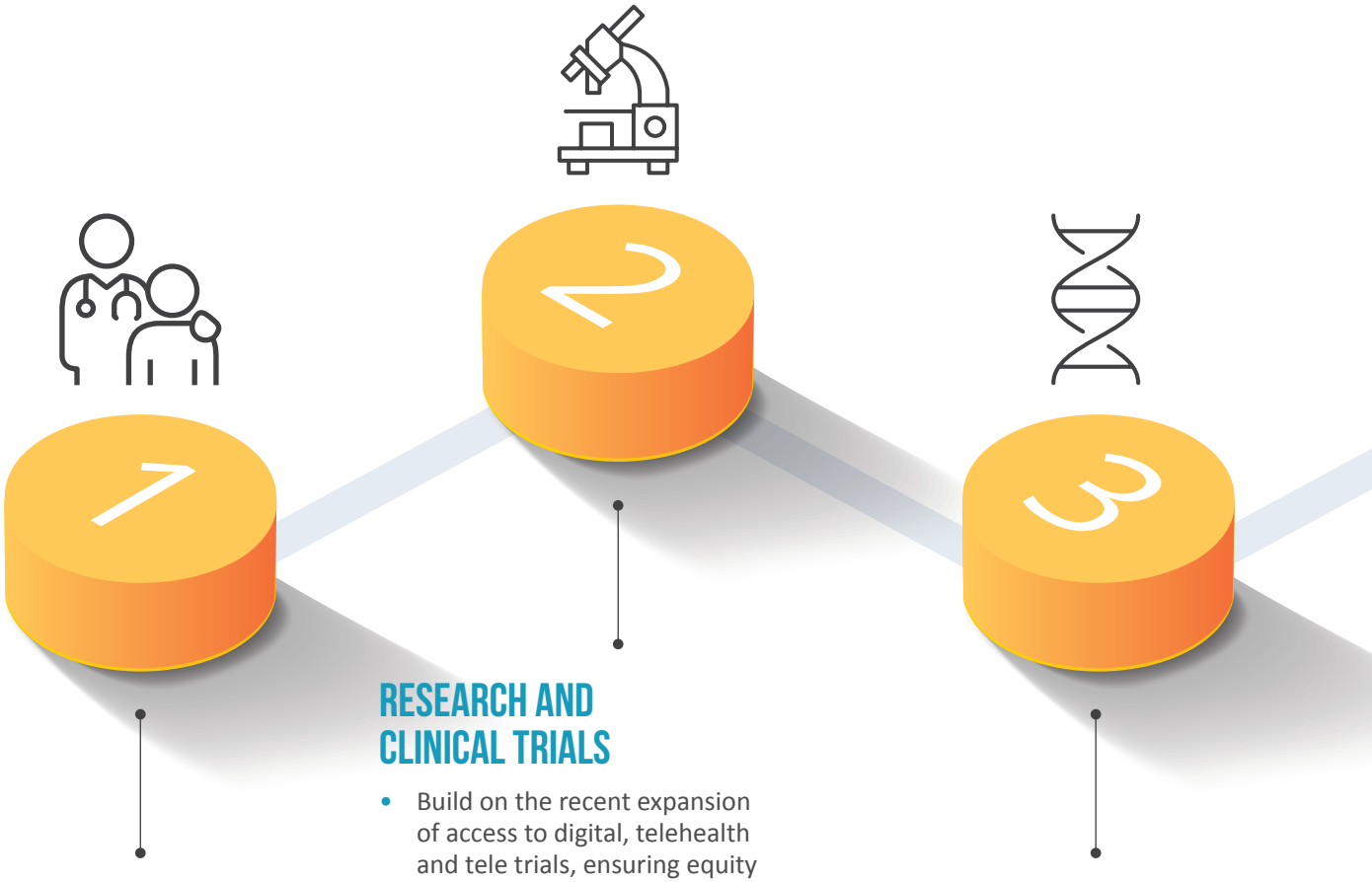
Patients have equitable, swift and affordable access to the best treatments and technologies.

There is greater than 90% survival rate across all cancer types and sub-types, regardless of rarity.

Australia has a thriving local biotechnology, pharmaceutical, medical technology industry.

Australia is recognised internationally as a country that models best practice for cancer research, treatment and management.

FRAMEWORK



PATIENT CENTRED CANCER CARE

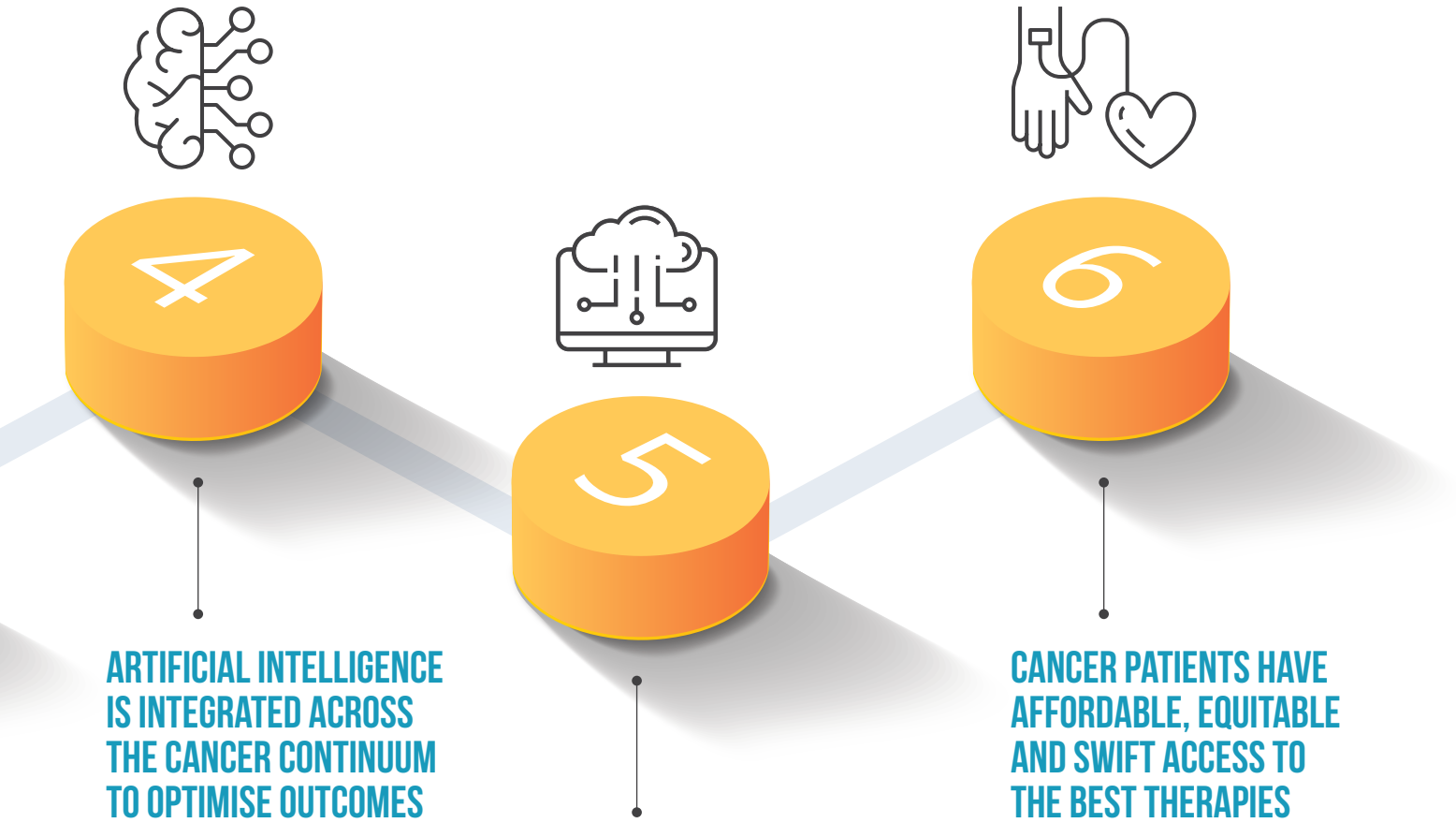
- Cancer patients are engaged and "central" to all aspects of their journey.
- Cancer patients have equity of access to understandable information to empower decision making, best medical teams and the support they need.
- Patient preferences are captured formally in evaluation frameworks that lead to decision making about resource allocation. Preferences can be embedded through rigorous modelling and patient reported outcome measures.

RESEARCH AND CLINICAL TRIALS

- Build on the recent expansion of access to digital, telehealth and tele trials, ensuring equity of access for patients regardless of disease type or geographical location. In particular, a plan to expand access to clinical trials to patients outside major metropolitan areas through tele trials.

GENOMIC SEQUENCING AND TESTING TO SUPPORT ACCESS TO PRECISION THERAPIES AND PAVE THE WAY FOR NGS INTEGRATION INTO THE HEALTH SYSTEM

- Provide genomic sequencing for cancer patients on non-curative pathways who are likely to benefit from analysis to inform optimum treatment, and linkage to clinical trial therapies where no funded therapies are available.
- Determine how to offer funded access to NGS, which will be needed as companion testing for emerging tumour-agnostic therapies.
- Explore the feasibility of establishing a national co-ordinated genomic centre of excellence.



ARTIFICIAL INTELLIGENCE IS INTEGRATED ACROSS THE CANCER CONTINUUM TO OPTIMISE OUTCOMES

- Develop the capacity for the use of AI across the cancer continuum and more broadly within the health system. Understand the breadth of its utility and current application. Develop frameworks for policy, governance, ethics and infrastructure.

DATA AND DIGITAL OBJECTS ACROSS THE CANCER CONTINUUM CAN BE SHARED AND ACCESSED VIA AN AUSTRALIAN CANCER DATA COMMONS

- Establish Australian cloud-based data platform that collects and houses comprehensive data, including around access to care, trends in survival, variation in practice and genomic data. This would allow stakeholders to store, share, access and apply AI to digital data and objects across the cancer continuum.

CANCER PATIENTS HAVE AFFORDABLE, EQUITABLE AND SWIFT ACCESS TO THE BEST THERAPIES AND TECHNOLOGIES

- A fast-track provisional reimbursement pathway (akin to TGA priority and provisional fast track pathways) with a risk-share funding mechanism for cancers with high clinical need.
- Streamlined reimbursement pathways for multi-indication targeted therapies.
- Comprehensive evaluation and funding pathways that are designed to meaningfully measure the value for money of newer therapies and technologies over the longer-term.

ACKNOWLEDGEMENTS

We would like to acknowledge all of the many individuals and organisations that helped make this report possible whether through financial support, written submissions at the start of this project, contributions through the workshop series or encouragement through this exercise.

We wish to emphasize that our acknowledgment does not imply that views expressed within the report are held by all who participated in the project. To the hundreds of contributors and supporters we simply wish to say

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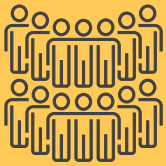
12 WORKSHOPS

37 SPEAKERS

1,200 ATTENDEES



1 AN AUSTRALIAN CANCER FUTURES FRAMEWORK

A UNITED VISION 20-30

The National Oncology Alliance (NOA) is an unincorporated not-for-profit alliance of cancer stakeholders founded by Rare Cancers Australia (RCA). Vision 20-30 is an initiative of NOA and RCA developed in partnership with The Minderoo Foundation

NOA engages the best experts across the entire cancer community. It aims to shape policy, ensuring Australians living with cancer get access to the best technology and treatments to extend their survival and improve their quality of life.

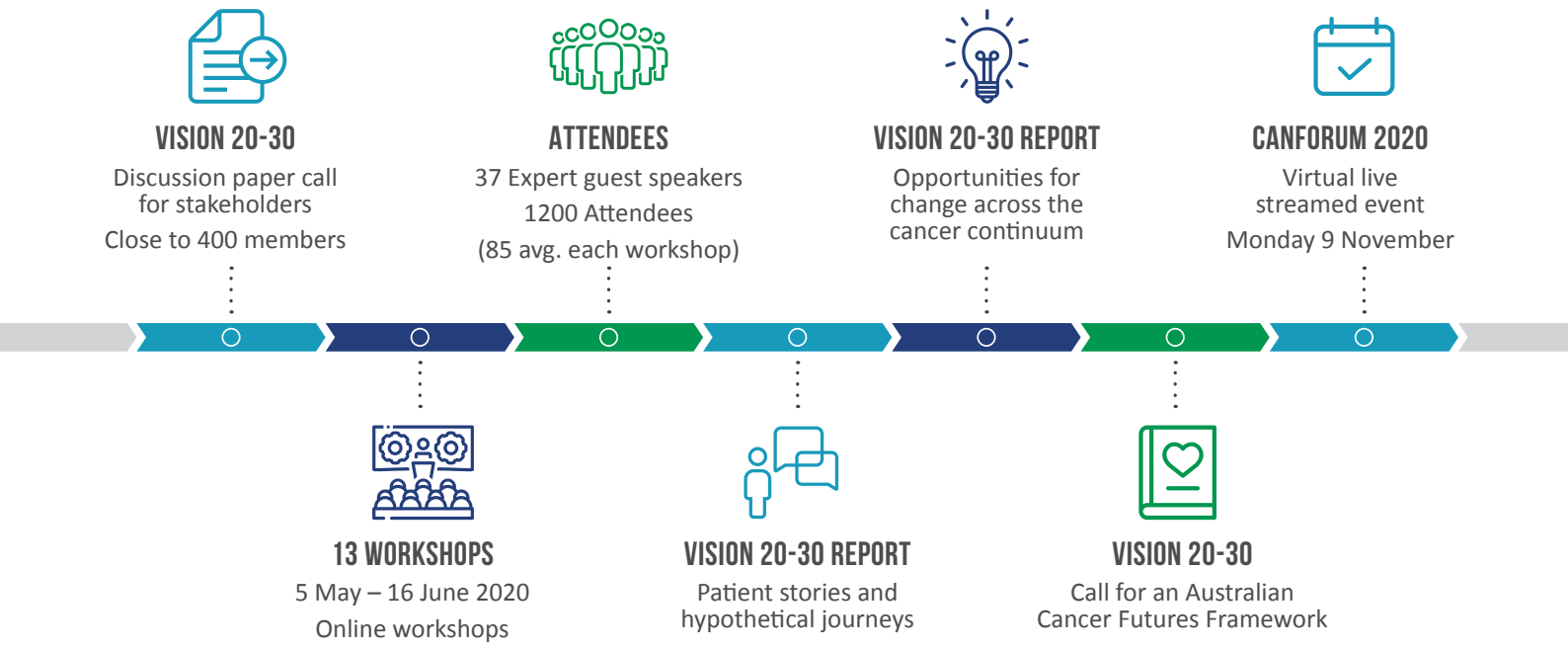
NOA has 400 registered members, including organisations and individuals. Members include patients, patient organisations, clinicians, hospitals, supplier organisations (including radiation oncology providers), the pharmaceutical industry and technology companies.

This report draws upon opportunities to deliver on an aspirational Vision 20-30 to save and extend the lives of cancer patients. The vision was informed by 12 NOA virtual workshops that spanned the cancer continuum. The process of extensive consultation of the best minds in cancer care provided the foundation for this report.

Cancer has a profound impact on patients, families and society from a physical, emotional, financial and economic perspective. It is a tragic and complex raft of diseases that remains one of Australia's most significant health challenges.

Over the next ten years, the transformational changes in cancer care will challenge the health system. The emergence of therapeutic discoveries in cancer together with the impact of a world-wide pandemic demand thoughtful consideration of where resources should be spent most efficiently. NOA seeks to ensure that cancer patients can access the best treatments and technologies consistently within the next decade. Now is the time to plan to make this a reality.

FIGURE 1. NATIONAL ONCOLOGY ALLIANCE VISION 20-30 FOR CANCER



↑90%

A higher than ninety percent survival rate across all cancers is achievable by 2030.

For the first time in the history of the complex set of diseases called “cancer”, there is much to be optimistic about.

The aspirations across the cancer continuum known as Vision 20-30 can be used to guide what needs to evolve within our health system. The united Vision 20-30 informed by the extensive workshop series is:

- To have a fully patient centred and driven health system.
- That all patients have access to the best therapies, technologies, care, medical networks and social supports – when they need them, at an affordable price, regardless of location or socioeconomic status.
- There is a greater than 90% survival rate across all cancer types and sub-types, regardless of rarity.
- Australia has a thriving local biotechnology, pharmaceutical, medical technology industry.
  - Australia is considered an attractive commercial destination by global manufacturers of cancer therapies and related technologies. Investment in clinical trial research attracts industry investments into the sector – creating jobs and stimulating economic returns.
- Australia is recognised internationally as a country that models best practice for cancer research, treatment and management.

BUILDING AN AUSTRALIAN CANCER FUTURES FRAMEWORK

This report explains that building an Australian Cancer Futures Framework can deliver the desired outcomes from Vision 20-30.

NOA's proposed Australian Cancer Futures Framework aims to increase the utility and availability of cancer treatments and technologies in the interest of saving lives. The Framework will provide a mechanism to conduct 'deep dives' into areas of significance that will complement existing cancer work streams.

The initial pillars fall into two broad categories:

- Integrating use of emerging technology and methodology for personalised cancer care
- Addressing the frameworks that underpin equitable and swift access to the best cancer care

Investing in the framework will deliver economic and social returns on investment that can be measured. The desired outcomes will be front of mind in building each key area of focus for the framework.

NOA stakeholders are invested in securing equity of access to the best treatments and technologies for the cancer patients of today and tomorrow, to ensure they have the best hope for long, healthy lives. Patients ARE the reason we seek to progress our systems, so that Australia can boast of being one of the leading countries in the world for cancer care and survival in 2030.

1 Patient centred cancer care

- Cancer patients are engaged and "central" to all aspects of their journey.
- Cancer patients have equity of access to understandable information to empower decision making, best medical teams and the support they need.
- Patient preferences are captured formally in evaluation frameworks that lead to decision making about resource allocation. Preferences can be embedded through rigorous modelling and patient reported outcome measures.

2 Research and clinical trials

- Build on the recent expansion of access to digital, telehealth and tele trials, ensuring equity of access for patients regardless of disease type or geographical location. In particular, a plan to expand access to clinical trials to patients outside major metropolitan areas through tele trials.

3 Genomic sequencing to support access to precision therapies and pave the way for Next Generation Sequencing (NGS) integration into the health system

- Provide genomic sequencing for cancer patients on non-curative pathways who are likely to benefit from analysis to inform optimum treatment, and linkage to clinical trial therapies where no funded therapies are available.
- Determine how to offer funded access to NGS, which will be needed as companion testing for emerging tumour-agnostic therapies.
- Explore the feasibility of establishing a national co-ordinated genomic centre of excellence.

4 Artificial Intelligence is integrated across the cancer continuum to optimise outcomes

- Develop the capacity for the use of AI across the cancer continuum and more broadly within the health system. Understand the breadth of its utility and current application. Develop frameworks for policy, governance, ethics and infrastructure.

5 Data and digital objects across the cancer continuum can be shared and accessed via an Australian Cancer Data Commons

- An Australian cloud-based data platform that collects and houses comprehensive data, including around access to care, trends in survival, variation in practice and genomic data. This would allow stakeholders to store, share, access and apply AI to digital data and objects across the cancer continuum.

6 Cancer patients to have affordable, equitable and swift access to the best therapies and technologies

- A fast-track provisional reimbursement pathway (akin to Therapeutic Goods Administration (TGA) priority and provisional fast track pathways) with a risk-share funding mechanism for cancers with high clinical need.
- Streamlined reimbursement pathways for multi-indication targeted therapies.
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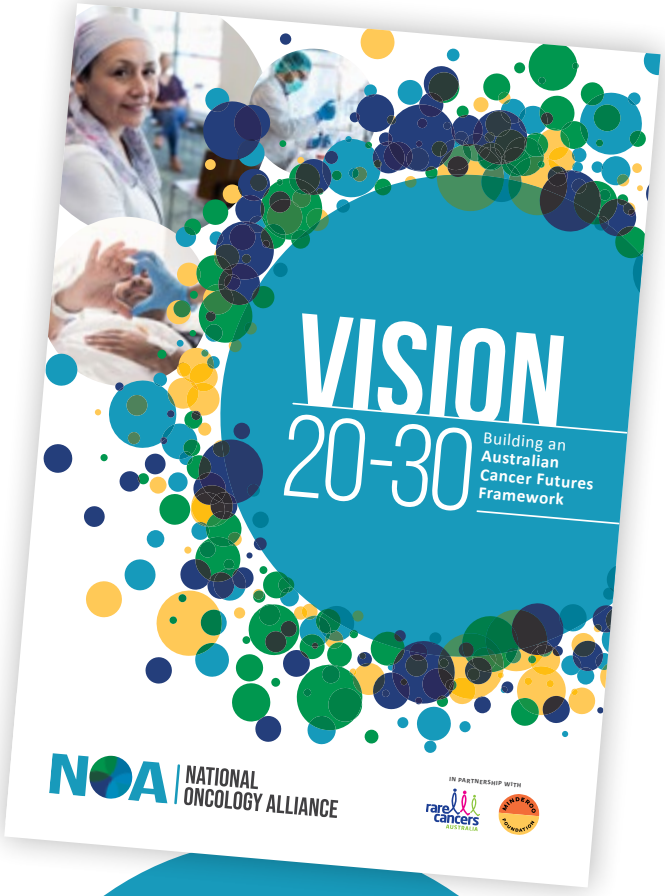
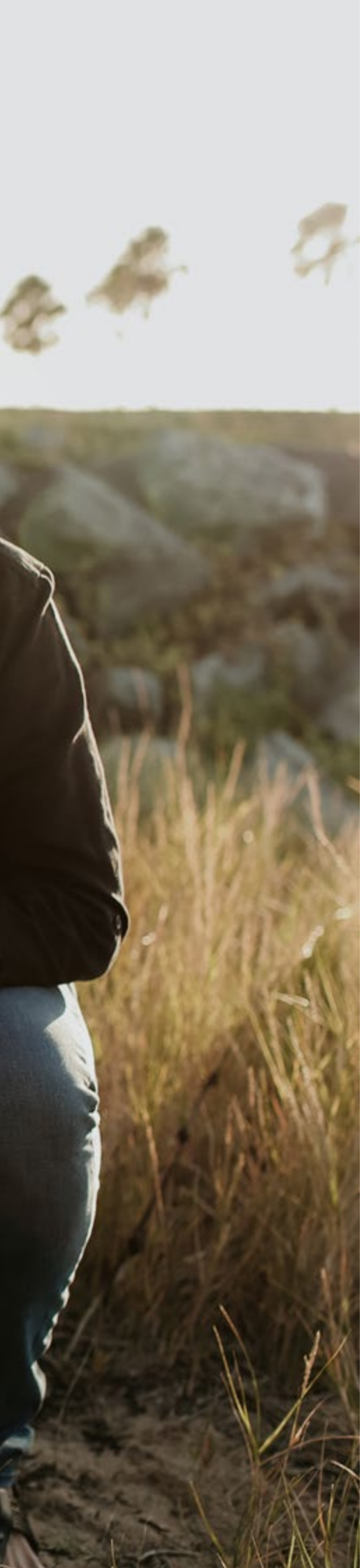


NOA stakeholders are invested in securing equity of access to the best treatments and technologies for the cancer patients of today and tomorrow, to ensure they have the best hope for long, healthy lives.

> Failing to Plan is Planning to Fail
>
> ***Benjamin Franklin***

Patient Journey

Not a day goes by when Jack and I don't talk about Scott, I will be forever grateful for the impact he had on our son.



SCOTT

Every night Scott would say goodnight to our son Jack. They had a ritual where Scott would say "*Whose boy are you?*" Jack would lovingly respond with "*Your boy*". Scott's life was Jack, he was the stay at home parent whilst I went to work and everything he did, he did for his boy. He was deeply passionate about Jack getting a good education and living a good life.

Scott's other great passion was St Kilda AFL club, after they drew in the grand final in 2010, Scott didn't speak for days! His partner Robyn describes how much better St Kilda are performing since Scott died earlier this year, and how she and Jack laugh that Scott would certainly be saying "*story of my life*". Scott's coffin and the box his ashes are housed in are both dedications to his favourite club.

Robyn goes on to describe Scott as "*the balancer, whilst I am the extrovert. He was the organiser and the stable influence. He was the guy we defaulted to for decisions and a rational perspective. He wasn't much of a talker but he was a very considered decision maker. When he brought our dog Bowser into our lives there were months of research that went into what kind of dog would fit our family.*"

Scott and Jack shared a passion for sports, Scott was his taxi driver and when he took up little athletics last year and Scott was worried it would interfere with cricket. He didn't stop it, found a way too balance it. Robyn shares that found a discuss in the wardrobe that Scott had bought before he died and didn't get a chance to give it to his son. Jack recently had his 12th birthday so it was a great gift specially from dad.

Scott wasn't always the sensible type, he had some quirks too, explains Robyn "*He always brushed his teeth before breakfast and was an irrational neat freak in the house but his shed looked as though a bomb had gone off.*" Despite his level-headedness, like all of us Scott had a distinct dislike for traffic and his impatience meant that Jack learnt a lot of choice words in their city commutes!

Not a day goes by when Jack and I don't talk about Scott, I will be forever grateful for the impact he had on our son, I'm sure that because of Scott, Jack will grow into a great man. We have wonderful memories from a trip we took to Broome before Scott died and we share those memories often.

2020 PATIENT JOURNEY

Scott

2013 DISCOVERY

- Scott felt pain in his calf muscle and couldn't work out what was wrong after experiencing symptoms for more than six months.
- He went to the doctor for an ultrasound thinking it was a blood clot.

2013 SCREENING

- Scott's Doctor orders an MRI and a Biopsy to find the cause of Scott's pain.

2013 DIAGNOSED

- To Scott's horror the results came back diagnosing him with a rare fast growing and aggressive Undifferentiated Pleomorphic Sarcoma. (53%, 5-year survival rate).

2013 INFORMATION

- Scott and his doctor are left without an optimal care pathway.
- Scott will now begin the scary unknown journey familiar to rare or less common cancer patients.

2013 TREATMENT – SURGERY

- Scott endures a painful surgery removing 2 out of 3 hamstring muscles in the back of his leg. He suffers nerve damage and, as a result, daily numbness and tingling down his leg to his foot.

2013 TREATMENT – RADIATION THERAPY

- Scott also undergoes 25 rounds of radiation therapy around the operated area to try and keep the cancer spreading.
- Radiation therapy does not work, and the sarcoma spreads to both lungs, with his two initial tumours having now multiplied into seven.

2013 TREATMENT – CLINICAL TRIAL

- Scott exhausts all family funds on immunotherapy (approx. $14,000).
- He enrolls in the MoST study, but no actionable mutation was found.

2018 TREATMENT – TARGETED THERAPY

- Despite Scott raising $29,000 the FDA approved drug is pulled from the global market due to inadequate evidence and the trials are terminated.
- Scott restarts the standard palliative chemotherapy and radiation until he could no longer drive himself to treatment

OCTOBER 2016 FUNDRAISING

- Scott has hope of a new Targeted Therapy drug approved by the FDA in the US.
- Scott must raise $174,000 for a 12-month supply. He manages to crowdfund $29,000, however this causes significant personal hardship for Scott and his family as they had been extremely private about their experience, in fact they had not even told Scott's son, Jack. Scott underwent extensive support to be able to have that conversation with Jack, he had no knowledge about how to tell him and did not want to distress his young son.

APRIL 2020

- Scott passed away leaving behind a loving partner and 11-year-old son.

2030 PATIENT JOURNEY

DISCOVERY

- A patient feels pain in his calf muscle and can't work out what is wrong after experiencing symptoms for six weeks.
- Patients have access to a standard MRI which is subsidised. The scan is funded via a shared model.

SCREENING

- The MRI shows a malignancy and a fine needle biopsy is taken from the small mass.
- Results show a tiny rare, fast growing and aggressive Undifferentiated Pleomorphic Sarcoma.

DIAGNOSED

- Patients and their doctors are not alone during the diagnosis and are assigned a Specialist Cancer Navigator who helps provide information and emotional support for patients and their families.
- Patients are able to better manage their symptoms by engaging early with palliative care services.

TREATMENT
GENOME SEQUENCING

- Before treatment commences patients undergo Whole Genome Sequencing, funded under a shared model which helps outline the best way to treat the cancer.
- Patient's GP's receive rare cancer management refreshers so are able to share care during treatment and follow best practice guidelines.

TREATMENT
MULTI DISCIPLINARY TEAM

- Patients are involved with a Multi Disciplinary Team (MDT).
- The results from the Whole Genome Sequencing show that a targeted therapy is best to treat the sarcoma.

INFORMATION

- With the Navigator assisting, patients can make informed decisions about their treatment options.
- Patients and their MDT agree the treatment objective is to keep the sarcoma from growing and reduce it in size. Patient preferences are recorded and guide the pathway of care taken.
- Patients do not need to undertake crowdfunding and therefore, can maintain their privacy.

TREATMENT
TARGETED THERAPY

- Patients access targeted therapy at no cost to their families. Targeted treatments have minimal side effects and are available close to home.
- Monitoring will be done via wearable devices and any changes will trigger a notification to the treating team and recorded in a registry.
- Side-effects are managed through a shared care model with GPs, this means patients have easy access to care and GPs and oncology teams are in close communication.

TREATMENT
GENOME SEQUENCING

- Patients undergo further screening to evaluate the success of the targeted treatment.
- The test reveals that the sarcoma is responsive to the therapy, and as a consequence, the patient enters the survivorship period. Survivorship involves routine checkups and extensive psychosocial support.
- The Specialist Cancer Navigator continues to collect outcomes of interest to patients and record this data in the registry.

SURVIVORSHIP CARE

Patients and their families are referred into a Survivorship Care program and receive ongoing support from a specialist team. Data collected from sequencing informs future monitoring for patients families and in the presence of a germline mutation, careful personalised surveillance is undertaken and the family are followed for prevention.

2 BUILDING THE CASE FOR CHANGE

CANCER IS ONE OF AUSTRALIA'S WORST HEALTH CRISES

The number of people who will die from cancer this year alone will be extraordinary – approximately 50,000 Australians of all ages. Almost 140 Australian cancer patients die each day. For every three people who die, one person will have lost their lives to cancer[1].

Historically, Australia has had one of the highest five-year cancer survival rates. Sadly, these survival benefits have not extended to all cancer types.

As an example of what is possible, patients with lung cancer in Australia have recently seen dramatic improvements in survival compared to many other cancers. This is because of greater awareness, earlier detection, and critically, the availability of new targeted interventions and immunotherapies. In great part, this improvement has been because of our understanding that lung cancer is not a uniform disease, but rather a collection of mutation driven sub-types that need specific therapies. This new science is increasingly being developed for many other cancer types, but change will be needed to make them available to all Australians.

Across the globe, billions of dollars are being poured into new models of cancer care. These emerging therapies will dramatically improve outcomes for cancer patients. The challenge for Australia (and the rest of the world) is how to assess and fund high-cost precision therapies and technologies across a range of cancer types.

Under the current structure of the health system, small patient populations make traditional assessment regimes impossible.

For Australians to benefit, the health system must develop and adapt in such a way that all Australians, not just the wealthy, have swift and affordable access.

In 2030 alone, close to 63,000[2] people are expected to die from cancer if nothing changes. However, if we adapt, plan and reform the system to maximise the new science, NOA estimates that half of these lives could be saved or extended each year (representing the rare or less common cancers patients for whom treatment options are limited)[3].

Australian state and federal governments, systems and communities can make swift and drastic changes when Australian lives and livelihoods are at risk. We have learnt this from COVID-19.

However, unlike COVID-19, breakthroughs in cancer treatment are being made, and our challenge is to ensure we take maximum advantage.

It is hard to overstate the impact cancer has on those whose lives it touches. It affects families, individual's mental health, their physical wellbeing, and finances. On a larger scale, it also affects the economy and health system.

Cancer is Australia's most fatal disease, affecting both adults and children[4]. NOA estimates that over 550,000 Australians will die from cancer between now and 2030 if nothing changes. There will also be around one million people living with the disease by 2030.

[1] Australian Bureau of Statistics Births deaths and Marriages

[2] Cancer statistics extrapolated from ABS data and AIHW cancer data

[3] Cancer statistics extrapolated from ABS data and AIHW cancer data

[4] Cancer statistics extrapolated from ABS data and AIHW cancer data

> **Genomic sequencing has unveiled many sub-types of cancers formerly considered "common". The phenomenon of breaking down of (histological) cancer types, like breast cancer, into multiple molecularly distinct entities – is well understood."**
>
> PROFESSOR DAVID THOMAS
> HEAD OF GENOMICS CANCER MEDICINE, GARVIN INSTITUTE FOR MEDICAL RESEARCH

Cancer can develop in any person regardless of gender, race, or life stage. Environmental, behavioural, or hereditary factors can be factors, but often the cause is unknown.

Cancer is hundreds if not thousands of different diseases. Advances in genomic testing mean that we are closer to understanding its unique presentations and biology. Up until recently, cancers were defined broadly by their anatomical location, but now they can be categorised according to their molecular sub-types.

The advancing genomic technology is revealing smaller subsets of cancers through molecular diagnosis, and discovery of new disease biomarkers – meaning that every cancer will inevitably be considered "rare".

Cancer is now defined by its molecular characteristics rather than tissue of origin. For example, lymphoma is considered a common cancer, yet more than 60 sub-types have been identified, and close to half of these have been genetically classified (see Figure 2 below).

Each lymphoma sub-type can be considered to be rare.

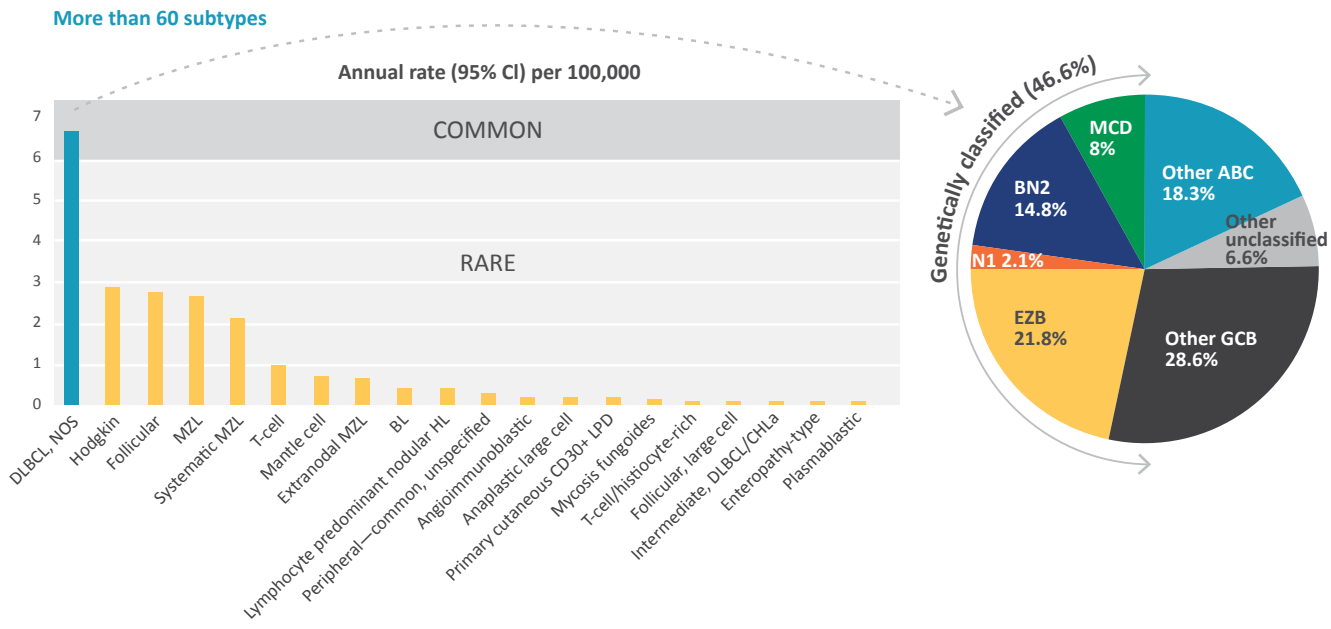
For some cancers, understanding the molecular make-up can uncover targets for developing new therapies, particularly in cases when the disease is associated with a single gene mutation or a known set of mutations.

Single treatments are in development that treat multiple cancers sharing a common molecular marker – pan tumours. All these developments give rise to personalised treatment approaches, which are otherwise known as precision oncology.

The profound impact of cancer on populations has driven global investment in research and technology that far outweighs the investment in any other therapeutic area.

While there has been enormous progress in research, the benefit will only be translated to the clinical setting and to patients equally and fairly if our systems, delivery frameworks and funding mechanisms evolve and are equipped to take advantage of these emerging treatments.

FIGURE 2. LYMPHOMA IS COMMON, BUT EACH SUB-TYPE IS RARE[5]



[5] Professor Stephen Opat, Vision 20-30 workshop: Schmitz R et al.. N Engl J Med 2018 Apr 12; 378:1396, Smith A, Br J Cancer. 2015 Apr 28; 112(9): 1575–1584

Patient Journey

As a father, he was devoted. He would look forward to coming home after a long day of hard work, because he knew his children would be there waiting for their Dad's return.

ASH

Ashley Robertson. Or Ash as he preferred, was the sort of man most people already know in their lives. He was a best friend; someone who would go on wild and exciting adventures at the drop of a hat, from blowing up a jet-ski to hanging out with mates in Byron Bay – he did it all. The kind of man whose infectious laugh would brighten a room to no end, and with whom everyone would quickly fall in love. There were many great times like that, filled with fun and laughs, but that's who he was.

He was in love, always, even in the beginning, when he planned a holiday for them both, only barely in a relationship. When they would go out, either together or with friends, they would have fun and just live together in that moment.

As a father, he was devoted. He would look forward to coming home after a long day of hard work, because he knew his daughter, Jaz, would be there waiting for her Dad's return. He lived to spend days packing his car with everything you could possibly need because he knew his son, Lachie, was excited for the single day of camping they could squeeze in together. United, they were an unstoppable team, going on grand adventures, such as the well-loved trips to Bunnings.

But the goal was always to have a place that they could retreat into, a place to spend time as family and enrich themselves with treasured memories. Even in the face of a possible returning cancer, Ash decided that it would not rule their lives, and so they bought a beach house together. Even though short-lived, the memories for his kids would be forever, and that was always the plan. He was just that sort of guy.

Even in the end, during his treatment in Boston, he pushed through the pain to make sure his family could see New York City at least once while they were there. They hired a minivan because the train was too expensive for their budget, and ended up off-roading it to avoid a traffic jam when on their way to collect his parents from the airport. He was the kind of man who's last plans were to have a simple BBQ, just to say thanks for what people had done for him.

Of course he loved his surfing and fishing, playing cards and camping, but compared to his family, it was as stark as night and day. Not even close. That's the sort of man, Ashley Robertson was.

2020 PATIENT JOURNEY

Ash

DIAGNOSED IN 2013

- Stage 1 Non-Hodgkin Lymphoma.
  - Surgery, 6 months of chemotherapy and radiation.
  - Advised he was in remission.

OCTOBER 2018

- Hospitalized with increasing back pain.
- Diagnosed with relapsed Lymphoma, stage 4 with extensive metastases throughout his body.

NOVEMBER 2018

- Intensive preparation for stem cell transplant: Chemo, cell harvesting, more chemo.

JANUARY 2019

- Weeks in hospital for grueling Stem Cell Transplant (SCT) process.

APRIL 2019

- Advised he was in remission.
- Had to return to paid work despite significant pain and fatigue.

MAY 2019

- Back pain returned and worst fears were confirmed: second recurrence diagnosed.
- No further lines of therapy available in Australia.

JUNE-SEPT 2019

- Ash has to come off steroids which control his pain in order to get a clear PET scan, required top access CAR-T in USA. He is in excruciating pain. Tumour is so close to his spine he can hardly walk. He undergoes more chemotherapy and radiation.
- Complicated arrangements are made by the family including MTOP and visa requirements, it is an extremely stressful time.

SEPTEMBER 2019

- Ash and his wife and two small children travel to Boston; T Cells harvested. 3 weeks of hospital admissions for increasing pain; finally reinfused with CAR-T cells.
- 11 days later Ash readmitted with neurotoxicity, a very serious side effect of CAR-T.

OCTOBER 2019

- Major spinal surgery performed to remove the tumour. It was confirmed that Ash would not walk again.
- Recovering from treatment, major spinal surgery and unable to walk, Ash and his wife were Medivac'd 17,000km back to Melbourne and after 35 hours landed at the Cabrini hospital. The other members of his family had to fly separately.

SEPTEMBER 2019

- Ash continues to be in and out of hospital with increasing pain, lethargy and loss of appetite. A PET scan shows Ash is cancer-free, a small lump is dismissed as insignificant.
- 5 days later a tumour was found wrapped around Ash's spine. His legs can no longer support him.
- Family is flown from Australia to Boston to support the young family.

NOVEMBER 2019

- Ash was made comfortable by his Australian treating team, but one week later he contracted an infection and he died the very next day surrounded by his wife and family.

2030 PATIENT JOURNEY

DIAGNOSED

Stage 1 Non-Hodgkin Lymphoma

- Whole Genome Sequencing is carried out.
- After surgery, six months of targeted therapy is accessed via a shared funding model.
- Patients and their families have access to support and navigation for their cancer experience.
- Monitoring and screening confirms remission.

TREATMENT

- Patients undergo close surveillance using MRI over the next five years and if relapse is detected, it is in the early stages.
- Patients and families are guided through their options with a Specialist Cancer Navigator and they're able to make informed decisions about subsequent lines of treatment.

SUPPORT

- The use of genomics provides increased capability of identifying suitable candidates for CAR-T therapy. Under the care of MDTs, patients access CAR-T cell therapy locally. Despite the difficult preparation and protocol for this procedure, patients are close to family and well supported by their GP and Cancer Navigator who provides whole family care.
- Early intervention with palliative care units allow patients to better manage symptoms and side-effects.

MONITORING

- Patients who experience signs of neurotoxicity are monitored by sophisticated monitoring AI-assisted wearable technology which detects it in the very earliest stages and interventions prevent further toxicity.
- Through ehealth records, GPs, the treating teams and families can all access important records.

SURVIVORSHIP CARE

- Patients living with side-effects of their diagnosis and treatment have access to comprehensive survivorship programmes which help with the physical and psychological effects of their cancer experience. Families have access to support.
- GPs are involved in shared care; they are trained in managing the effects of the disease and side-effects.
- Patient information including clinical data and real-world experiences are kept in registries.
- Data analysed from these repositories inform how patients pain is best managed after CAR-T. Patients diagnosis and treatment are recognised to have significant impact on their ability to work. Families are well supported with financial mechanisms via safety nets that address financial toxicity when cancer impacts people from rebuilding their quality of life.
- Patients can enrol in studies to detail family-important information; these studies inform any future treatments with personalised information and to add to data registries.
- Personalised surveillance in the following years is carried out.
- The patient can provide informed consent for his personal health care data to be accessed for future use.

3 THE FUTURE OF CANCER CARE

AN ERA OF PERSONALISED CANCER CARE

The nature of current and emerging therapeutics and technology has changed in an astounding way. So has the way patients are being treated, now and into the future. By logical connection, health frameworks and systems will need to change too.

Even how we define a "medicine" is up for debate – cellular therapies or "living medicines" are now part of the treatment armament.

Innovations will offer cancer patients new hope for survival. The differences compared to conventional treatments will challenge current health system frameworks.

Historically, cancer care adopted a 'blanket' population-based approach to treatment and management. Patients received a combination of conventional surgery, radiation, and chemotherapy. Treatments were not selective for patient or disease characteristics. They were highly toxic and many people failed to benefit.

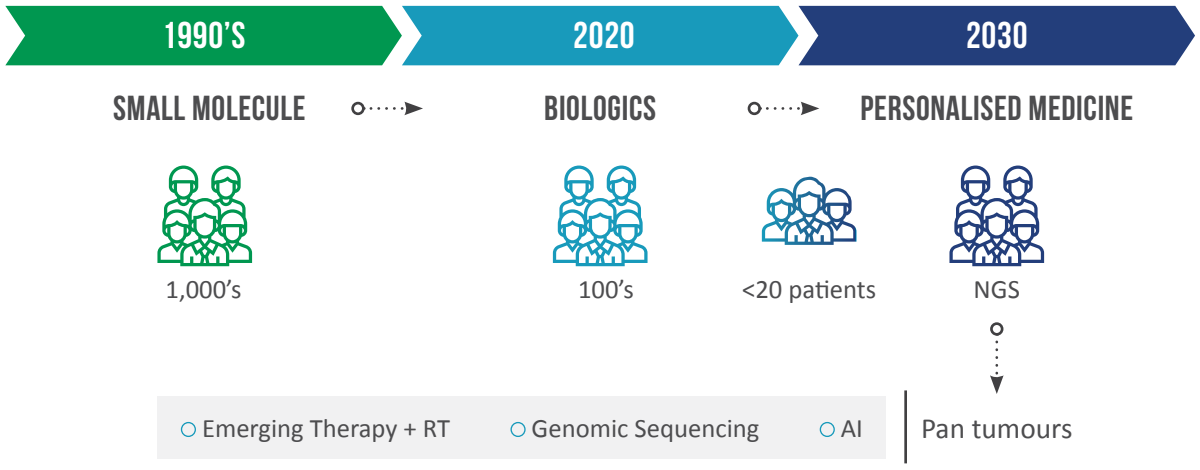
The new wave of personalised cancer treatments, or precision therapies, work in two main ways. They selectively block the action of enzymes, proteins and other molecules that promote the growth of cancer cells or they harness the immune system to kill cancer cells. This type of treatment is vastly different from previous approaches, as it is tailored to the patient's DNA or the molecular characteristics of their cancer. Astoundingly, more than 75% of cancer therapies in development are "personalised treatments"[6].

Personalised cancer treatment is more than just the targeting of new treatments. It also extends to genomic or other screening programs, preventative health measures using biomarkers or tests based on algorithms, as well as patient preferences.

The Vision 20-30 virtual workshops, which showcased emerging therapies and progress in radiation therapies, provided an overview of how enhanced treatment approaches could lead to greater survivorship for cancer patients. Personalised cancer treatment will be integral to all cancer care by 2030.

Studies have shown that survival benefits double when patients receive a therapy matched to a gene or sequence of genes compared to a non-targeted approach[7].

FIGURE 3. THE DRAMATIC SHIFT IN TREATMENTS AND TECH



[6] Personalized Medicine Coalition, "Personalized Medicine at FDA: The Scope and Significance of Progress in 2019," http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_The_Scope_and_Significance_of_Progress_in_2019.pdf

[7] Schwaederle et al., Impact of Precision Medicine in Diverse Cancers: A Meta-Analysis of Phase II Clinical Trials. J Clin Oncol 2015 Nov 10;33(32):3817-25

Some of the advances, like genomic screening, the discovery of new biomarker targets on cells, and immuno-oncology, will deliver outcomes that were not possible just a decade ago.

The possibilities for cancer patients over the course of the next 10 years are not entirely uncertain. Manufacturers' research and development pipelines and clinical trials are visible. Clinical trials are underway for new therapies and combinations that will be ready for use in 2030.

Providing equal opportunities to all cancer patients for best treatment poses some challenges that require contemplation and careful planning.

TABLE 1

	THEN (1970s)	NOW
Chemotherapy	Chemotherapy not targeted to each cancer type. Little understanding of how best to combine therapies. Severe side effects requiring hospitalisation.	Chemotherapy tailored to cancer sub-types. Used in the adjuvant setting. Combinations effective in reducing cancer size. Treatment administered out of hospital with manageable side effects.
Radiation therapy	Standard photon external beam radiation therapy, highly damaging to surrounding tissues.	Targeted radiation to a individual's tumour type and morphology. Increased precision and minimal exposure of normal tissue with fewer side effects. Shorter courses of treatment.
Surgery	Radical surgery removes large amounts of surrounding tissues as well as the cancer.	Sophisticated reconstructive surgery, less invasive surgical options.
Targeted therapy	None	Small molecule drugs or antibodies that block the action of enzymes, proteins, and other molecules that promote growth of cancer cells. Or therapies that help the immune system to kill cancer cells.
Immunotherapy and cell therapy	None	A therapy that harnesses the body's own immune system to destroy cancer cells. Cell therapy transplants viable cells into patients to fight cancer- these may be immune cells or transformed cells.
Targeted tumour agnostic therapy	None	A therapy that targets the same genetic mutation (change) or biomarker across multiple cancer types.
Regenerative therapy	None	Includes gene therapies, RNA, cell therapies and tissue-engineered products, designed to repair, replace, or regenerate organs, tissues, cells, genes and metabolic processes in the body.
Genomic sequencing of cancers	None 2000s single gene tests.	Genomic hot spot panel testing for known disease markers. Genomic sequencing of some cancer types and whole genomes. Next generation sequencing (NGS) methodology can be used for hotspot panels to whole genome sequencing.
Artificial intelligence	Established in the 1940s	Uses machine learning to mimic human actions and reasoning by having the capacity to interpret patterns in extraordinary volumes or data, images or natural language.

TREATMENT ADVANCES

Surgery

Surgery is the oldest intervention for cancer, dating back hundreds if not thousands of years. Yet it has changed remarkably over time.

Historically, surgical procedures were radical and more invasive, resulting in significant complications, long hospital stays and sometimes disfigurement. It involved removing large amounts of tissue surrounding tumours, leading to impaired quality of life.

The availability and advancement of imaging technology has enhanced the precision of surgical techniques, enabling surgeons to determine where the tumour ends, and the healthy tissue begins. The goal of any surgery to excise a cancer is to have clear margins of healthy tissue.

Personalised cancer surgery has become a reality using chemotherapy and robotic, laparoscopic, and reconstructive surgical procedures.

Minimally invasive and robot-assisted surgery is evolving. Precision surgery guided by molecular imaging is one of the newer areas of surgical advancement.

There has also been a vast improvement in adjuvant therapies to reduce the extent to which surgery is needed to remove every trace of cancer[8]. An adjuvant is a therapy that is used to enhance the effects of the first treatment.

Surgery will always be important in treating operable cancers.

Chemotherapy

Chemotherapy gained significant traction in the 1970s and was typically used to destroy small tumours that could not be treated with surgery or radiotherapy. Chemotherapy is associated with an extensive array of side effects because it is cytotoxic to most cells – killing both cancer and normal cells.

Adjuvant chemotherapy and combination therapy were adopted in this era. In cancer, adjuvant chemotherapy is given to ensure that residual cancerous cells are destroyed following surgical resection or radiation therapy.

Combination therapy, while toxic and associated with side effects, was more effective in treating specific types of cancers than chemotherapy alone.

Oncologists still use chemotherapy widely, and in some instances, it can be very effective when combined with newer more targeted agents.

Chemotherapy combinations can now be administered out of the hospital setting. Researchers and physicians often report that it is now associated with a "manageable safety profile" yet the patient experience speaks to a different reality.

A patient says of her experience with chemotherapy:

"When I first began chemotherapy, I felt quite well, not sick at all. The accumulative effect of the chemo made me feel more and more ill. As expected, my hair fell out, but I did not know how uncomfortable that would feel. The nausea, even when under control, was never absent. Everything from my mouth to my fingernails hurt, and the stomach problems were probably the worst things of all."

[8] Wyld, L; Riccardo A A and Poston G. The evolution of cancer surgery and future perspectives. Nature Reviews. Clinical Oncology 2015 (12) 115 -124

Immuno-oncology

Immuno-oncology (I-O) uses the body's own immune system to recognise, control and destroy cancer cells anywhere in the body.

Professor Jonathon Cebon, Olivia Newton-John Cancer Research Institute, presented on the up and coming immunotherapies in the first workshop of the Vision 20-30 series. In his presentation, he said:

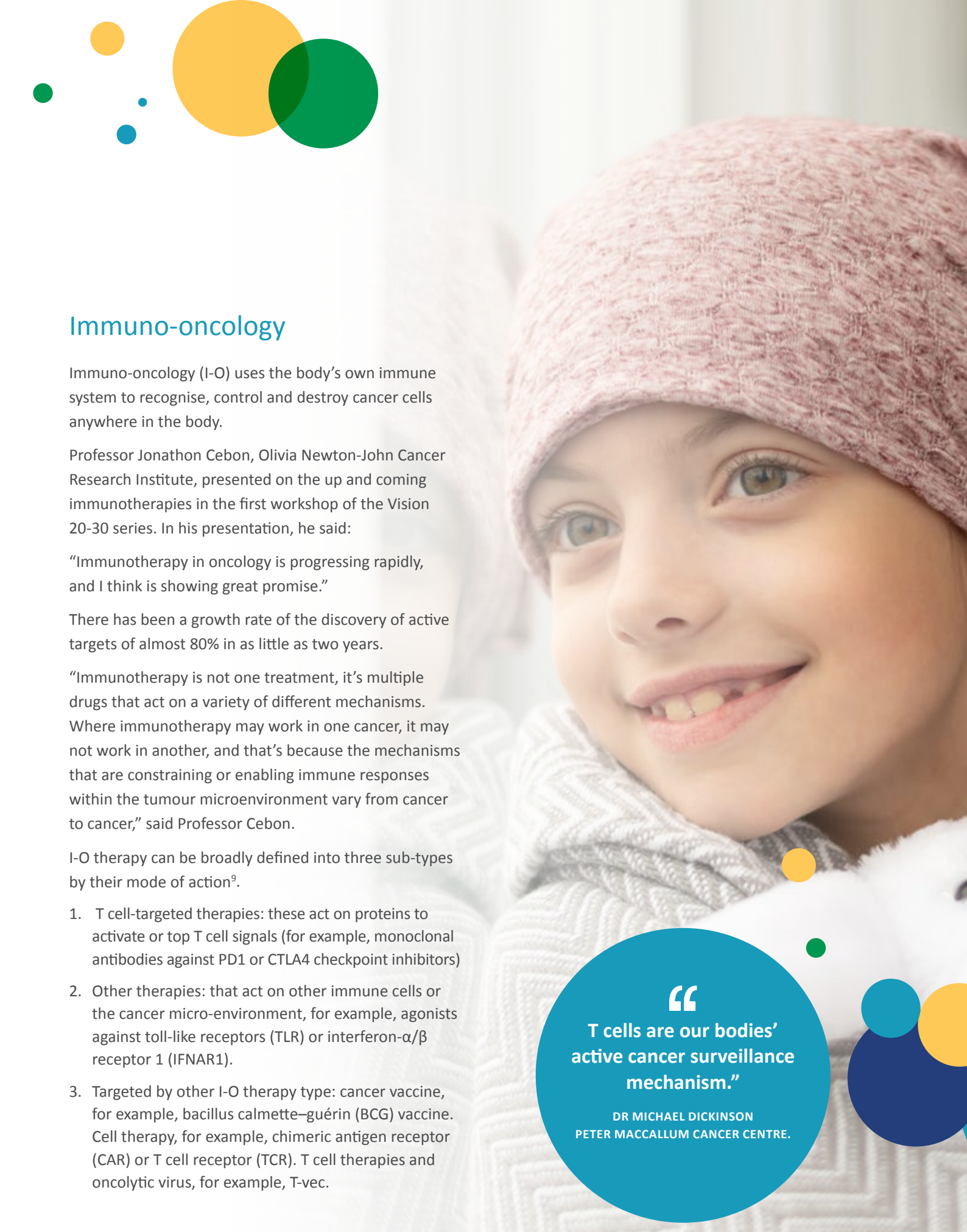
"Immunotherapy in oncology is progressing rapidly, and I think is showing great promise."

There has been a growth rate of the discovery of active targets of almost 80% in as little as two years.

"Immunotherapy is not one treatment, it's multiple drugs that act on a variety of different mechanisms. Where immunotherapy may work in one cancer, it may not work in another, and that's because the mechanisms that are constraining or enabling immune responses within the tumour microenvironment vary from cancer to cancer," said Professor Cebon.

I-O therapy can be broadly defined into three sub-types by their mode of action[9].

1. T cell-targeted therapies: these act on proteins to activate or top T cell signals (for example, monoclonal antibodies against PD1 or CTLA4 checkpoint inhibitors)
2. Other therapies: that act on other immune cells or the cancer micro-environment, for example, agonists against toll-like receptors (TLR) or interferon-α/β receptor 1 (IFNAR1).
3. Targeted by other I-O therapy type: cancer vaccine, for example, bacillus calmette–guérin (BCG) vaccine. Cell therapy, for example, chimeric antigen receptor (CAR) or T cell receptor (TCR). T cell therapies and oncolytic virus, for example, T-vec.



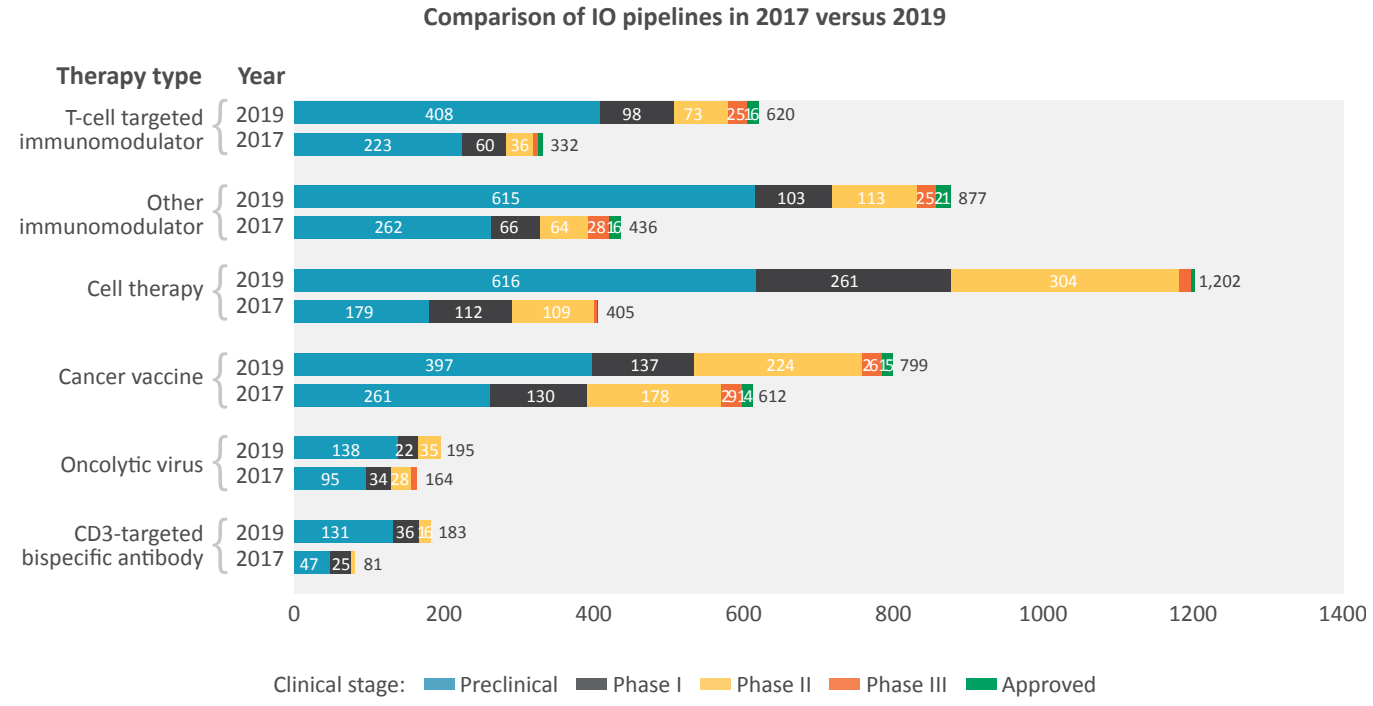
> **"T cells are our bodies' active cancer surveillance mechanism."**
>
> **DR MICHAEL DICKINSON**
> **PETER MACCALLUM CANCER CENTRE.**

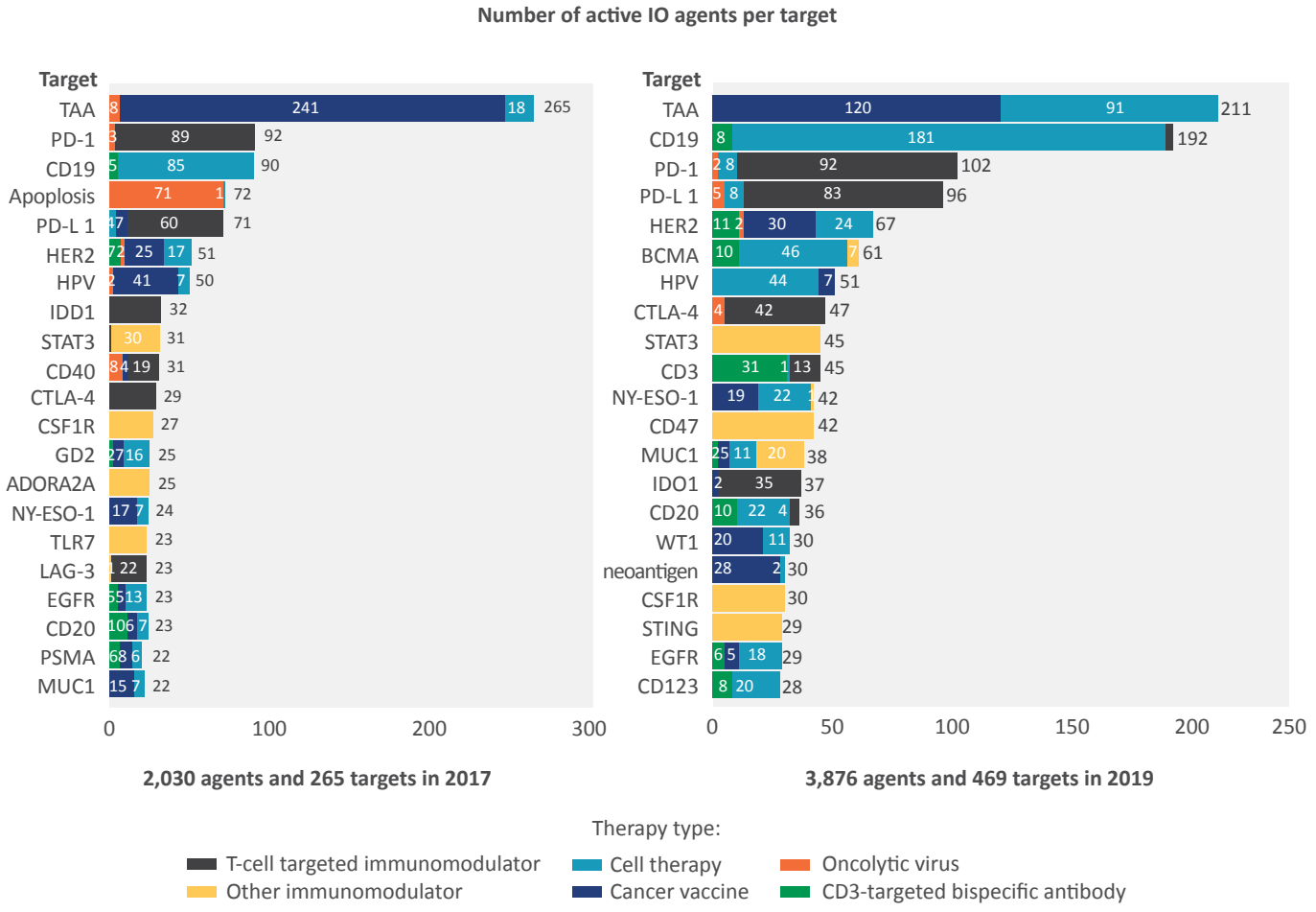
[9] Cancer Research Institute (2020), Immunotherapy Treatment Types. https://www.cancerresearch.org/immunotherapy/treatment-types

FIGURE 4. IMMUN-ONCOLOGY DEVELOPMENT PIPELINE

Published by Jun Tang & Annie Yu on Sep 27, 2019

Sources: CRI Analytics, Cinicaltrials.gov, iAtlas and GlobalDate





Checkpoint inhibitors

In the last few years, there has been extensive progress in the development of therapies called checkpoint inhibitors.

Checkpoint inhibitors prevent cancer cells from "turning off" the immune response by binding to the checkpoint proteins, PD-1, PD-L1 or CTLA-4.

The first checkpoint inhibitors targeting CTLA-4 increase the number of activated T cells that migrate to the tumour by turning off a signal on the T cell that normally tells them to stop.

PD-1 or PDL-1 inhibitors enhance the ability of immune cells to fight cancers that express these markers by preventing the cancer from evading the immune system.

MSD's KEYTRUDA (Pembrolizumab) and Bristol-Myer Squibb's (BSM) OPDIVO (nivolumab) were the first PD-1 inhibitors. These were initially recommended for advanced melanoma by the Pharmaceutical Benefits Advisory Committee (PBAC) in 2015 as single use therapies. The PBAC recommended BMS's YERVOY (ipilimumab) for the same indication in 2012.

These treatments have offered patients new hope. Those with advanced cancers expressing PD-l/1 were very likely to respond to treatment despite it being introduced late in the course of their disease.[10]

The use of these therapies was extended to each cancer type one at a time, based on new clinical trial evidence. However, the benefit can increasingly be translated across all cancer types expressing the marker PD1/L – re-classifying them as pan tumour therapies.

The clinical trial pipelines reveal the future applications of these therapies are across multiple tumours, in combination with new therapies directed against other targets to enhance durability and prevent resistance. A combination therapy approach can target the cancer through multiple mechanisms, enhancing effectiveness. The number of combination trials has doubled in the past two years, and PD1/L is fast becoming the new "backbone I-O therapy."

Remarkably, around 2,700 trials are combining 300 different types of drug targets with PD-1/PD-L inhibitors.

In mid-June 2020, the US Food and Drug Administration (FDA) granted accelerated approval for Merk's KEYTRUDA (pembrolizumab) for metastatic solid tumours or those not suitable for surgery, where the tumour tested positive to a high tumour mutation burden (TMB).

This is not just an exciting advance for children and adult cancer patients in the US. It is important for Australia too. It is a sign of progress in gaining registration for use of therapies in multiple cancers that share the same marker of disease.

"It is the second time a therapy that targets a common tumour marker has been approved in the US, regardless of tumour type – a tumour agnostic therapy," Professor David Thomas, Garvin Institute of Medical Research.

The development is significant because most emerging therapies are only approved for one cancer subpopulation at a time – not multiple cancer types. This highlights further opportunities, that will be discussed later.

Cell therapy

Cell therapy has seen the largest growth in research and development in the last two years compared to other I-O therapies. [11] There are close to 1,500 agents in development, an increase of a third in just one year. The US and China dominate the cancer cell therapy pipeline. The number of agents in development in China is approaching the number of agents under development in the US .

The first cell therapy – Novartis' KYMRIAH (tisagenlecleucel) chimeric antigen receptor (CAR) T-cell therapy – was approved for use in Australia by the Therapeutics Goods Administration (TGA) in 2018.

In April 2019, federal Health Minister Greg Hunt announced support for children with acute lymphoblastic leukaemia (ALL) through Commonwealth state and territory funding agreements. It is expected that 30 children will be treated per year through public hospitals, according to Dr Michael Dickinson, Peter MacCallum Cancer Centre.

A year after TGA approval, both KYMRIAH and Gilead's YESCARTA (axicabtagene ciloleucel) received funding approval for treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Between 200 and 400 patients will receive treatment each year.[12]

[10] Wu et. Al. The efficacy and safety of combination of PD-1 and CTLA-4 inhibitors: a meta-analysis. Experimental Hematology & Oncology,(2019): 8(26)

[11] Yu et al. (2019). Immuno-oncology drug development goes global. Nature Reviews Drug Discovery, 18, 899-900

[11] Dr Michael Dickinson, Vision 20-30 workshop series

The combined state, territory, and federal funding model, as well as the need for capable tertiary specialist centres to deliver the therapy, has presented significant challenges in making these therapies available across Australia. It is a very slow process that is still being implemented today.

Historically, medicines have been funded at a federal level through the Pharmaceutical Benefits Scheme (PBS). Yet CAR-T did not "fit" the conventional evaluation pathways because it was not considered a "medicine". Internationally, it has been considered a "living medicine".

The CAR-T therapies were much anticipated because early results showed they were able generate responses in late-stage blood cancers that had not been possible before. The patient's own immune T cells are modified and re-infused to enhance their ability to recognise cancer cells and destroy them.

Dr Michael Dickinson spoke about the anti-CD19 CAR-T therapies in one of the Vision 20-30 workshops.

"These are reprogrammed cytotoxic T cells which are genetically modified to enable them to target a cancer by directing themselves against one or more antigens on the surface of the cancer," he said.

"CAR-T therapy has offered hope for many patients who would have had no other treatment options. Before CAR-T came along, patients were cured with autologous stem cell transplantation around half the time. But if they fail autologous stem cell transplantation, that would generally be considered incurable and they would be offered palliative treatments."

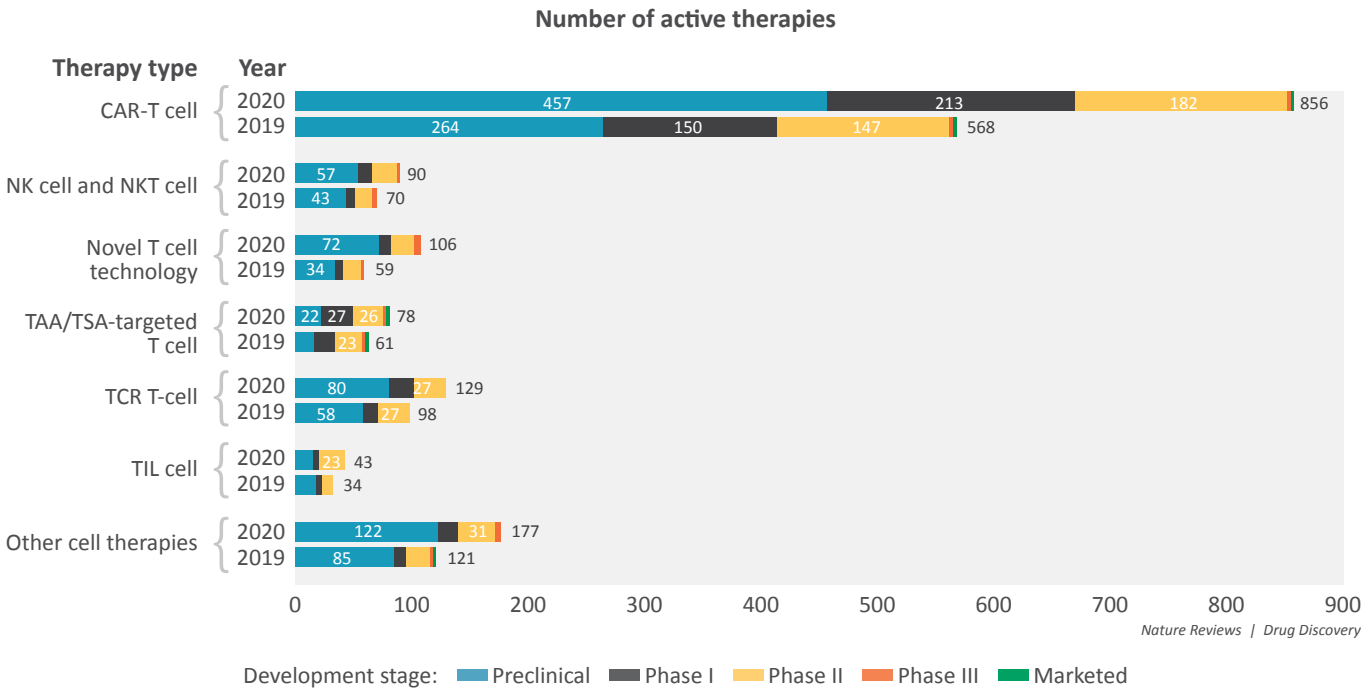
It is a therapy that has offered great hope and promise, as seen from the results of JULIET, the first clinal trial for KYMRIAH.

"JULIET was an early phase study. Most patients (in the study) had had three or four prior lines of therapy, and up to seven prior lines of therapy. This is a patient population where we would have expected perhaps a 10 -15% durable complete remission with chemotherapy, and we saw this 40% or so durable complete remission", said Dr Dickinson.

Some of the first patients to receive KYMRIAH in clinical trials have shown no signs of relapse for more than five years[13] .

While CAR-Ts offer remarkable results for some patients, they are not without their nuances or limitations. The technology is its infancy in so many ways, and there are many more developments using CAR technology in the pipeline that we expect will greatly surpass these current treatments by 2030.

FIGURE 5. TRENDS IN CANCER CELL THERAPY PIPELINE



[13] Murray, AB, Hviland JS et al; Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. The Lancet (2020). Volume 395(10237), p1613-1626

Autologous CAR-Ts that use an individual's cells are associated with limitations from manufacturing time, use in patients with late-stage aggressive cancers only and variable potency to dangerous side effects.

"The cell therapy doesn't work in everyone. When it does work, there are on-target effects, such as cytokine release syndrome. This presents a bit like a serious infection with fevers, which can then progress to low blood pressure, a fast heart rate and admission to the intensive care unit."

Yet we are just at the start of discovery in this exciting new field.

Internationally, there are over 250 clinical trials underway or planned using CAR technology, mostly in cancer. Clinical trials of the next generation CAR therapies focus on enhancing the durability of effectiveness but also avoidance of cytokine release syndrome. Promising research uses CARs with a type of lymphocyte other than B cells or T cells – natural killer cells.

Another promising advance is the use of "off-the-shelf" or "one-size-fits-all" CAR-T treatments. These are known as allogeneic CAR-Ts because they use pre-prepared cells not from the patients.

Dr Dickinson explains: "Healthy donors can provide T cells which are then modified so that they don't attack the patient but do attack the patient's cancer. We have just started a clinical trial of these allogeneic CAR-Ts where there's no manufacturing wait time. We have the CAR-Ts on the shelf, and those trials have already commenced in Australia."

BOX 1: DR MICHAEL DICKINSON, PETER MACCALLUM CANCER CENTRE, EXPLAINS CD19 DIRECTED CHIMERIC ANTIGEN RECEPTOR T CELL (CAR-T) THERAPY

HOW IS IT MANUFACTURED?

The way it works is that we ask patients to participate in a donation procedure, which is apheresis. We use an apheresis instrument and collect peripheral blood mononuclear cells. Those cells are sent either frozen or fresh to the manufacturing facility. Cells are isolated as T cells and activated and then transfected, usually with a virus designed to insert this new designer receptor, called the CAR, the Chimeric Antigen Receptor. CAR is like a hybrid T cell receptor and an antibody, so that you get both the T cell killing activity of the immune system, but also the antibody specificity. Those cells are grown up in the lab and then sent back to the treatment site several weeks later, and infused into the patient as a single product, single infusion.

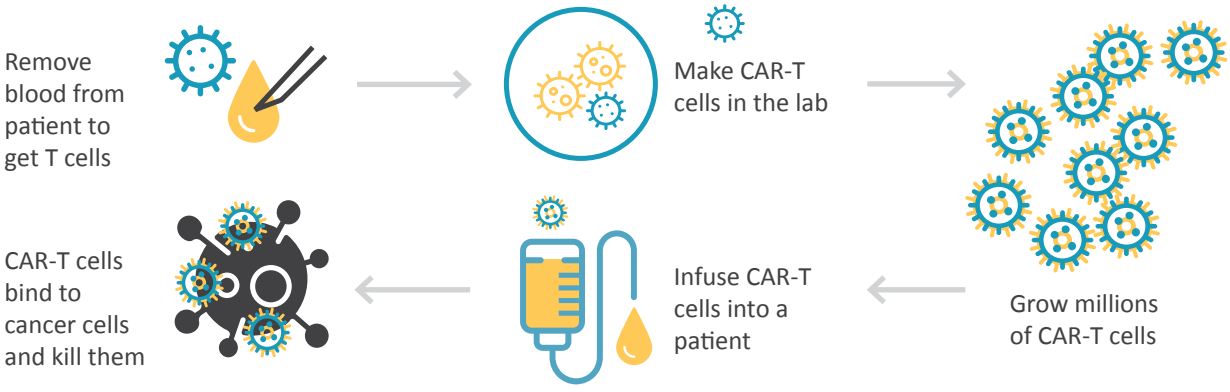
HOW DOES IT WORK?

What happens is CAR-Ts see their target, expand within the patient, and kill the target. The available CAR-Ts are anti-CD-19 to target B cell cancers, CAR-Ts, CD-19 is a protein on the surface of B cells. When we give these reprogrammed T cells, they kill B cell cancers (diffuse large B cell lymphoma, acute lymphoblastic leukemia) as well as normal B cells.

WHAT NEEDS TO BE DONE?

One of the future directions is to improve the outcome of the product, make it less toxic and more active, broaden the range of antigens that we're targeting, speed up manufacturing, and deliver it at a lower cost. We need to develop networks for referring patients, and we also need to develop clinician familiarity with the modality and help everyone pick the patients who are most likely to benefit from this treatment.

HOW CAR-T THERAPY WORKS



Adapted from NIH, National Cancer Institute, "T-Cell Transfer Therapy"

Cancer vaccines

Many of the vaccines designed to treat cancer have shown promise in early clinical trials, but are not yet approved by regulatory agencies overseas or in Australia.

Dendreon's PROVENGE (Sipuleucel-T) for advanced prostate cancer is one of the very first to offer hope. It is available in the US, but not yet approved in Australia by the TGA.

Cancer vaccines are quite remarkable. Except for the cervical cancer vaccine, they challenge the traditional concept of a vaccine that is designed to be preventative on a population basis.

A cancer vaccine is a treatment, rather than a preventative measure. These vaccines generally use a non-active version of disease to stimulate ongoing immunity to destroy active cancer.

Some cancer treatment vaccines are made up of cancer cells, parts of cells or antigens. The vaccine is injected in the body to heighten the immune response against cancer cells. It involves ongoing treatment to selectively maintain and establish immunity and harness immunological memory.

There are currently more than two dozen ongoing Phase I and Phase II trials using different vaccine platforms targeting rare cancers in the pipeline.

There are primarily four types of cancer vaccines in development: dendritic cell vaccines, tumour cell vaccines, antigen vaccines and vector-based vaccines (Box 4).

BOX 2: TYPES OF VACCINES TO TREAT CANCER

DENDRITIC CELL VACCINES

Have so far shown the most success in treating cancer – evident by the recent FDA approval of Dendreon's PROVENGE (Sipuleucel-T) for advanced prostate cancer. Dendritic cells engulf proteins expressed by cancer cells, break them down, and present them to T cells that then multiply, and can attack and eradicate the cancer cells.

TUMOUR CELL VACCINES

Are harvested from the patient (autologous) or from an existing cell line (allogeneic). They are altered, killed and then injected back into the patient. The patient's immune system then attacks these and any similar cells still in the body.

ANTIGEN VACCINES

Use a couple of proteins expressed by cancer cells rather than the entire cell to stimulate the immune system.

Regenerative therapy

Regenerative therapies are designed to treat the root cause of cancer to destroy it.

These include gene therapies, RNA, cell therapies and tissue-engineered products designed to repair, replace, or regenerate organs, tissues, cells, genes and metabolic processes in the body.

Regenerative therapy trials are mostly in cancer.

Types of regenerative therapy include gene therapy, gene editing, gene addition and gene immunotherapy.

BOX 3: TYPES OF REGENERATIVE THERAPIES

GENE THERAPY

makes changes to DNA in certain cells to help treat, or potentially even cure, a disease. The changes can be permanent or temporary.

GENE EDITING

works by silencing or modifying a gene to interrupt a disease process or correct genetic expression. An example of this technology is Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR – Box 4).

GENE ADDITION

involves a one-time treatment to replace the function of a faulty gene with a healthier copy of the gene delivered within a cell using a vector (vehicle).

GENE IMMUNOTHERAPY

introduces a new or modified gene into a patient's immune cells to help treat disease (CAR-T therapy).

RNA THERAPY

RNA interference (RNAi) and antisense RNA can turn off or modify the expression of genes. RNA therapies can potentially block the mechanism of disease-causing proteins.

There is six times the number of regenerative therapy trials in cancer compared to other disease areas. In the US alone, one in every two gene or cell therapies in development is for cancer (Figure 6).

Over 500 cell and gene therapy clinical trials are underway in various cancers. It is an exciting and overwhelming prospect because cell and gene therapies have already offered great hope, for example, CAR-T therapy.

BOX 4: CRISPR – GENE EDITING FOR THE FUTURE[14]

CRISPR is a rapidly evolving gene-editing technology that allows researchers to alter DNA sequences and modify gene function by altering the genome.

CRISPR therapy works by inserting a cut or break in the DNA and introducing the desired change. The enzyme, in this case Cas9, acts as molecular scissors. It is directed by a particular RNA sequence that guides it to a target sequence of genetic code and cuts DNA at precise locations. It can carefully edit the genes of selected cells extracted from patients and develop better engineered cells. Research in the future is aimed at more comprehensively editing immune cells, to improve their performance so that they can more effectively identify and respond to cancerous cells, after a single administration.

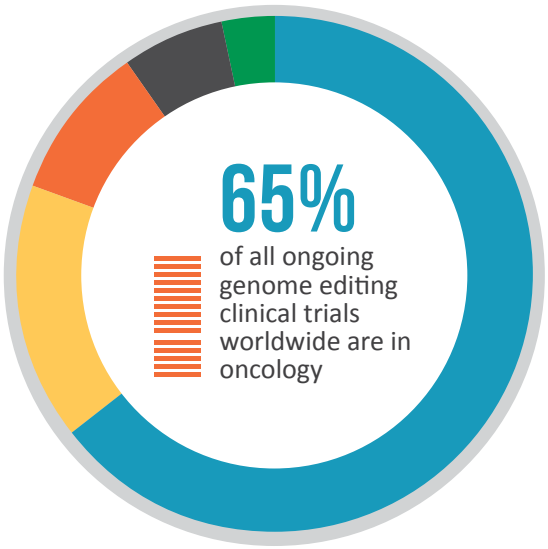
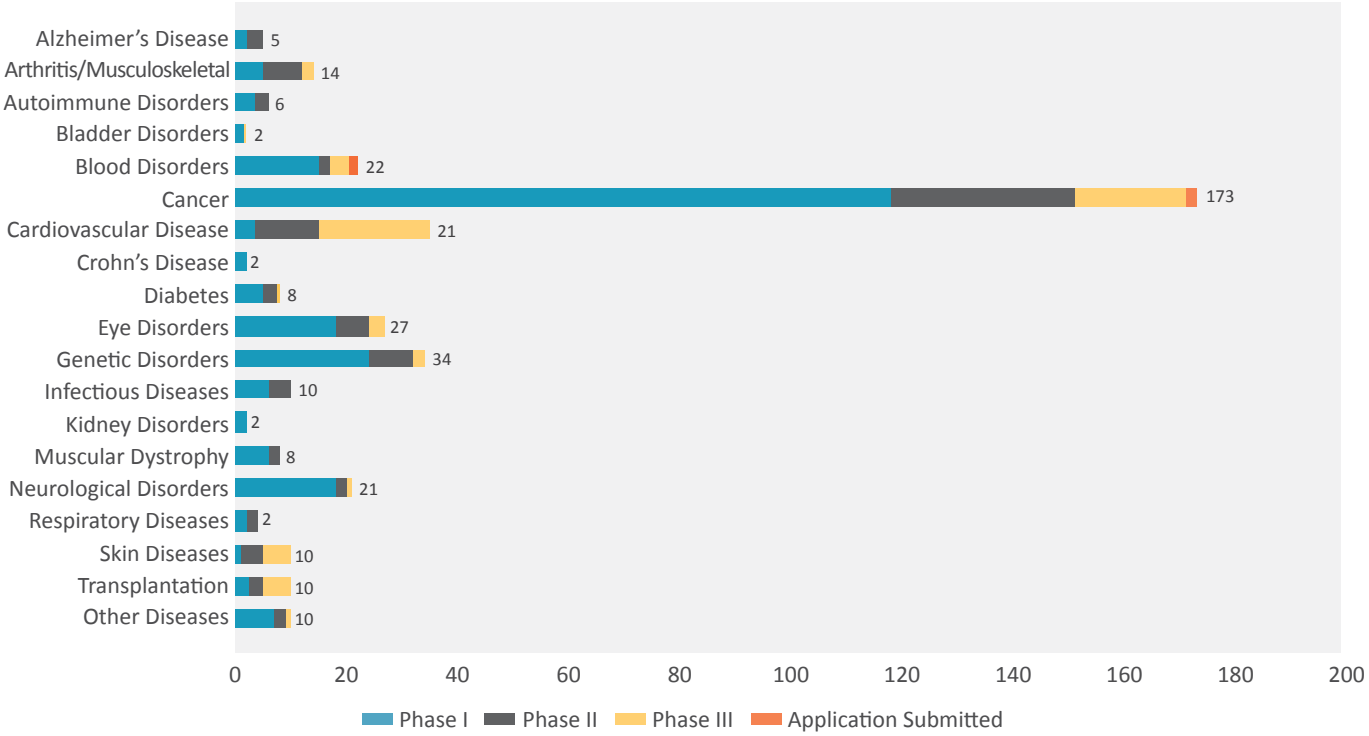


FIGURE 6. NUMBER OF GENE AND CELL THERAPIES IN DEVELOPMENT BY DISEASE IN THE US[15]



[14] 2019, Alliance for Regenerative Medicine, CRISPR Therapeutics, Intellia Therapeutics: The Future of Therapeutic Genome Editing

[15] Medicines in Development (America's Biopharmaceutical Companies) 2020 Report, Cell and Gene Therapy

Radiation therapy

Radiation therapy has been used in cancer care for decades. Yet there have been remarkable advances in technology leading to major improvements in the accuracy of radiation therapy delivery. The precision provided by combining radiation therapy with MRI and functional imaging, tailoring the dose for individual cancers and managing motion during treatment, translate into better patient outcomes. These developments have meant that higher doses can be safely given to the cancer and lesser doses given to surrounding tissues resulting in fewer side effects. Cure rates have increased, and quality of life improved for patients having radiation therapy.

Advances also mean that some patients require fewer treatments, daily treatment times are shorter, and less time is spent in treatment centres.

Hypofractionation is the term referring to a reduced number of treatments with the same efficacy. For instance, for prostate cancer patients having radiation therapy, the number of treatments can standardly be safely reduced from 40 down to 20, or even less.

Most commonly, radiation therapy is delivered through beams of high energy photons (x-rays) or electrons directed from outside the patient's body into the cancer to kill cancer cells. Other heavier particles e.g. neutrons, protons and carbon ions can also be applied in this manner. All these forms of treatment are called external beam radiation therapy.

Brachytherapy is the other type of radiation therapy. It uses radioactive sources of various types that are put into, next to, or around cancers or organs containing cancers.

Particle radiation therapy – a precise adaptive treatment

Conventional radiation therapy uses photon beams while more recently protons or carbon ion beams are being applied for some clinical situations. During the workshop series, Associate Professor Verity Ahern, Sydney West Radiation Oncology Network explained the agility of proton beam therapy and how it can deliver bundles of energy with greater precision compared to photon therapy. Like photon therapy, proton therapy can be adapted as the tumour evolves and changes in morphology.

"Protons use very fine pencil beams that 'paint' an individual cancer with a dose of radiation. The radiation beam starts at one portion of the cancer and then gives a slightly lower strength beam to the next part of the cancer and so on. In this way protons are 'dose sculpting' – directing their energy exactly where you want that dose to go. Virtually no radiation is delivered beyond the cancer (compared to photon therapy)," she said.

This type of precise radiation therapy allows the dose to be escalated to give patients a better chance of cure. Proton and carbon beam therapy may prevent damage to normal tissues adjacent to the cancer better than photon therapy in some clinical scenarios.

In her presentation, Associate Professor Ahern explained that the technology offers a remarkable opportunity to treat cancers that are in sensitive locations including those close to vital or developing tissues. Radiation therapy is useful for cancers that are inoperable and/or as an alternative to surgery.

> **"Sparing normal structures is hugely important around the brain as an example. For children, this could mean that they have a better ability to keep learning, and they have better hearing outcomes after treatment."**
>
> ASSOCIATE PROFESSOR VERITY AHERN
> SYDNEY WEST RADIATION ONCOLOGY NETWORK

For a child with a brain cancer, the level of radiation exposure to healthy tissues might be reduced, for example, by 60% for proton beam therapy compared to conventional radiation therapy, resulting in a better outcome and quality of life for patients[16].

Associate Professor Ahern explained that carbon ions can be an even sharper tool than protons and kill cancer cells in a different way than proton or photon therapy. They are effective for some rarer types of cancer that are resistant to conventional photon treatment.

"The National Institute for Radiological Sciences in Tokyo, Japan has been using carbon ions for more than 20 years. They're well advanced in giving even common cancers shorter courses of treatment with fewer side effects as well as using carbon therapy to treat radioresistant cancers," she said.

[16] https://www.cancer.net/navigating-cancer-care/how-cancer-treated/radiation-therapy/proton-therapy

How does it work?

Radiation therapy both directly damages cancer cell DNA and causes chemical changes within the cell that indirectly lead to DNA damage, which stops cells dividing.

Radiation therapy may be used with the intent of cure as a single therapy, or in combination with chemotherapy, hormone therapy or other treatments. Often, it is an appropriate alternative to surgery, for instance for prostate cancer, skin, and head and neck cancers. It is less invasive than surgery, preserves important organs e.g. bladder or voice box, and can result in improved quality of life. Radiation therapy is commonly given in the adjuvant setting before or after surgery to target microscopic cancer cells that may be left behind. Radiation therapy has a very important role in the palliative setting to control patients' pain, bleeding, or other symptoms of incurable cancer.

Advances in imaging have opened a new paradigm in determining the location and spread of cancer in the body and defining the regions requiring irradiation.

Associate Professor Sandra Turner, Westmead Hospital, Radiation Oncology Network, explained what she expects "adaptive radiation therapy" will be able to do in the near future, coupled with advances in AI.

"We will be able to hone in, using imaging, to work out where the cancer may be more active or more resistant within an organ or cancer. We can use imaging for accurate treatment delivery to overcome organ motion and to tailor our treatments day-to-day according to what is happening in that biological system and in that patient's body", she said.

Theranostics

Theranostics combines a unique target, identified via diagnostic scanning with a personalised nuclear therapy, which is delivered systemically to the patient. The therapy delivers radiation to areas where disease target is expressed with less off-target damage to healthy tissue. According to Associate Professor O'Brien, GenesisCare, the therapies can target primary and secondary cancers, including those not visible or treatable with conventional imaging and current therapy.

"The major advantage here is that we know that we're only treating patients who demonstrate that target. Targeted, personalised nuclear medicine using tumour markers labelled with diagnostic or therapeutic radionuclides," he said.

Professor O'Brien highlighted that international industry-led R&D programs are underway to commercialise novel theranostic agents as monotherapy and combination treatments to improve clinical outcomes in cancer patients.

Therapies are exploring a range of therapeutic radioisotopes such as copper, rhenium, lutetium, thorium, scandium, tin, actinium, and lead with various technologic approaches including radiopeptides, antibodies and interventional administration for example.

Radiation therapy underutilised in Australia

"There is an opportunity to benefit all patients in whom radiation therapy would be medically indicated. Awareness of modern radiation therapy is low in the general community, amongst patients, families and even health care workers compared to knowledge of other cancer treatments. Education across the board and ensuring patients are referred to radiation oncologists for a discussion of the value of radiation therapy in their care is a priority. In addition, if we have resources to invest in the newer technologies and improve access for regional patients to services we will start to close the gap between actual and optimal use of radiation therapy in our community," Prof Turner said.

"Many Australians miss out on life-saving or palliative quality of life-improving radiation therapy. The number of patients who still miss out on treatment in Australia in 2020 is frightening."

Forty per cent of all cancer cures involve radiation therapy with radiation alone, or in combination with other treatments. Yet the treatment is very much under-recognised and underutilised across the cancer continuum, irrespective of patients' geographical location.

> "In Australia, only one in three patients receive radiation therapy while evidence shows one in every two patients would benefit."
>
> **ASSOCIATE PROFESSOR TURNER**

There is low awareness of radiation therapy in the community even amongst other health professionals. During her presentation, Associate Professor Turner went on to explain: “we have very little education around radiation oncology, so people may not get appropriately referred. They may have fears or misunderstandings about the risks of radiation therapy and other issues. It is a very safe treatment if used properly. In addition, radiation therapy is highly cost-effective, particularly compared to newer systemic agents. Radiation therapy can be used for patients of all ages, from babies to elderly people.”

“There is a need to empower patients and their families to more effectively and meaningfully engage, not only with their diagnosis but in the development of their treatment plan and options for supportive care. We also need to consider the development of platforms to capture patient reported outcomes and harness ways that these can inform clinical care more effectively.”

TIFFANY BOUGHTWOOD
AUSTRALIAN GENOMICS

Genomic testing: diagnosis, prognosis and directing treatment

Advances in genomic sequencing are providing the means to characterise molecular sub-types of cancers and are the foundation for personalised treatment approaches.

Genomics is a rapidly advancing and complex field, with multiple applications. Genomic testing is used to screen for familial risk of developing certain cancers, molecular diagnosis, disease prognosis and to direct the best course of treatment.

The testing yields information about gene mutations, patterns of mutations, and other alterations to the genetic code inside tumour tissue. This can lead to the identification of disease relevant markers, enabling manufacturers to develop targeted treatments.

Genomic testing is far from being widely available in Australia. There is a long way to go to integrate it into routine clinical practice and this is because there is a range of tests that yield varying amounts of data. There is debate around the value of these tests and their varying validity for different cancers.

The NOA Vision 20-30 consensus is to champion research efforts to provide greater opportunity for patients, and to translate these into clinical practice in the longer term.

NOA commissioned Health Technology Analysts Pty Ltd (HTAnalysts) to undertake the Genomic Testing for Cancer Patients: Blueprint Assessment. This comprehensive report is intended to assist in understanding the complexities, utility, clinical and economic value, key players, technologies, and collaborations in this exciting field. It will serve as a foundation to inform progress and highlight opportunity for further collaboration.

This section will elaborate on the fundamental areas of relevance that arose through the Vision 20-30 workshop series. More in-depth information is available in the Genomic Testing report.

Next generation sequencing

Next generation sequencing (NGS) is a high-throughput method of sequencing genetic material (DNA or RNA). It is much faster and dramatically cheaper than the earlier Sanger method, taking days instead of weeks.[17] The decreasing cost together with the demand for genomic information is driving the demand for comprehensive genomic testing.

According to the NOA – Genomic Testing report, NGS is valuable in three key ways:

1. Identifying patients who are likely to benefit from existing or investigational targeted agents.
2. Understanding prognostic information about the patient's cancer.
3. Identifying new potential targets for research (especially when sequencing large enough sections of DNA that incidental findings occur).

NGS is being used in many ways from whole genome sequencing (WGS) and whole exome sequencing (WES) to comprehensive genomic profiling (CGP) using panels of 100s of genes, and multi-gene or hotspot panel tests (disease-specific panel tests of five to 50 genes).

A summary of the types of tests is provided in Table 2.

TABLE 2. TYPES OF TESTS USING NGS[18]

Test	Genetic material	Number of genes / base pairs	Purpose
Hotspot panel	DNA	5 to 50 genes	Targeted panels consist of well-known common driver mutations. They are often used to understand which targeted therapies, if any, a patient would be eligible for.
CGP) panel	DNA +/- RNA	300 to 500 genes	Comprehensive panels contain genes known to be involved in cancers. These panels provide information not only on mutations, but also structural issues such as TMB, microsatellite instability (MSI), and/or loss of heterozygosity (LOH).
WES	DNA	Whole exome (1% of genome)	The exome, which is the protein-coding region of the genome, is thought to contain most disease-causing mutations. WES can be considered an efficient method of genomic testing, given that it targets the sections that have a higher probability of containing pathogenic mutations. (15)
WGS	DNA	Whole genome	As the most comprehensive form of DNA sequencing, WGS can detect single nucleotide variants, insertions/deletions, copy number changes and large structural variants across the entire genome. This is currently used mostly in research settings.
RNA sequencing (RNA-Seq)	RNA	Short read: 100-300 bp Long-read: >1000 bp (length of full mRNA)	RNA-Seq is a catchall term for various approaches to RNA sequencing, such as differential gene expression (DGE) or detection of fusions.
Methylation analysis	DNA	1000 base pairs to whole genome	Methylation analyses can characterise DNA methylation at single bp resolution to provide epigenetic information.

Bp, base pair; CGP, comprehensive genomic profiling; DNA, deoxyribonucleic acid; LOH, loss of heterozygosity; mRNA, messenger ribonucleic acid; MSI, microsatellite instability, RNA, ribonucleic acid; TMB, tumour mutational burden; WGS, whole genome sequencing; WES, whole exome sequencing

[17] https://www.garvan.org.au/research/kinghorn-centre-for-clinical-genomics/learn-about-genomics/for-gp/genetics-refresher-1/genomics-and-genomic-testing
[18] October 2020, The National Oncology Alliance commissioned HTAnalysts report: Genomic Testing for Cancer Patients:Blueprint Assessment

Patients currently must pay out-of-pocket to access large-scale genome analyses or obtain these tests through participation in a clinical trial. NGS testing in cancer is not currently funded via the Medical Benefits Schedule (MBS). According to the NOA – Genomic Testing report, just two MBS items for whole genome sequencing or whole exome sequencing were listed for children in May 2020.

Only a few centres of excellence (CoEs) in Australia currently offer comprehensive NGS tests through their research. These include the Peter MacCallum Cancer Centre, the Garvan Institute of Medical Research, and the Monash Cancer Centre. (See section 9.4 of the NOA – Genomic Testing report for further details of the current research landscape in Australia).

The timing of the use of NGS for genomic sequencing is a topic of much debate amongst stakeholders. NGS for genomic sequencing will be needed for emerging tumour agnostic therapies, however it is not clear what an ideal tumour agnostic panel might look like.

Combining NGS with and AI and machine learning may have the potential to map out entire clinical pathways[19].

Liquid biopsy vs. solid tissue biopsy

An early and accurate diagnosis can mean the difference between life and death for cancer patients. A patient's cancer journey is heavily influenced by how quickly their cancer is detected and diagnosed, and what the overall prognosis will be. Genomic sequencing soon after diagnosis or to confirm diagnosis is valuable to inform the treatment plan for patients as early as possible.

Needle aspiration biopsy is the conventional approach to tissue sampling. Patients find this an invasive and painful procedure. This technique is difficult to repeat, preventing characterisation of ongoing changes to a cancer's phenotype or distribution.

A liquid biopsy detects circulating cancer cells, tumour DNA (Ct-DNA) and exosomes as a source of genomic and proteomic information from blood and body tissues.

The great advantage of liquid biopsies is that they can be repeated after diagnosis to provide ongoing information about how the cancer has changed or progressed and inform the risk of relapse.

The technique has advanced from single-gene analysis to being able to detect a broad range of genes due to the increased sensitivity of NGS. This enables application in a wide range of settings, including the response or lack of response to targeted treatments, monitoring of tumour changes in real-time, and detection of residual disease and risk of relapse.

Liquid biopsy is not a routine test in clinical practice, but it can be sourced privately or via clinical trials. Advantages of liquid biopsy include faster testing, non-invasive, lower cost, and real-time monitoring of changes compared with conventional biopsy.

Screening for risk

Historically, genetic tests were limited to the identification of particular genes such as those linked to a known cancer mutation.

Testing for "known" genes linked to cancer predisposition is available in Australia for selective cancers that have a well-characterised molecular profile. For example, in breast cancer, patients or family members may have a high risk of having inherited a faulty gene such as BRAC1 or BRAC1 linked to a family history of breast cancer. Gene screening for prevention and identifying family risk factors is crucial but is beyond the scope of the initial proposal for an Australian Cancer Futures Framework.

The prognostic value of early genomic sequencing

Early genomic sequencing can inform which treatments will benefit patients through the identification of genomic alterations that indicate the likely response. This type of testing can prevent patients from receiving treatments that are not likely to work, prevent their cancer from progressing while not responding to treatment, and increase the cost effectiveness of treatment.

For example, Professor Andrew Spencer and his colleagues at the Alfred Hospital are running clinical trials testing samples from patients with multiple myeloma across Australia. These show how early genomic testing can provide vital information to inform a patient's treatment and prevent unnecessary expenditure on therapies that won't work for particular states of multiple myeloma.

[19] May 2020 Value In Health

"Early and accurate genetic testing that could provide important prognostic information is critical to support discussions with patients and their families to enable realistic and informed treatment choices, viz, SoC versus alternative approaches. This, in turn, could lead to cost savings for the health system by using treatment more effectively, for example, discontinuing treatment where it is unlikely to be of any clinical benefit," said Professor Spencer (Box 1).

Molecular markers and personalised treatment

WGS, CGP or hot spot panel tests are giving rise to the discovery of biomarkers or tissue-specific disease-related mutations.

The immediate value of genomic sequencing in a treatment setting is limited by the ability to match a marker-biomarker to a targeted therapy that is available via the (PBS), MBS or within a clinical trial.

In the research setting, the molecular data from the tumour can be compared to the patient's whole genome to identify potential targets or disease modifiers as opportunities for development of new targeted therapies.

Cancer is an extremely complex set of diseases, and there is a tendency for the cancer to develop resistance to targeted treatment. The latest research suggests that a combination therapy approach focused on multiple biological drivers may be more effective.

The value of genomic testing lies in rare or less common cancers, advanced cancers and cancers that have spread beyond the primary tumours. Metastatic cancers are multi-clonal, meaning there are multiple types within a sub-type. For this reason, a druggable target may help slow the progression of the disease and generate a response. Curative measures are likely to require combination therapy approaches that employ a targeted therapy with alternative agents to treat residual cancer clones.

The discovery of mutations that are common to multiple cancers are giving rise to the development of pan cancer or tumour agnostic therapies. This is an exciting prospect for cancer patients, as it means many different cancers with the same characteristics are very likely to respond to the targeted treatment. An example of this is Bayer's VITRAKVI (larotectinib). The first pan-tumour therapy to harness genomic profiling to target and treat adult and childhood cancers with NTRK fusions was approved by the TGA in September. VITRAKVI will treat as many as 30 different kinds of cancers if it successfully navigates the pathway to PBS listing. The availability of VITRAKVI also relies on a suitable "companion diagnostic" genomic test to determine the cancer has the relevant target for treatment. These therapies increase the importance of NGS sequencing. Overexpression of TRK proteins can be detected using surrogate tests, although FISH or NGS are used to confirm the result[20]. Some pan tumours can only be detected using NGS sequencing methodology, highlighting the need for a national plan for implementation.

Generation and interpretation of genomic data

WGS sequences all the genes within the DNA of an individual and yields massive amounts of data – most with unknown relevance. The data requires interpretation to realise the value of the test. This can be carried out by experts on Multidisciplinary Molecular Tumour Advisory Boards (MTBs) or through automated reports on the test findings. Increasingly, boards may use bioinformaticians to analyse raw data. However, this practice involves large amounts of time. In future, MTBs may leverage artificial intelligence algorithms and machine learning.

The resultant data must be stored in data banks, data clouds or registries with privacy and ethical protections in place for personal health information. Registries can inform research and best clinical practice and enable a patient's disease to be matched to targeted treatments where such treatments are available. Currently, data is being accumulated across a range of public and private data banks, which will present a significant challenge.

An added layer of complexity lies in the intellectual property, or legal ownership of the information. Who owns the data and how readily it will be shared has an impact on delivering the best outcomes to cancer patients. This is particularly true in the case of the discovery and patenting of genetic signatures that have known linkages to important disease characteristics of a particular cancer subtype.

[20] 2020, National Oncology Alliance: Genomic Testing for Cancer Patients: Blueprint Assessment

Working toward a national approach for genomic sequencing

The federal government has recognised the importance of genomic research, supporting multiple endeavours, including:

- $50 million in funding over five years for the expansion of the Australian Genomic Cancer Medicine program at the Garvan Institute of Medical Research. The program matches therapies to individuals with rare and less common cancers based on their unique genetic information. In Molecular Screening and Therapeutics (MoST) clinical trials, the genome of each patient is compared with the genome of their tumour to discern the underlying cause and target treatment accordingly. Patients without a targetable driver of their cancer are offered immunotherapies. In addition, the program's RisC trial develops surveillance protocols for those at a genetically high risk of cancer[21].
- $54.8 million in funding to the ZERO Childhood Cancers research program in April 2020. The additional funding extends the genetic testing of the ZERO program from 20% of paediatric cancer patients to all Australian children diagnosed with cancer by 2023. The federal funding is in addition to $12.2 million from the Minderoo Foundation.
- Cancer is one of the priorities of the $500 million Genomic Health Futures Mission that will be rolled out over the next 10 years. The initiative supports research through the Medical Research Future fund to integrate genomic knowledge and technology into clinical practice. $20 million was awarded to ProCan in 2020 to develop a comprehensive research database of genomic information related to cancer. It will help develop technologies and tools to diagnose and treat individual cancer patients more precisely. This will improve survival rates and avoid unnecessary treatments. ProCan is comprised of cancer researchers from across Australia and around the world.

The Australian Cancer Futures Framework would include a study on the feasibility of establishing a national co-ordinated genomic centre of excellence.

[21] https://www.garvan.org.au/research/genomic-cancer-medicine-program/molecular-screening-clinical-trials

The gap between research and the clinical setting is widening. This means only some cancer patients who qualify for clinical trials will benefit. There is an opportunity to close the gap through further investment in research and consideration of progressive evaluation and funding mechanisms (more on this in access and funding). These must consider access to NGS screening and emerging tumour agnostic therapies that can treat multiple cancers.

The NOA – Genomic Testing report identified that patients with rare and less common cancers are most likely to benefit from NGS-based genomic testing using large panels or CGP. The needs of this population are the greatest. As more sub-types of cancer emerge, this need will grow.

Innovative approaches will be required to translate molecular advances into clinical care.

An Australian Cancer Futures Framework could bring together a dedicated taskforce of expert stakeholders across the entire cancer community to support a national approach to genomic screening for rare or advanced cancer patients.

Genomic testing is a rapidly advancing and complex field. In Australia, there are many players in the field of genomic testing. Each has competing or complementary goals and aspirations along with differing opinions about potential applications and utility within research and clinical settings.

The NOA – Genomic Testing report can be used by the Department of Health, supported by NOA, to deliver a model to progressively roll out and integrate genomic testing for advanced and rare cancer patients.

BOX 5: MMPROFILER WITH SKY92 - PAVING THE WAY FOR EARLY AND ACCURATE GENETIC TESTING OF MULTIPLE MYELOMA

Professor Andrew Spencer is the Head of the Malignant Haematology and Stem Cell Transplantation Service at The Alfred Hospital, and is Professor of Haematology at Monash University.

Multiple myeloma (MM) is an incurable, clinically and genetically heterogeneous cancer arising in the bone marrow[1].

In Australia, the real-world outcome for newly diagnosed MM (NDMM) patients is systematically monitored via the Myeloma and Related Diseases Registry (MRDR), a clinical quality registry established in 2012.[2] Two recent analyses of real-world data from the MRDR highlight persisting obstacles to the delivery of effective treatment for Australian NDMM patients. A study of >1500 Australian NDMM patients presented at the 2019 American Society of Hematology Annual Scientific Meeting demonstrated that 22% relapsed within 12 months of commencing standard of care (SoC) treatment. These patients had a median overall survival from diagnosis of only 16.8 months, starkly highlighting the inability to salvage these patients with alternative treatments once they had embarked on SoC, and then relapsed.[3] A more recent analysis has shown that only 50% of Australian NDMM patients have access to genetic (chromosome) testing at the time of their diagnosis.

This problem is confounded by a lack of standardisation in testing approaches and the fact that in the majority of cases, the results are not available at the time of initiating treatment.[4] Early and accurate genetic testing that could provide important prognostic information is critical to support discussions with patients and their families to enable realistic and informed treatment choices, viz, SoC versus alternative approaches. This in turn could lead to cost savings for the health system, for example by discontinuing treatment where it is unlikely to be of any clinical benefit.

An alternative strategy for the genetic characterisation of NDMM patients is to utilise gene expression profiling (GEP), specifically the SKY92 MMprofiler platform. SKY92 is based on an extensively validated algorithm, and can accurately identify NDMM patients with 'high risk' disease and who demonstrate significantly shorter survival with SoC.[5] The Myeloma Research Group at The Alfred Hospital has incorporated SKY92 profiling into a range of investigator-initiated treatment trials over the past three years. These have confirmed the utility of the platform, and the capacity to generate results within 72 hours of receiving a patient bone marrow sample.

Importantly, the MMprofiler SKY92 assay has now been approved for diagnostic purposes in the EU and US.
The diagnostic value of SKY92 profiling has recently been highlighted by the results from the UK Medical Research Council's MM XI trial involving >4000 NDMM patients. It was clearly demonstrated that SKY92 high-risk patients derived no survival benefit from the use of the high-cost immunomodulatory agent lenalidomide.[6] Lenalidomide provides the mainstay of NDMM treatment in Australia, and is PBS funded for both first-line and maintenance treatment. In this context, the availability of a standardised and validated genomic diagnostic platform for NDMM, such as MMprofiler with SKY92 algorithm, would have obvious and wide-ranging implications clinically and economically. It would enable more personalised treatment approaches, and the avoidance of the ongoing funding of ineffective high-cost therapies. MMprofiler with SKY92 algorithm is aligned to the federal government's strong commitment to genomics, helping people to live longer through access to genomic knowledge and technology to diagnose, treat and monitor disease.

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[1] Cowan AJ, Allen C, Barac A, et al. Global Burden of Multiple Myeloma: A Systematic Analysis for the Global Burden of Disease Study 2016. JAMA Oncology 2018: 4(9): 1221-1227.

[2] Bergin K, Moore E, McQuilten Z, et al. Design and development of the Australian and New Zealand (ANZ) Myeloma and Related Diseases Registry. BMC Med Res Methodol. 2016 Nov 9;16(1):151.

[3] Spencer A, Mollee P, Blacklock HA, et al. Real-world outcome for newly diagnosed patients with functional high-risk myeloma – a Myeloma and Related Diseases Registry analysis. Blood 2019;134(suppl 1):269.

[4] Myeloma and Related Diseases Registry. https://www.mrdr.net.au/ Data on file.

[5] Kuiper R, van Duin M, van Vliet MH, et al. Prediction of high- and low-risk multiple myeloma based on gene expression and the International Staging System. Blood 2015; 126(17): 1996-2004.

[6] Shah, V, Sherborne AL, Johnson DC. et al. Predicting ultrahigh risk multiple myeloma by molecular profiling: an analysis of newly diagnosed transplant eligible myeloma XI trial patients. Leukemia 2020. https://doi.org/10.1038/s41375-020-0750-z

ARTIFICIAL INTELLIGENCE AND DATA

What is AI, and why does it promise to be transformational in cancer care?

Artificial intelligence (AI) is the name given to computer systems that have some capacity to make independent decisions and can learn from past examples. AI encompasses myriad technologies that exhibit some aspects of intelligent human behaviour and decision-making. AI can learn, plan, predict, interpret, act and process natural language.

AI already plays a significant role in our everyday lives. Our smart phones, apps and social media use AI to tailor what they do to match our personal profiles. Everyday AI examples include shopping sites that suggest items we might personally be interested in, chatbots that help customers on websites, voice assistants like Siri and Alexa that learn to recognise our voices, and Pinterest's LENS tool that can identify products in images.

There are many clinical tasks where AI can be used, including:

1. Identifying and classifying features in an image. For example, deep-learning systems can outperform radiologists and pathologists at detecting cancer and abnormalities in clinical images.
2. Recognise human speech. Modern AI systems have reached human level performance on single speaker tasks and allow computer systems to be run by speech rather than keyboard and mouse.
3. Predict future events such as risk of death in hospital or adverse events. After training a machine-learning system on the outcomes of care from past patients, AI systems can accurately predict what will happen to future patients. The humans using these predictions to make decisions will need clear ethical frameworks to guide the weight they place on them[22].

AI has the potential to transform cancer diagnosis and treatment and will revolutionise traditional models of healthcare delivery.

Medical expertise in cancer care can be enhanced by the agility and precision of machine learning and deep learning over the next 10 years. The success and ability to harness the profound potential of AI in cancer care will depend on how well it is integrated into healthcare frameworks.

BOX 6: MACHINE LEARNING AND DEEP LEARNING EXPLAINED

MACHINE LEARNING

Machine learning is the process of training a computer to identify patterns and make decisions with minimal human intervention by churning through large amounts of data. Compared with traditional computing, machine learning does not rely on a human developer to write code to instruct the machine. The machine is trained on data from images, audio, video, and data banks.

DEEP LEARNING

Deep learning is a subset of machine learning. Deep learning relies on neural networks that loosely mimic neurons in the human brain. These extended networks have huge layers and are trained using massive amounts of data. It relies on interconnected layers of algorithms, called neurons, which feed data into each other, with the output of the preceding layer being the input of the subsequent layer. Each layer can be thought of as recognising different features of the overall data. Deep neural networks have enabled computers to carry out tasks like speech recognition and computer vision.

Most excitingly, AI promises a new era of productivity, accuracy, and vastly improved outcomes in cancer care. It is already transforming the way cancer is diagnosed and will increasingly predict risk and which cancers will respond to certain therapies. AI also has application in research and development, directing the discovery of new therapies and assisting in their clinical validation.

[22] Professor Enrico Coiera, Director, Australian Alliance for AI in Healthcare, Director, Centre for Health Informatics, Australian Institute of Health InnovationMacquarie University, Director, NHMRC Centre for Research Excellence in Digital Health

As an example, Max Kelsen, an Australian analytics company, is using AI to predict the effectiveness of cancer treatments using WGS with an initial focus on immunotherapy treatment for melanoma and small cell lung cancer.

Another exciting application of AI for cancer patients is the use of "real-time" information using imaging. A patient's cancer is constantly evolving, changing its phenotype, genomic composition, and through the metastatic spread, its location[23]. AI radiographic biomarkers (radiomics) can provide information on the entire tumour in a non-invasive way as it evolves and changes.

AI is also enhancing logistics in all areas of the cancer supply chain – from payer to patient to product manufacturer – and optimising areas such as scheduling, billing, marketing, and distribution logistics. Table 3, provided by Cameron Bean, Health lead, Max Kelsen, summarises how AI is shaping cancer care in 2020, and what it may offer in 2030.

The use of big data to inform cancer care

Healthcare produces a steady and growing data stream from research, medical records, devices, prescription data, MBS item claims, past preferences for services, genomics, biology and more. This data will be key in delivering patient-centric personalised cancer care by 2030.

Big data is essential for the development and testing of new predictive treatment algorithms. Data samples from many small populations can be combined, enabling and enhancing research and evidence generation which was previously impossible with traditional clinical trials. International data sharing opens the possibility of vastly improved outcomes for patients with rare cancers and emerging cancer sub-types by better understanding their disease and best therapies.

Max Kelsen has reported that a single genome amounts to almost 300 gigabytes. The company is using Google Cloud's computing power to sort through data using TensorFlow, which was initially developed by the Google Brain Team for internal use.

Cloud platforms in addition to Google, such as Amazon Web Services and Microsoft Azure, provide all the infrastructure and services capable of holding the vast amount of data needed to train machine-learning models, services to transform data to prepare it for analysis, visualisation tools to display the results clearly and software that simplifies the building of models[24].

Data generation, data storage and its use within the Australian healthcare setting will require governance to prevent misinterpretation and inequities across the cancer population.

An Australia-wide approach to AI integration

A national approach is needed to transform the healthcare system into a modern, adaptive and consumer driven system for the wellbeing of all Australians. A new collaboration, the Australian Alliance for AI in healthcare (AAAAiH), championed by Professor Enrico Coiera[25], have been working to identify the nature, scope and scale of a national response needed to seize the opportunities and meet the challenges that AI brings to healthcare[26].

AAAiH recently highlighted lack of a "cohesive national approach to maximise the benefits of AI in healthcare through better health outcomes and efficiencies and the absence of an ethical or regulatory framework to protect consumers when technology is unsafe or threatens their legitimate interests such as their privacy, and no workforce strategy."

There is an opportunity to plan to integrate AI into the health system in line with the MRFF's "Digital Health Intelligence" priority. AAAiH predicts that this would benefit all Australians, including those in rural or remote regions and those managing chronic illness and rare diseases. It is also expected to boost the economy through jobs and growth.

The goal of AAAiH complements the NOA vision for building a national approach to AI that will benefit cancer patients, particularly those with an advanced disease or with rare cancer sub-types.

[23] https://www.jto.org/article/S1556-0864(19)30737-3/fulltext

[24] https://www.zdnet.com/article/what-is-ai-everything-you-need-to-know-about-artificial-intelligence/

[25] Professor Enrico Coiera, Director, Australian Alliance for AI in Healthcare Director, Centre for Health Informatics, Australian Institute of Health Innovation, Macquarie University. Director, NHMRC Centre for Research Excellence in Digital Health

[26] August 2019 AAAiH, Briefing Paper, Proposal for a MRFF funded national mission for Artificial Intelligence in Health Care

The overwhelming incidence and the rapid advances in personalised treatments mean that cancer would be an ideal pilot disease area for building an AI framework that could be complementary to the National Mission for AI in Healthcare proposed by the AAAiH.

An Australian AI Cancer Framework is expected to offer numerous benefits, some of which have been highlighted in the AAAiH proposal:

- Re-purposing innovative and economically beneficial treatments.
- Creating safe, effective and personalised primary health services and
- Optimising the power of consumers to navigate the health system through personalised digital navigators.

A national framework would allow technology companies, health service providers and policymakers to propose guidelines for the integration of AI and data sharing. Standardised protocols for data protection and storage will allow data to be consolidated and compared meaningfully.

An AI and data taskforce could consider the issues of data custodianship between different institutions and private enterprises, and how to ethically share data for wider use.

Australia is in the unique position to plan for the integration of AI into cancer care and the health system. An overarching collaborative and national approach is necessary to ensure that appropriate transparency, regulatory, ethics and governance frameworks are in place to manage the complexities and optimally harness the technologies to provide improved survival for cancer patients.

TABLE 3. THE CURRENT STATE OF AI FOR CANCER CARE IN 2020

DIAGNOSTICS/DISCOVERY	INTERVENTIONS	PATIENT OUTCOMES
• Image recognition and interpretation[a] • Molecule development[b] • Genomics[c] • Pathology[d] • EMR[e]	• Treatment identification[f] • Treatment outcomes to inform interventions[g] • Clinical trial matching[h] • Drug dosing and care plans[i] • Scheduling[j] • Logistics – treatment availability[k]	• Treatment outcomes • Initial real-world evidence gathering[l] • Multimodal data integration[m] • PREMS / PROMS[n]

TABLE 4. FUTURE STATE OF AI FOR CANCER CARE IN 2030

TECHNOLOGY	SOCIETAL EXPECTATIONS AND REGULATION
• incorporation into diagnostic machines • rise of applicable quantum computing • AI-specific chip sets • more energy and computationally efficient methods • fundamentally new algorithms • distributed networks	• data sovereignty • ability to replicate services regionally so that they reside in multiple data centres • governance of data ownership • data privacy and disclosure to third parties (i.e. insurers)

• Tables supplied by Cameron Bean, Max Kelsen. For references see Appendix

Artificial Intelligence promises a new era of productivity, accuracy, and vastly improved outcomes in cancer care.

Patient Journey

Madonna was the embodiment of a mum, finding ways to help with calm and thoughtful words. She's described as the glue that held the family together, a truly beautiful person.

MADONNA

A story of peace and patience

Saying that Madonna was the backbone of the family would be understating it. You would be hard pressed to find someone who could carry the weight of family as she did. She never complained or whinged about a situation, instead accepted things for what they were and got on with it. That internal strength was ever-present, shining like a beacon, even in her final weeks. There were never any complaints about the unfairness of it. There was no lashing out or complaints about the pain. When others would speak on her behalf, they were met with that same calm resilience; “Its ok love, it is what it is, can’t do anything about it”

That’s who Madonna was – a kind, caring woman, with no end to her patience or strength – or her wicked sense of humour. It was because of those qualities that she thrived as a Police Officer, serving over 16 years, from the age of 19. She’d loved to have gone on to become a teacher, if family needs didn’t come first. Instead, she would raise her family, and care for both her mother and ill grandmother.

Madonna was the embodiment of a mum, finding ways to help with calm and thoughtful words. She’s described as the glue that held the family together, and never had a harsh or cruel word for anyone. It was her life motto, ‘Least said, soonest mended” and she truly lived up to it. She also loved to spoil her kids, with most of them still having Santa sacks well into their 20s! Being a mum was everything to Madonna.

She met her husband, Greg, when she was still in primary school. He was in the all-boys school across the road, and in a true to life fairy-tale, one day he slipped a note in her bag, an invitation to a party. Together, they shared nearly 50 incredible years of love and romance. She had a certain magic about her that even her old school friends remember, with some reaching out after her passing and reminiscing about how Madonna touched their lives.

She was a truly beautiful person and to say much more, would simply go against her motto, so we leave you with the words of her devoted daughter, Stephanie.

“Mum loved us with a deep and abiding love, she sacrificed her career to care for her family, she was selfless and unique and we couldn’t be more blessed to have had her for the time that we did… There is a gaping hole in all our hearts that cannot be filled with anyone else.”

2020 PATIENT JOURNEY

Madonna

2018 DISCOVERY

- Madonna is a 61 year old grandmother living in Queensland.

2018 SCREENING

- Madonna undergoes a CT scan

2018 DIAGNOSED

- Madonna is diagnosed with angiosarcoma in the heart.
- Madonna and her family are devastated and confused.

2018 INFORMATION

- Madonna and her family are left without an optimal care pathway.
- Madonna will now begin the scary unknown journey familiar to rare or less common cancer patients.

SEPTEMBER 2018 TREATMENT – SURGERY

- Madonna undergoes cardiac surgery to remove the angiosarcoma.
- A 6cm sarcoma is removed but unfortunately the cardiothoracic surgeon does not gain a clear margin.

SEPTEMBER – DECEMBER 2018 TREATMENT – RADIATION THERAPY

- Madonna undergoes 26 radiation treatments with no other direction.

EARLY 2019 TREATMENT – CLINICAL TRIAL

- Madonna investigates her own options and hears of Pazopanib, a promising drug for angiosarcoma. Her oncologist does not believe pazopanib is a good option.
- An actionable mutation is found through MoST and she is accepted onto a clinical trial of Erubilin at the Chris O'Brien Lifehouse at RPA in Sydney.

DECEMBER 2019 TREATMENT– TARGETED THERAPY

- Madonna undergoes chemotherapy and is given 8 sessions of Paclitaxel. Although It prevents progression in her back, the lesions in her lungs, hips and liver increase.
- Madonna develops the side effect of a worsening of peripheral neuropathy and treatment is stopped.

APRIL TO NOVEMBER 2019 FUNDRAISING

- Madonna flies from QLD to SYD with her carer every 3 weeks to attend the clinical trial.
- After 3-4 months she encounters financial difficulty in paying flights and accommodation for two people.
- RCA pays for flights so she can continue
- Madonna has good results for several months (April- November) until a new lesion in her ribs appears. She is devastated as now she is excluded from the trial.

APRIL 2020

- Early 2020 in a last attempt to diminish her pain, Madonna resorts once again to radiation.
- The extreme radiation burns her throat which leads to an infection. Madonna is unable to eat and loses 20 kilos. She picks up a virus and requires monthly blood transfusions.
- Madonna passes away leaving her family heartbroken.

2030 PATIENT JOURNEY

DISCOVERY

- Patients with rare conditions such as angiosarcoma, thanks to the use of AI and diagnostics via liquid biopsy, are diagnosed at an early stage.

SCREENING

- Patients undergo whole genome sequencing to uncover molecular features which can guide decisions such as targeted therapies. Families are assigned Specialist Navigators to ensure patients understand their choices and are fully informed and supported.

DIAGNOSED

- Patient data is all recorded in a registry which contributes to knowledge for optimal care pathways for sarcoma treatment.

INFORMATION

- Patients and their families together with an MDT collaborate through a rare cancers portal and may decide on treatment options such as robotic surgery which is minimally invasive. The portal allows patients to stay with their local oncologist close to home and receive care guided by leading sarcoma experts.

TREATMENT TARGETED THERAPY

- Because patients remain close to home, they are able to spend quality time with close supports and family when they are most vulnerable and family are most anxious.
- Using genomic data, targeted therapy is carefully selected to match the patient's molecular profile.
- Patients are referred to the services of a palliative care team, to better manage symptoms and enhance quality of life.

TREATMENT SURGERY

- Surgery, and subsequent targeted therapy in administered in local hospitals, and are provided via a shared funding model. Tele trials are central to care delivery, and GPs are involved in shared patient care.

TREATMENT FOLLOW-UP

- Specialist Cancer Navigators record patients experiences and preferences throughout diagnosis and treatment which contributes vital real-world evidence to the registry. Patients preferences are also recorded. The data can be used to demonstrate that the treatment is effective in the real world and may be used to justify ongoing value. In addition, the data can be used for optimal care pathways for future patients.

TREATMENT FINANCIAL

- The support mechanisms in place include: access to a financial safety net which relieves expenses and supports the family ensuring the financial toxicity that used to come with cancer is a thing of the past.

SURVIVORSHIP CARE

Patients can continue to access clinical trials using tele trials and receiving support from their own GP throughout and after treatment. Support is provided from the Specialist Cancer Navigator to ensure continuity of care. This allows patients to continue to work and enjoy spending time with the people close to them at home

4 WORKING TOWARDS SAVING THE LIVES OF CANCER PATIENTS

PATIENT-CENTRED CANCER CARE

What is the patient perspective on patient centricity within the health system?

A cancer diagnosis can be devastating and terrifying for patients, their families and caregivers. There are many unknown obstacles to navigate in the quest to prolong the patient's life. This is particularly true for patients diagnosed with advanced, or rare and less common cancers.

It is unanimous throughout the sector that patients and their caregivers should be central to their cancer treatment journey, as well as policies that relate to the provision of treatment and care. Do patients have enough information, feel heard and have choices in practice? Are the preferences of cancer patients sufficiently integrated into decision making frameworks underpinning access to therapies and technologies?

The feedback from the Vision 20-30 workshop series highlights that there is a potential to do a lot more.

Patients and their carers are often self-educated in oncology. They have no choice but to invest time in learning how to obtain the best care and best treatment teams to increase the chances of survival.

Jelena Magic has a little son Marko, who was diagnosed with very aggressive neuroblastoma in 2018. She said she felt comforted by the notion that the Australian system was promoting person-centred care. Yet Jelena's experience as a carer was far from ideal in respect to the "centralised patient model". Jelena is a passionate patient advocate for her son and other families both in Australia and overseas, and has learnt that the idea of centralised patient care does not really translate into reality in the clinical practice setting.

"There is room to improve continuity of care so that messages do not get lost along the way, to ensure trustworthy relationships are forged between patients, physicians and their broader cancer care team," Jelena explained.

A patient member of NOA outlined similar challenges when it comes to communication and transparency. Patients are sometimes the last to be told of the status of their condition, which means it is almost impossible to make informed decisions effectively and with confidence.

BOX 7: CHRISTINE COCKBURN – PATIENT NAVIGATION EXPERT AT RARE CANCER AUSTRALIA – TALKS ABOUT HER DAILY DISCUSSIONS WITH CANCER PATIENTS

People who seek out our support range broadly from highly health literate to worryingly ill-equipped to operate in the healthcare space they find themselves in. Regardless of where people fall on this spectrum, there are challenges with decision making, and much of this comes down to access to information and awareness of their options. People are rarely encouraged to seek out further options and are placed in a position of having enormous trust in medical teams. The power dynamic is such that the patient is not in the position of authority or considered an "expert". This is compounded by the anxiety and vulnerability experienced by patients and their families when they enter the oncology world. It can be a terrifying time.

We spend a lot of time talking to anxious people about the information they have received, how they feel about it and the questions they should ask to find out more.

They are, more often than not, aware of time pressures in the clinical setting, learning a whole new language as they go and reluctant to challenge specialists to explore alternative options. This results in disempowerment and increased vulnerability. It really is little wonder that in the current model, patients are not viewed as capable of informed decision making – the knowledge gaps are problematic.

There is significant opportunity with an Australian Cancer Futures Framework to place greater emphasis on the role of the patient in decision making; to meaningfully consider their preferences and to incorporate their experiences in care and treatment planning. Meaningfully including the patient in the treatment team can only result in a better patient experience and greater efficiencies in cancer care delivery.

Patient choice is becoming broadly recognised within cancer circles as being valued and important. Yet within the clinical setting, patients are often completely unaware of all their options. Patients often feel lost and confused and not "armed" with the tools and information they need to make a decision that is vital to their treatment outcomes, quality of life and emotional wellbeing.

It is essential to understand what information patients and their families want, how it be presented to them, and what decisions they can make when they are empowered to speak up.

An Australian Cancer Futures Framework can provide the vehicle to effectively and consistently deliver on patient-centred care and empower patients and their families to make informed choices. Patient experiences could be analysed in a systematic way to understand what patients want and need. There is an opportunity to explore how complex medical and scientific information can be clearly and more readily explained, as well as to enhance the patient-physician relationships.

As more lives are saved, further support frameworks will be needed to deal with survivorship. There are many psychological challenges in the early and ongoing stages of cancer survivorship, as well as the prospect of potential comorbidities. These challenges can include pain, fatigue, anxiety, depression, memory and cognitive changes. The need for support in the period after cancer survival will increase in 2030 if an Australian Cancer Futures Framework is successful in delivering better outcomes.

Harnessing patient preference to have a truly patient-centred health care system

Real world evidence and patient preferences must play an increasing role in the allocation of financial resources across the cancer continuum. There is growing recognition that as taxpayers and the direct recipients of healthcare, the patient's perspective is becoming increasingly important. This has never been more so than now, when financial resources are scarce and in the context of an era where clinical evidence may be less mature to support decision making.

While real world data is becoming more central to registration and pharmacovigilance evaluations, there is growing need to formally integrate it into value-based comparative assessments to support funding decisions for therapies and medical technologies.

It may have been difficult to contemplate how to achieve this in the past, but there is a growing body of tools capturing patient preferences and outcomes to support formal integration into the health system.

Simon Fifer from research group CaPPRe demonstrated that it is possible to understand what patient's value and how that links to engagement through trade-off surveys, otherwise known as discrete choice experiments. These value measures can then be used by various stakeholders to keep the patient's preferences at heart when navigating complex treatment pathways, as well as at the policy level in determining the allocation of financial resources.

In addition, patient reported outcomes (PROMs) can support patient-centric decision making. PROMs are validated studies that focus on various aspects of health, such as symptoms, daily functioning and quality of life[27]. There has been significant growth in the tools to measure PROMs. There are approximately 40 generic templates available and around 275 condition specific ones, according to Colman Taylor, from HTAnalysts, who presented on real world evidence in the Vision 20-30 workshop series.

While there is increasing recognition of the value of PROMs in providing patient perspectives to treatment outcomes, they are not prioritised within the health technology assessment (HTA) clinical assessment frameworks. They are, however, important measures, as they provide the patient perspective where conventional clinical outcomes cannot.

As well as being used to support funding decisions, PROMS can measure and monitor how well the health system is performing.

According to Dr Colman Taylor, more consistent and rigorous PROMs data would allow us to consider interpreting clinical data differently and provide an entirely patient-centric perspective on what is important and meaningful.

It should be noted that there is already work being done in this area. Cancer Australia has commissioned the University of Sydney to harmonise how PROMs are measured.

Through the Australian Cancer Future Framework, stakeholders would consider how most effectively to embed PROMs and patient surveys into evaluation frameworks that underpin the health system.

[27] Colman Taylor, HTAnalysts Vision 2030 Outcomes Presentation

CHILDHOOD CANCERS — WHY ARE THEY DIFFERENT?

Childhood cancers are unfathomable in the eyes of families. Those of us with healthy children struggle to put ourselves in the shoes of parents that must face a cancer diagnosis, the rollercoaster of the treatment journey and the disruption to everyday life.

Children are very resilient, and most children with cancer are cured. But the pathway to cure is incredibly taxing, emotionally and psychosocially.

Parents must actively navigate treatment choices and the ups of signs of response or recovery, then manage big toxicities such as hair loss, low blood counts, infections, sepsis, and latent effects. It is a rough road for parents and children, who are often left with lasting consequences after recovery.

There are some children, like little Ned, who endure intensive therapies and side effects and then, despite remissions, still do not make it. It is simply devastating.

Dr Emily Isham, oncology parent, talked about the decisions she and her husband were faced with during Ned's treatment journey. Ned was diagnosed with ALL at only two years of age.

"I remember having to make pretty enormous decisions about taking risks for procedures and treatments that I would normally take a lot longer to consider and weigh out. But in the pursuit of Ned's life, we just had to kind of flippantly consent to a lot of things. It is not for want of us being given the information, but we did not really have a lot of choice, it was the lesser of two evils. So, all those long-term effects and risks to his heart, eyes, years, fertility, all of that. Of course, the psychological trauma of all this was significant," she said.

Dr Isham discussed the difficulty in trying to manage the demands and upheavals the resulted from Ned's various treatments. This included travelling in Australia and overseas, as well as having to keep Ned free from infection in vulnerable periods. This meant long periods of isolation for up to 60 days at a time after bone marrow transplants.

Childhood cancer is terribly burdensome, as it will affect a child's physical and psychological development for the duration of their life. Survivor concerns relate to employability, insurability, cognitive and physical side effects, organ damage, secondary cancers and loss of fertility. There are additional struggles for parents and siblings who lose a child to cancer. They need to recover from the trauma of the treatment journey and manage their feelings of loss.

Cancer is the second biggest cause of premature death among children and young people aged five to 14 years, after accidents[28]. According to Dr Geoff Cowage from Westmead Children's Hospital, one in 600 children will develop cancer or leukaemia throughout their childhood up to about 16 years of age. There are no known environmental or lifestyle factors that can be addressed to aid prevention strategies for childhood cancer. Only a relatively small proportion of childhood cancers are inherited – around 8%.

The good news is that 80% of children with cancer are permanently cured[29]. The progress in childhood cancers has been made in the past two decades, mostly due to clinical trials (around 50% of treatments are provided via clinical trials).

Yet there is an opportunity to do more for children with cancer in the next ten years. One clear area of need is for children's cancer to be treated differently and distinguished from adult cancer.

[28] Bond M and Pritchard S. Understanding clinical trials in childhood cancers. Paediatrics Child Health (2006); 11(3): 148–150

[29] Howlader N, SEER Cancer Statistics Review 1975-2012

CHILDHOOD CANCER ALTERS THE LIVES OF ALL FAMILY MEMBERS

By Jelena Magic, oncology parent

Childhood cancer dramatically alters the lives of all family members, it indiscriminately robs the childhood from the young patient as well as their siblings. Trips to the park, bike rides and playtime are replaced by endless hours at the hospital. During his treatment journey, Marko and his brothers could not understand what was happening and why. Childhood cancer causes parents to question every decision they have ever made and there is an overwhelming sense of fear of what is to come. Unanswerable questions constantly present themselves, like "Will my child survive? If my child dies, how can life possibly go on?" "If he survives, how do I explain to him, that his life will never be normal because of the long term impact from toxic cancer treatments, and that he may never be able to have his own children as a consequence"?

Even for the most optimistic person, when your child is sleeping next to you semi-unconscious and drooling from the toxic therapy not even designed with their little body in mind, it is hard to ward off terrible thoughts that leave you picturing their last moments.

Alongside all of this, there are still practical decisions to be made. Our cancer care team was wonderfully supportive, but the current healthcare system was over-reliant on bureaucratic procedures and statistics, rather than making sure our child's needs were front and centre. Maintaining quality of life during treatment, exchanging opinions with other experts in the field and minimising long-term side effects were equally as important to us as "curing" the cancer.

Information was important given the extremely rare expression of Marko's disease. We felt we were not empowered to make informed decisions about Marko's treatment. We sent emails to our care team that were often left unanswered. As a result, we had to do our own "research". We were forced to negotiate a complicated healthcare system, spend hours on the phone and internet as well as reading medical journal databases at the same time as caring for a tiny baby with an aggressive cancer. We later discovered that best option for Marko's recovery was to participate in a clinical trial led by a reputable cancer research centre in the US. When we learnt that the only option was to crowdfund to cover the exorbitant costs and no support, we felt almost defeated.

Our little hero Marko's smiles and goodness together with his unrelenting will to live and thrive despite the odds, helped us find strength and energy to persist through the most difficult of times. He inspired us to find hope, happiness and pride while striving to find better ways to fight his disease and improve his chance for survival to lead a life with a future of schooling, relationships, etc.

For this reason, we did not give up. Supported by our community and a bit of luck, we succeeded in raising sufficient funds to provide our little boy with a chance at life through the clinical trial treatment overseas. It has been an arduous journey, but it should not be like that. Patients and families should be better supported by their care team to understand the nuances of treatment for rare diseases, to have knowledge of all treatment options even if not available in their hospital, to be empowered to ask difficult questions and challenge the existing frameworks if they are no longer relevant.

Investment into research and kinder, more effective therapies is paramount to achieving these goals in future. An equal emphasis must be given to helping the patients of today. It is not fair nor right to leave families to navigate the global cancer care landscape by themselves.

Picture Courtesy of Jason Edwards/Herald Sun)

Denying these most vulnerable of children the mere opportunity to try an existing new, promising therapy is denying them the opportunity to maximise their odds of leading a healthy, joyful, and productive life.

Unfortunately, childhood cancer protocols are usually an adaptation of adult versions, despite their cancer and downstream consequences being entirely different. During the Vision 20-30 workshops, Dr Cowage stated that "everything you think you know about adult cancer you mustn't apply in childhood".

Childhood cancers don't predominantly present as carcinomas like adults do, 30% are leukaemia and 20% are brain tumours. There are also rare cancers you never hear about in adults, such as neuroblastoma, various lymphoma, sarcoma of bone and soft tissue and tumour of the kidney.

Childhood cancers are rarer than adult cancers. The discovery of even rarer cancer sub-types and potential disease-related targets means that children will need better access to clinical trials for treatment.

According to Dr Cowage, there are some trials conducted in Australia that involve international collaboration to recruit the required number of patients.

"There are groups that specialise in particular diseases like medulloblastoma from Saint Jude, neuroblastoma from NANT, TACL does acute leukaemia trials. There are multinational consortia, the International BFM, US Children's Oncology Group and many of us (paediatric oncologists) do a lot of our trials with them," he said.

According to Dr Cowage, conducting clinical trials for childhood cancers in Australia is difficult.

"Running trials, good trials that are ethically conducted, is very expensive. There are a lot of regulatory hurdles. There is a problem with funding, hospitals don't recognise it as their core business, so they don't fund it. We rely on getting grants from all over the place and philanthropic groups to support our research," he said.

Profiling the tumour and using whole exome sequencing and whole genome sequencing to try to identify a drug target has additional complexities. Targets for childhood cancers are sometimes different to adult cancers. When there is a common marker, the size of the population may be simply too small for a manufacturer to conduct a trial and seek to register and market a treatment for children. This leaves an evidence gap, and no means to have therapies reimbursed and available on the PBS.

Sometimes, the only feasible option when available treatments for a rare childhood cancer have failed is an overseas study. Jelena Magic, an oncology parent and advocate, discussed having to go overseas and fund an expensive clinical trial therapy for her son Marko (see page 61).

The future of childhood cancer

NOA believes that more can be done to ensure children have a better experience of the treatment journey. Greater awareness of the distinguishing experiences and features of childhood cancers is needed. Protocols and information need to be developed, so children are not faced with adapting regimens designed for adults. The workshops highlighted the importance of local clinical trials for children as a treatment option. NOA advocates for greater support of research for childhood cancers, so that Australian children can access treatment in their home country.

NOA advocates for greater support of research for childhood cancers, so that Australian children can access treatment in their home country.

CLINICAL RESEARCH: DISCOVERY, ACCESS AND ECONOMIC GROWTH

What are clinical trials

Clinical trials provide therapeutic opportunities for patients and clinical answers to physicians. They inform standards of care and commercial opportunities for manufacturers of therapies and technologies.

Approximately one third of clinical trials in Australia are investigator-initiated via international centres, small consortia and state-wide networks. Two thirds are commercially led by private industry.

Broadly, investigator-led studies help provide answers to clinical questions while commercial trials test efficacy, safety and quality of new interventions to support development, registration and commercialisation.

These types of trials fulfil different purposes, but both are very important in creating opportunities for patients to receive new treatments and uncovering new uses for existing treatments.

Clinical trials providing treatment opportunities for patients

Clinical trials have the most immediate impact on healthcare compared to any other type of research, according to Professor John Zalcberg from the Australian Clinical Trials Alliance. Clinical trials have become the new "standard of care" for many cancer patients who have exhausted other options, or for whom no beneficial treatments are available. Clinical trials provide a means for patients to have early access to potentially life-saving treatments at no cost (in Australia) and provide healthcare professionals valuable experience with the new treatments.

Historically when patients have exhausted treatment options, clinical trials are the last or only resort. Unfortunately, the option of participating in a clinical trial is not universally transparent to all doctors and patients, and this needs to change.

At a recent seminar, Professor Zalcberg talked further about the importance of embedding clinical trials into everyday clinical practice.

"We must also look at how we embed trials into clinical practice. This must form part of the care we provide, and the community must be informed of this. We need patients and the community asking – 'is there a clinical trial for me and where do I access it?' If patients drive it, we will bring change," he stated.

The patient experience of participation in a clinical trial is very different to navigating the healthcare system. Kate Vines, co-founder of Rare Cancers Australia, provides some insights on what could be done to improve this and embed clinical trials into the health system from a patient perspective (Box 8).

BOX 8: KATE VINES, CO-FOUNDER OF RARE CANCERS AUSTRALIA EXPLAINS HOW IMPORTANT FINDING THE RIGHT CLINICAL TRIAL CAN BE

"I was diagnosed with metastatic Medullary Thyroid Cancer (MTC) in July 1991. At that time, my doctor said to me: "I haven't seen this type of cancer before and I'm not sure how to treat it."

A comment that rare and less common cancer patients unfortunately still hear in 2020. The only treatment option available to me was surgery. There was no chemotherapy available and radiation had limited success. The cancer had already spread to lymph nodes in my neck and chest. I underwent several surgeries in the following years.

Fast forward to 2006. I was in unbearable pain from bone metastases in my chest. There were still no drug treatment options available for MTC. My oncologist at the time suggested that we try one of the old cytotoxic chemotherapies in the hope that this might help, so I agreed to four cycles of Doxorubicin. Fortunately, the first cycle relieved the pain, but the following cycles did nothing to reduce my tumour load or stop the slow spread of disease.

Fast forward again to July 2019. There were still no drug treatments for MTC listed on the PBS. There were two potential drugs indicated to treat MTC, but only one was registered for use in Australia and neither had been considered for PBS listing.

There were no compassionate access programs or available clinical trials in Australia to enable me to access these therapies at a reduced cost.

To be treated with them, I would have needed to pay tens of thousands of dollars and this simply was not an option. Subsequently, I was fortunate enough to be eligible for the MoST trial at OMICO, where my tumour sample was sequenced, and it was discovered that I had a RET mutation. A new drug, Loxo-292 (Selpercatinib) had recently been developed and there was a phase 2 clinical trial running in Sydney. To my great relief, I was eligible for this trial. For the first time in 28 years, there was finally hope for a treatment. Had I not been able to have my tumour sequenced, I would never have found a suitable treatment.

Staging scans for the trial showed that the cancer had been steadily progressing and I now had metastases in my lungs, liver, bones and possibly a lesion in my brain. I started on the trial and like all drugs, there were significant side effects. Monthly visits to the hospital in Sydney for scans and blood tests to determine how I was responding to the drug were quite a strain on me, both physically and mentally, as we lived over 100km from the hospital. The main side effects that troubled me were extreme fatigue and abdominal swelling. I felt quite unwell most of the time and this affected my ability to work and manage normal duties at home.

With the advent of COVID-19 lockdowns, I transitioned to monthly telehealth consultations with the trial doctor and co-ordinator. Fortunately, I was able to have the blood tests and scans done locally. But there were difficulties getting copies of the scans to the hospital – they were not connected digitally to the radiology company. The radiologist was also not familiar with the special criteria of reporting the scans for the sponsor company, so they had to be re-reported once they were received at the hospital.

Phone consultations were the only way that I could meet with my doctor, but I feel now that I wasn't able to fully communicate how sick I had become in the ensuing months. As we were not using video conferencing, my doctor wasn't able to see that my face had become swollen. I think if we had been able to include my local GP in my MDT, we might have recognised what was happening to me far quicker than waiting until I was admitted to hospital, where it was identified that I had mild heart failure, most likely due to the Doxorubicin in 2006.

I live in the Southern Highlands of NSW. For remote and regional patients, being able to access a medical professional in their local community that is familiar with their treatment plan would assist both the patient and the clinical trial doctor in keeping up with what is happening with a patient on a much more frequent basis. I also feel that a more personalised approach to general wellbeing would be very helpful. Every month I filled out a "wellbeing diary", but this was solely related to a particular aspect of my cancer. If the diary was more broadly questioning how I was managing overall on a day-to-day basis, I feel that the trial team would have been able to either direct me to additional psych-social assistance, or perhaps helped to manage the ongoing side effects before it led to a hospital admission.

I'm very grateful that after 29 years, I'm finally on a treatment that has stabilised the cancer growth, and in some areas, has reduced my tumour load. I have always been a very optimistic person, but now I feel that I will have many more years to spend with my family and grandchildren, thanks to this clinical trial and other drugs that are being developed. But it is still disappointing and frustrating that so many drugs that have been developed for rare or less common cancers are not available in Australia at all, or that there are not enough clinical trials. Patients are being denied treatment that could be life extending or lifesaving.

Accessing clinical trials overseas

When patients have not had local options for clinical trials, they have looked overseas. There are many complicating factors with accessing clinical trials outside of Australia. It is often expensive, and out-of-reach for many people (see Box 9). International travel restrictions may be in place for many years because of COVID-19, imposing further barriers and re-directing patient focus back to Australia. Clinical cancer research within Australia is now more critical for cancer patients than ever.

Why local clinical trial research is important

During the Vision 20-30 workshop series, Professor Zalcberg explained the importance and relevance of clinical trials, particularly in informing decisions and strategies for care in cancer medicine.

Investigator-led studies help define standard of care by providing evidence to support the most effective use of multiple therapeutic modalities.

"Multiple and complex interactions of drugs, devices, radiotherapy, surgery etc need to be coordinated in a way that reflects how we manage patients in the real world," he said.

Investigator-driven research can explore new uses for generic or older therapies.

It can identify components of treatment that are harmful and ineffective, thereby improving processes and strategies of care.

As important as clinical research is to patients and the broader community, there is a funding imbalance. Fundamental academic research (not for clinical trial purposes) takes up around 75% of the overall research budget in Australia. Only around 25% (approximately $75 million) is allocated to clinical trials through the National Health and Medical Research Council (NHMRC). Yet the more investment in clinical research funding, the better the survival of patients[30].

The MRFF has allocated $20 billion over 10 years for research in therapeutic areas of need, as well as to the Australian Clinical Trials Alliance (ACTA), NHMRC schemes, and state and territory infrastructure. Three percent of the total MRFF has been allocated to rare cancers and rare diseases over the course of ten years.

Not only does research have the potential to transform lives, but it also provides jobs, and will help re-build the economy and contribute to strengthening the health system.

Clinical trials are estimated to contribute $1 billion to the Australian economy each year[31] and were reported to support close to 7,000 highly skilled jobs in 2015. Ultimately, there are more extensive societal benefits to trials than just patient health, including higher workforce participation.

Keeping Australia an attractive destination for clinical trial research

The evidence generated through clinical trials and research supports the longer-term integration of novel technologies and therapies into clinical practice.

Internationally, selection of location for clinical trials has become increasingly competitive[32]. NOA members agree that to keep Australia a visible and attractive clinical trial destination, harmonisation across the states and territories is needed. It's also vital to ensure regulatory and commercialisation pathways can be navigated easily by overseas investors and manufacturers.

Harmonisation encourages consistency within and between jurisdictions for the conduct and execution of clinical trials across multiple centres. Harmonisation would reduce complexity, increase the speed of clinical trials and promote equity of access and enrolment of eligible patients across the country.

[30] Sumit R. Majumdar, MD, MPH; Matthew T. Roe, MD, MHS; Eric D. Peterson, MD, MPH; et al. Better Outcomes for Patients Treated at Hospitals That Participate in Clinical Trials, Archives of Internal Medicine. 2008(6):657-662

[31] https://www1.health.gov.au/internet/main/publishing.nsf/Content/Clinical-Trials

[32] 2016–2017 Clinical Trials Jurisdictional Working Group, FRAMEWORK FOR NATIONAL AGGREGATE STATISTICS (NAS) SECOND ACTIVITY REPORT ON CLINICAL TRIALS IN AUSTRALIAN PUBLIC HEALTH INSTITUTIONS 2015–16

The place for clinical trials within a Cancer Futures Framework

Australia has always been able to boast of having a world-class health system. If we take COVID-19 as an example, Australia is faring well overall compared to the rest of the world. There is an immediate opportunity for Australia to raise its profile internationally in cancer research, as other countries have been forced to stop clinical trials given their health systems are overwhelmed by COVID-19.

If Australia wishes to maintain its good record in cancer survival, and health more broadly, then the systems will need to attract ongoing investment in local and globally funded clinical research.

Clinical trials are a vital treatment option to extend the lives of cancer patients.

An Australian Cancer Futures Framework would consider harmonisation, embedding clinical trials into clinical practice, supporting patients on clinical trials and planning to ensure Australia is an attractive destination for clinical research for overseas manufacturers.
A large part of keeping Australia an attractive clinical trial destination globally also hinges on the ease of market entry and commercialisation of new therapies and technologies.

BOX 9: THE PROBLEMS ASSOCIATED WITH ACCESSING CLINICAL TRIAL TREATMENTS OVERSEAS – A CARER PERSPECTIVE

When there are no viable clinical trial opportunities in Australia, patients may be forced to look overseas. The costs are astronomical, and out-of-reach for many people. Jelena Magic shared her experience as carer for her son Marko, who had an aggressive form of neuroblastoma, during the Vision 20-30 workshop series.

Jelena talked about the need to crowdfund to raise $470,000 so that Marko could participate in a clinical trial in New York. Given the high relapse rates for neuroblastoma and the lack of treatment available within Australia, Jelena and her family, with the support of Marko's physician, felt there were no other options.

"What choice do I have if this is the only option for me to improve my child's chance of long-term survival? It's an impossible decision," Jelena said during her presentation.

Jelena provided insights on the emotional toll associated with crowdfunding – the loss of privacy, dignity and having to expose your family to the scrutiny of media.

Crowdfunding creates inequality, as not all people will be able to raise the amount of money needed to be treated with an experimental therapy overseas. Crowd funding is also more successful when it's on behalf of a child with cancer rather than an adult. Many adult cancer patients fail to raise sufficient funds.

While Jelena and Marko's need to travel abroad to access the best treatment option may seem to be an outlier to everyday Australians, it is becoming more common.

CANCER REGISTRIES: WHY REAL-WORLD EVIDENCE PROVIDES A WAY FORWARD

The value of registries

Clinical registries provide the opportunity to collect data on patterns of disease and treatment, and variation in outcomes (both survival and quality of life), in the real world of everyday care. In this way, every patient's information contributes to developing a picture of the condition in Australia.

Real world evidence collected in registries can provide evidence for treatments for rare cancer sub-types, where it may be almost impossible to run a robust phase III clinical trial that meets the needs of regulators and funders.

Registries enable clinicians to benchmark against national and international standards, and evaluate the uptake of new scientific knowledge and treatments into long-term outcomes. This includes health economics analyses relevant to the Australian setting.

The Lymphoma and Related Diseases Registry (LaRDR) was established following on from the Multiple Myeloma registry. Both registries demonstrate the increasing value and multiple utilities of real world disease-based data. The registries are fully annotated, and the participating sites can download their own data. Twice a year, the sites also receive data and analysed reports comparing outcomes to the data collected from the rest of the country.

Improving treatment and outcomes for patients is the aim of the Lymphoma and Related Diseases Registry

LaRDR collects comprehensive information on adults newly diagnosed with non-Hodgkin lymphoma, Hodgkin lymphoma and related diseases, including chronic lymphocytic leukemia (CLL). The registry is expanding rapidly since it was established with a pilot study in mid-2016. More than 2,800 people have agreed to participate from 21 centres around Australia.

The registry is run by Monash University's Department of Epidemiology and Preventive Medicine, in partnership with participating hospitals and clinicians. It monitors access to care and trends in survival, explores variation in practice, process and outcome measures, benchmarks outcomes and acts as a resource for clinical studies.

"Data from this registry will help us understand variations in care across treatment centres," said Professor Stephen Opat of Monash Health, chair of the LaRDR Steering Committee.

"According to jurisdictional cancer registries, people in rural and remote areas have worse outcomes than those living in cities. However, the cancer registries only initially record diagnosis, whereas this registry looks at variations in care with detailed information about treatment and what happens for each person over time."

The registry operates on an 'opt out' consent basis. This means the sample isn't biased, "as nearly all people who are approached to participate are willing to do so", said Gayathri St George, LaRDR Senior Research Officer at Monash University.

"Each patient is given information on the purpose of the registry, and if they don't want to participate, they let us know and their data is not recorded."

But the more people who participate, the better for everyone.

Participating hospitals enter data securely online. Information collected includes:

- Patient demographics, diagnoses, health status and laboratory and imaging results at diagnosis.
- Therapy (including chemotherapy and stem cell transplantation, and supportive care)
- Outcomes (overall and progression-free survival, duration of response and time to next treatment)
- Quality of life measures.

Long-term outcomes will be captured by ongoing follow-up and through linkages with other cancer and death registries.

"The registry will be valuable to governments and many other organisations when planning health and support services, such as accommodation for patients and families, because it will provide an Australian 'map' of lymphoma diagnoses, treatment and outcomes nationally," said Professor Erica Wood of Monash University.

"And because we capture detailed information on diagnoses, including molecular results, we can paint a really detailed picture of lymphoma in Australia and better understand how diagnosis influences outcomes."

"It's difficult to do clinical trials in uncommon or rare cancers but, through the registry network, we can bring many sites together across the country and see the full picture of how many patients might need treatments for these different lymphomas, and what resources will be required to support them. We can also conduct faster and more efficient clinical trials using the established registry network and infrastructure," she said.

Professor Opat said: "This registry represents a wonderful collaboration from around Australia and New Zealand focused on improving care for patients with lymphoma. We thank all the patients for taking part, and the expert clinicians on the steering committee for their input."

Taking a national registry one step forward – establishing a Australian Cancer Data Commons

Given the increasing demand for real world evidence and its value, there is an opportunity to explore the feasibility of establishing an Australian Cancer Data Commons under the Cancer Futures Framework.

The Cancer Data Commons could use a cloud-based platform to collect and house comprehensive data, including access to care, trends in survival, variation in practice and genomic data. This would allow multiple stakeholders to store, share, access and apply AI to digital data across the cancer continuum.

NOA stakeholders agree that in order to make significant progress and optimise availability of new therapies and technologies, it is vital to develop a central source of data. This would bring together information about the impact of testing, clinical best practices and the effectiveness of therapies, and provide a research base that would invigorate development of genomic science and integration of AI.

EQUITABLE AND AFFORDABLE PATIENT ACCESS TO THE BEST CANCER MODALITIES

ACCESS TO CANCER TESTS AND TREATMENT LEADS TO GREATER POSSIBILITIES

The most that communities can do for cancer patients is to provide them with EQUITABLE access to the BEST therapies and technologies WHEN THEY NEED THEM, to increase their chances for survival. It may sound simple, but there are many complexities.

Richard Vines, Chief Executive Officer of Rare Cancers Australia, has often said that "treatment delayed is treatment denied for cancer patients". The aggressive nature of cancer means that patients are often left with only one option for a chance at life. This is particularly true for advanced and rare or less common cancers. NOA expects that this experience will increase as more sub-types of cancer emerge, giving rise to smaller sub-populations of cancers sharing similar characteristics.

In the context of Vision 20-30, NOA has defined equity in cancer care to mean that "All patients have access to the best therapies, technologies, care, medical networks and social supports when they need them, at an affordable price, regardless of geographic location or socioeconomic status".

The notion of timely, equitable and affordable access to medicines is the foundation of the National Medicines Policy (NMP) that was established 20 years ago.

The first stage of a review of the policy's terms of reference, conducted early in 2020, generated discussion among stakeholders that suggested these principles are equally important today.

The four central pillars are:

1. Timely access to the medicines that Australians need, at a cost individuals and the community can afford.
2. Medicines meeting appropriate standards of quality, safety and efficacy.
3. Quality use of medicines.
4. Maintaining a responsible and viable medicines industry.

However, the NMP only extends to medicines categorised as traditional "drugs" by the National Health Act 1953 – it currently doesn't capture many of the newer therapies such as CAR-T. The update of the policy to potentially broaden its scope and consider wider changes was put on hold due to the unforeseen impact of COVID-19.

For the purposes of the discussion in this chapter, we are considering equity of access as it extends to medicines, treatments, devices, technologies and tests. This is because cancer treatment is multi-modal, with all these being used in combination more frequently than not.

This also offers unique opportunities to consider the structure of approval pathways and the tools that lie within them to capture value, and value for money.

While there is consensus on the core value of equity of access, more needs to be done to ensure that this will be a reality for patients in the years ahead. Experience suggests that we risk falling short of this goal, and will face many challenges.

Ensuring that equity of access becomes a reality by 2030 is the ultimate opportunity to secure greater survivorship for Australian cancer patients. To understand how this can best be achieved over the next ten years, it is important to unpack what this means for patients and the evaluation frameworks that underpin our health system, in light of the phenomenal changes that have been presented in the proceeding chapters of this report.

Overview of the frameworks that underpin the health system

The Therapeutics Goods Administration (TGA) is the regulatory body in Australia. Its role is to ensure that therapeutic goods offered in Australia are of an acceptable standard in terms of effectiveness, safety and quality. The TGA developed two fast track approval pathways for the registration of new prescription medicines. This initiative was thought necessary to increase alignment with overseas regulators, which offered accelerated assessment processes.

The two pathways are:

1. Priority review; and
2. A provisional approval pathway.

The objective is to achieve earlier access to certain novel prescription medicines that address unmet clinical needs. To be eligible for the priority pathway, a cancer medicine must be a major advance compared to other medicines available for the defined group of patients. This shortens the approval time for registration to around eight months instead of around 11 months.

Under the provisional approval pathway, therapies may be "provisionally registered" up to two years sooner than under the standard framework. This gives manufacturers time to generate and collect evidence to support listing on the Australian Register of Therapeutic Goods, while the therapy is already available to patients.

The provisional pathway provides significant opportunity for emerging personalised treatments. Many of these treatments will have very promising results in early trials conducted in small patient populations. Given the rarity of cancer or the cancer sub-type, patients presenting with these cancers will have few if any treatment alternatives.

Unfortunately, the point of market entry or patient access in Australia is not at the point of registration. It is at the point of reimbursement, when the treatment is subsidised through the MBS, the PBS or in the case of medical devices, through private health insurance via the Prostheses List. Equity of access cannot be achieved through fast-tracked registration pathways alone.

Patient access to new medicines can't be fully expedited in systematic ways without analogous fast tracked, or more importantly, provisional reimbursement pathways. These would result in patients with advanced or rare and less common cancers having access to novel treatments two to four years earlier than under traditional pathways.

TABLE 5. CRITERIA FOR THE PROVISION REGULATORY APPROVAL FOR PRESCRIPTION MEDICINES[33]

Eligibility	Evidence required
It must be a new prescription medicine or a new indication for an existing medicine.	It must be a new prescription medicine or a new indication for an existing medicine.
It must provide a favourable comparison against existing therapeutic goods.	Ensure all applications for approval include a plan on how the drug company will conduct more research on the medicine's safety and efficacy.
It must provide a major therapeutic advance.	Monitor the medicine more closely so that any issues are identified.
The sponsor (manufacturer) must provide evidence of a plan to submit comprehensive clinical data.	Limit, suspend or cancel the approval if there are major patient safety concerns.

[33] https://www.tga.gov.au/publication/australian-regulatory-guidelines-prescription-medicines-argpm

The frameworks that underpin the reimbursement system are the most time and labour intensive pathways for a new medicine or treatment to navigate. The Medical Services Advisory Committee (MSAC) and the PBAC make funding representations for treatments and services to the health minister.

Medicines recommended and approved by the PBAC are funded and listed on the PBS. Services and tests are generally provided via the MBS. These include GP visits and subsidised specialists' visits when referred by a GP, procedures and diagnostic tests, and companion diagnostics. Services and tests are evaluated by the MSAC, however, the remit of the committee has broadened. The MSAC is increasingly becoming the "go-to committee" for anything not defined as a medicine within the legislation, such as CAR-T therapy (considered a class 4 biologic).

Technologies and treatments – the role of Health Technology Assessment

The task of maintaining a high quality, innovative health system established on the principles of equity, timely access and affordability is extremely challenging when the budget is finite. The rising cost of new cancer treatments, combined modalities, and companion tests – and competition for health dollars – creates tension within the system.

Health technology assessment (HTA) is the conventional value-based decision-making methodology that underpins access to therapies and technologies. Used around the world, HTA helps in the allocation of resources and addresses the difficulty in servicing the health needs of society by informing which technologies offer the best value for money.

Australia was a world leader when it first implemented HTA through the PBS in the early 1990s.

Fundamentally, HTA considers the value of a medicine or technology as a function of its clinical benefit, minus the cost compared to an existing treatment. It also includes the willingness to pay for the benefit (budget impact or cost to the Commonwealth), and how to manage the "uncertainty."

TABLE 6. PRECISION THERAPIES AND CHALLENGES IN HTA BASED DECISION MAKING

Challenges in measuring value	Examples of additional value measures
Lack of robust clinical evidence – surrogate outcome measures.	• Real world evidence and innovative approaches to trial design. • Patient reported outcomes and discrete choice experiments. • Formalising patient advisory committees and their input. • Evidence obtained from Cancer Data Commons. • Clinical trials in small patient populations – where there will never be sufficient patients.
Lack of suitable comparators – technologies are too different or there are combined modalities or pan tumours.	Cost-effectiveness assessment evaluation over time or post market entry.
Meaningful cost-effectiveness evaluation is not feasible.	Societal impact measures included in cost effectiveness considerations economic impact.

Conventional HTA approaches were originally designed to inform decisions about reimbursement of interventions – which were small molecules, for population-based conditions or diseases such as hypertension. The system was designed to evaluate evidence from trials that recruited hundreds or thousands of patients. Patients received a tested intervention compared to a standard of care, typically within a phase III randomised controlled clinical trial. If the medicine most likely to be displaced by the proposed treatment was not included in the primary clinical study, then an indirect comparison could be made with relative statistical reliability across similar trial populations that shared a common arm. These statistical analyses translated into informative cost effectiveness evaluations, with an element of uncertainty.

The rise of precision treatment for cancer substantially increases the level of uncertainty of decision making using conventional methodologies. Simply too much has changed in the nature of emerging treatments and the types and sizes of disease populations, since these methods were first introduced.

The main cause for uncertainty is the lack of robust evidence that HTA demands. This will never be available in a clinical trial setting, due to the smaller sample sizes of sometimes < 20 patients with rare cancers or emerging cancer sub-types. The clinical trials conducted in pan cancers, where one biomarker exists in multiple cancers may help. But then there is the added complexity of measuring value across multiple diseases with no suitable comparator therapies to reliably measure incremental benefit.

Adapted HTA methodologies will need to consider different levels of evidence as well as novel trial designs such as basket trials or umbrella trials that consider multiple targeted therapies across multiple cancers. Globally, an increasing number of precision therapies are going to market with phase II data based on promising evidence. In these scenarios, there is a greater reliance on real world evidence to support ongoing evaluation when more data is available. This approach has already been adopted in the MSAC's recommendation to the health minister for CAR-T therapy funding. This method could be explicitly formalised within reimbursement guidelines.

Adaption of HTA approaches for emerging scenarios, pan tumours, combined modalities, larger genomic panel tests and integration of AI will be needed. Evaluating all the relevant pathways, populations and comparators could be infeasible, and will likely require a greater reliance on real world evidence, patient input and clinical expert opinion.

The changes in precision medicines and other technologies require an evolution of Australia's current approach to evidence and cost, and a change to the PBAC's current legislative framework that mandates cost effectiveness.

HTA assessment could formally include broader concepts such as patient preferences, or the social/psychological aspects of living with cancer, the use of technology and the economic benefits associated with the delivery of more certain outcomes for fewer patients.

One of the challenges is that there are two different pathways that evaluate tests (MSAC) separately from precision therapies (PBAC). A single committee may reduce risk of variable and disconnected assessment of the evidence where there is co-dependence or convergence of multiple modalities.

Whatever the solution, there is a need to evolve the HTA methodology or its place in decision making. **There is no doubt that evidence assessments should still support decisions about value for money when it comes to new therapies or technologies**. But consideration of how to realistically conduct these assessments in a meaningful and informative way is needed. There are varying views on what constitutes sufficient evidence to demonstrate value. Measurements of cost-effectiveness may require ongoing or later assessment using different types of evidence than traditionally considered at the point of market entry. Under an Australian Cancer Futures Framework, a more pragmatic and flexible approach to cost-effectiveness can be considered.

Many of these precision treatments and technologies are expected to deliver "more reliable" outcomes, and prevent treatment being given to patients who won't derive a clinical benefit. Outcomes could be measured more reliably as return on investment, as more people become "well" and begin contributing once more to society.

Closing the gap on equitable and fast patient access

NOA recommends a deep dive into HTA value measures, their reliability and the evolution of guidelines or evaluation frameworks. This would inform recommendations around precision cancer treatment, not limited to a single therapy or a companion test but including combined therapies, combined modalities and pan tumour treatments.

A thoughtful deep dive would also consider use of promising therapies in multiple cancers when clinical guidance suggests it may save lives. This could be part of a provisional approval mechanism while evidence is being generated to support funding and cost effectiveness over the long term.

The recent overlap of the PBAC and MSAC remit and the differences between the committees calls for consideration of whether harmonisation would increase efficiency, equity, accountability and reproducibility of funding recommendations.

Access to the best treatments – rural and remote patients

There is a clear need to establish systems to serve rural and remote communities to ensure patients can access new therapies and technologies. There is a clear opportunity to leverage the successful roll out of telehealth and eHealth during the COVID-19 pandemic to these underserviced areas. One of the greatest opportunities is to promote the ease of access to clinical trials for cancer patients who live outside of metropolitan areas.

Smaller treatment centres often miss out on participating in clinical trials either because of distance or lower patient numbers to attract clinical trial sponsors.

The Australasian Tele-Trial Model developed by the Clinical Oncology Society of Australia (COSA) has been successfully implemented in NSW, Victoria and Queensland. It has widespread support from state governments, health institutions and sponsors. This model could be adopted more broadly in rural and remote areas of Australia.

A Cancer Futures Framework proposes to prioritise the use of tele-trials and telehealth in solving the problem of equity and improved outcomes in rural and regional areas.

A Cancer Futures Framework proposes to prioritise the use of tele-trials and telehealth in solving the problem of equity and improved outcomes in rural and regional areas.

FUNDING EMERGING THERAPIES AND TECHNOLOGIES

Spending on health

As taxpayers, Australian cancer patients expect to have access to affordable care and the best treatments available when they need them. This expectation is grounded in Medicare. Under Medicare, the Commonwealth has been providing free or subsidised health services and medicines to the population since the 1980s.

At the state level, healthcare is separated into public and private sectors. Public hospitals are owned and managed by state and territory governments providing free treatment and accommodation. Private hospitals receive subsidies via health insurance taken out by the individual. Around half of the Australian population has private health insurance[34] with varying levels of financial rebates depending on the type of cover and the annual premium. Prescription treatments are rarely covered by private health insurance. Most providers have an ancillary fund that provides a small nominal amount for medicines.

In 2018-19, expenditure on medication through the PBS was $11.7 billion (excluding rebates). The total benefits paid for tests and services on the MBS was $24.4 billion[35]. Under the National Blood Agreement (NBA) between the federal government and the states and territories, 63% of funding is provided by the Commonwealth and the remaining 37% is provided by the state and territory governments. The funding of the national blood supply and the operations of the NBA was $1.2 billion dollars in 2018-19[36]. In addition, vaccines funded through the Australian Immunisation Register accounted for $9.5 million in 2018-2019.

The health budget represents approximately 16% of total government expenditure. At a federal level, the PBS and MBS are the largest funding pools for therapies and tests. These two account for approximately 9% and 20% respectively of yearly health expenditure . From a budget perspective, the PBAC and the MSAC's jobs are to manage risks and financial impact on the Commonwealth.

The federal government almost solely funds prescription medicines minus the patient co-payment ($40.40 for individuals or $6.50 for concession card holders) through the PBS. Manufacturers often provide compassionate supply for particular patients prior to commercialisation for a defined period. These arrangements may provide wholly-funded therapies but can require significant out-of-pocket costs from patients.

These are some of the gaps in the system that may provide opportunities for change:

- Siloed funding buckets – exploring whether the model will serve the cancer community into the future.
- Universal health – the governments are the primary funders of therapies and services. Should this be a shared obligation? Consideration of alternative funding models.
- Inability to measure "investment" as financial, social and economic returns associated with a healthy life compared to an expense within the health budget.

[34] https://www.health.gov.au/sites/default/files/documents/2019/10/department-of-health-annual-report-2018-19_0.pdf
[35] https://www.servicesaustralia.gov.au/sites/default/files/annual-report-191019-v2.pdf
[36] https://www.blood.gov.au/pubs/1819report/sites/default/files/publication/nba-annual-report-2018-19.pdf

The discrete buckets of government funding

There are discrete sources of funds for health items that sit within different silos in the MBS, PBS, Australian Immunisation Schedule (AIS), NBA and the PL. While the separation into medicine, device and test has served the system in the past, it may no longer work into the future, given the degree of overlap between definitions of a therapy, blood product and vaccine. The example of evaluation and recommendations for CAR-T therapy through MSAC highlight that the system is moving beyond its Commonwealth funding model and evaluation by the PBAC for everything considered "medicinal". CAR-T, considered a class 4 biologic and living therapy, was evaluated via the MSAC and is funded through state and federal agreements.

Convergence of therapies with companion tests or diagnostic sequencing panels, radiation oncology and AI also challenges the siloed funding and evaluation model. A therapy may be funded through one stream and its test through another – and it becomes more complex from there.

Alternative funding models

The impact of COVID-19 and the competition for allocation of resources may call for novel funding approaches so that the needs of cancer patients can be met, and Australia continues to be on par with other developed countries in providing the latest technologies and treatments.

- Consideration of roles for manufacturers, private health insurers, government and individuals (through establishing healthy savings accounts akin to superannuation for example) to share funding responsibilities.
- Value-based payment models.
- Novel risk share arrangements, or coverage at risk, pay for performance or divided payment models as adopted in the US for gene therapies.
- A separate fund for cancer therapies and technologies akin to the UK.

Investment in health in cancer – not an expense

Spending on health is considered an expense and not an investment, which is very problematic. Greg O'Toole from Astra Zeneca, a former employee of the health department, said in the Vision 20-30 series, "The PBAC process exhaustively quantifies the benefit of a drug in terms of health resource cost, which can have a dollar value put to it. But in accounting terms, the budget only accounts for what was spent on the drug. There's no recognition that a future benefit has been purchased."

A formal consideration of social and economic impact and the potential for return on investment in the creation of jobs and the return to health and work of patients would provide a holistic view of the value of spending. However, it is not so easy to bring this type of evaluation into the mix.

"Consideration of societal benefits sit outside the framework of the health portfolio," explained Mr O'Toole. The social and economic impact would need to be considered by a whole of government discussion including the health, finance and social service ministers.

There is an opportunity to consider this through the Cancer Futures Framework. It will become increasingly important to demonstrate the holistic value of financial outlays in an era of precision therapy, genomics, AI and big data, and in light of a finite health budget.

Funding: a NOA perspective

An Australian Cancer Futures Framework proposes to bring stakeholders together to explore:

- Novel funding models;
- The value of measuring social impact and return on investment studies;
- The integration of these into decision making; and
- Supporting the Department of Health and other stakeholders in considering streamlined funding models.

The rise in high-cost therapies and technologies need not require additional healthcare expenditure, but considered and more efficient funding solutions.

Patient Journey

He was bright, cheerful, and imaginative, and brought no end of joy and smiles to those lucky enough to have him in their lives, simply enjoying their company.

NED

While only young, Ned was brimming with life, affection and love, even despite the suffering he endured. That was one of the most the beautiful things about him – his attitude never soured; his resilience never waned. He was bright, cheerful, and imaginative, and brought no end of joy and smiles to those lucky enough to have him in their lives, simply enjoying their company.

His family was his world; he adored his siblings and was the glue between them. He made friends easily and loved being around people. To his older sister, he was a confidante, chatting in the dark after bedtime, sharing stories and ideas under the cover of night. She was the one who looked out for Ned, always trying to include him by bringing home extra party bags and cake when he so often missed out. His younger sister, playmate and his most devoted fan, would guide him through her imaginative games. But he was most gentle in his role as a big brother to his baby brother – he would snuggle with him on the hospital bed during treatments, and adored entertaining him, showing him toys, and watching him as he started interacting with the world.

Though he was mature in many ways, to his parents, he was their 'little man'. With mum, he looked for comfort and consolation when he was upset or worried; someone to ask his questions ranging from what the day's treatment schedule held, or how things in life worked, to the more philosophical questions, like what heaven looked like. She was the one who'd cuddle, comfort and reassure him, even in the middle of the night. His father was his creative outlet, his playmate and teacher. He was easily found in the loungeroom building epic LEGO constructions, battling superhero action figures against their dreaded archenemies, with voice-overs for extra entertainment, or outside, giving Ned wheelbarrow rides and helping him dig holes.

Ned also had a quieter side – he loved reading for hours, constructing puzzles, and especially loved animals of all sorts, particularly his pet guinea pig, Tommy, whom he hated leaving when he went on prolonged trips away from home for treatment. He even had plans to name two new family members, a pair of chickens, Egg Machine and Tilly.

Ned was creative, playful, gentle, sensitive and caring. Even in the end, when the last relapse was diagnosed and he could see his Mum's eyes brimming with tears, he placed his little hand on hers, patted it, and let her know it would be okay.

2020 PATIENT JOURNEY

Ned

2014 DISCOVERY

- Just after his 2nd birthday, Ned stopped walking.
- Ned's mother, Emily, a GP, took Ned to various specialists and clinicians to see what was wrong as no one could figure it out.

25 JULY 2014 DIAGNOSED

- Ned's mother Emily had referred Ned to a pediatrician who immediately ordered a blood count.
- Ned was diagnosed with Acute Lymphoblastic Leukemia.
- Ned became febrile that day.

2014 INFORMATION

- Ned's mother and father both worked full time while Ned's mother was pregnant.
- Ned's mother and father would be forced to go on to Centrelink to care for Ned while he received treatment.

2014 TREATMENT – CHEMOTHERAPY

- Commenced treatment immediately, chemotherapy and steroids.
- Subjected to brutally regular tests, blood prick analysis.
- Was not responding to treatment well and was reclassified as high risk leukemia.
- After 9 months, Ned went into remission.

2017 TREATMENT – TRANSPLANT

- Ned had relapsed and needed to be immediately sent to Melbourne from Tasmania for 10 months for a Bone Marrow Transplant.
- Ned and his family had to pack their things in one day and relocate to Melbourne.
- Ned required heavy doses of chemotherapy to wipe out his current bone marrow.
- Unfortunately the transplant did not work.

2017 TREATMENT – CLINICAL TRIALS

- Participated in various clinical trials in Melbourne.

2018 TREATMENT – CAR-T

- The only option for treatment was CAR-T, at that time only available in Seattle, USA.
- Ned and his family had to move to Seattle.
- Ned's T-cells mutated during this time, making it difficult to determine whether Ned would respond to the CAR-T therapy.
- Ned fortunately responded well to treatment and would be eligible for a second transplant back in Australia.

2018 TREATMENT – SECOND TRANSPLANT

- Ned and his family returned to Australia for a second transplant.
- Ned responded well to the transplant and was cleared of leukemia.

2018 FUNDRAISING

- CAR-T therapy would cost $600k.
- MTOP would normally cover the cost of treatment, but Ned and his family could not get approval in time.
- Ned's family were forced to crowdfund all expenses to pay for his treatment, trip to and from Seattle and living expenses.

2019

- Unfortunately Ned's disease returned and he entered palliative care.
- On March 29th 2019 Ned passed away shortly before his 7th birthday.

2030 PATIENT JOURNEY

DISCOVERY

- Developments in AI and diagnostic technology flag the issues in children experiencing challenges walking and sleeping and generate an alert for further investigation.

DIAGNOSED

- Due to early detection and diagnosis of childhood cancers such as acute lymphoblastic leukaemia, there is a promising survival rate.

SCREENING

- All children are eligible for whole genomic sequencing, fully subsidised under a shared model as the optimal standard of care.
- This would flag children's cancer mutations (eg CDs 19, 22 and 24) and allow clinicians to plan accordingly when determining treatment.
- Data collected can be shared with national registries, contributing to improving treatment and diagnostics for children.

INFORMATION

- Families are assigned a Specialist Cancer Navigator to help them navigate social supports covering areas such as financial, legal and support needs for children and their carers.
- GPs are part of the shared care for managing children and their treatment side-effects.

TREATMENT
MULTI DISCIPLINARY TEAM

- Families of paediatric patients are consulted by a multi-disciplinary team, including a palliative care unit to assist them in managing symptoms.
- The team determines using genomics who the appropriate candidates are for CAR-T, which is available locally or with concierge assistance and subsidised under shared models.

TREATMENT
TARGETED THERAPY

- Patients eligible for targeted therapy such as CAR-T based on the results of previous genomic sequencing, know exactly what, if any, side-effects may be experienced and reduce possible damage to other organs that may occur with preparation chemotherapy.
- Overall health of childhood cancer survivors is considered in treatment choices so that damage to fertility, cardiac health and cognition is minimised.

TREATMENT
CAR-T OR SIMILAR TARGETED THERAPY

- Children undergo CAR-T therapy in an inclusive, safe and accessible facility close to home.
- Treatment continues to be subsidised under shared models, minimising the financial strain on Australian families.
- During this time, the Specialist Cancer Navigator collects relevant experiential data and outcomes of interest to families which improve standard of care.

TREATMENT
MAINTENANCE

- Following successful CAR-T therapy, children receive subsequent treatment which amplifies the effects of the CAR-T cells and ensures sustained efficacy. Support via the Specialist Cancer Navigators mean families also get holistic support including sibling's needs, and financial support for parents/carers.

SURVIVORSHIP CARE

Children move into specialised survivorship programmes with ongoing support and care provided to families. As children grow older, they are routinely monitored for minimal residual disease via non-invasive sequencing and scanning which tests for new mutations, adding further data to childhood cancer projects, and increasing survival rates. Fertility and long term side effects are minimally impacted due to the nature of personalised treatment in 2030.

5 THE WAY FORWARD

NOW IS THE IDEAL TIME TO BUILD AN AUSTRALIAN CANCER FUTURES FRAMEWORK

The priority areas outlined within this report focus on seizing the advances in technology to deliver better and more uniform survivorship across all cancer subtypes, irrespective of rarity. The framework seeks to ensure that the health infrastructure and evaluation pathways evolve and are equipped to deliver these advances to patients in a fiscally responsible way.

Cancer is an insidious group of complex diseases that have had tragic consequences for the patients we profiled in this report (Ned, Ash, Madonna and Scott) and so many more. For the first time in human history, we are embarking on the prospect of tailored treatment leading to potential remission and possibly a future cure.

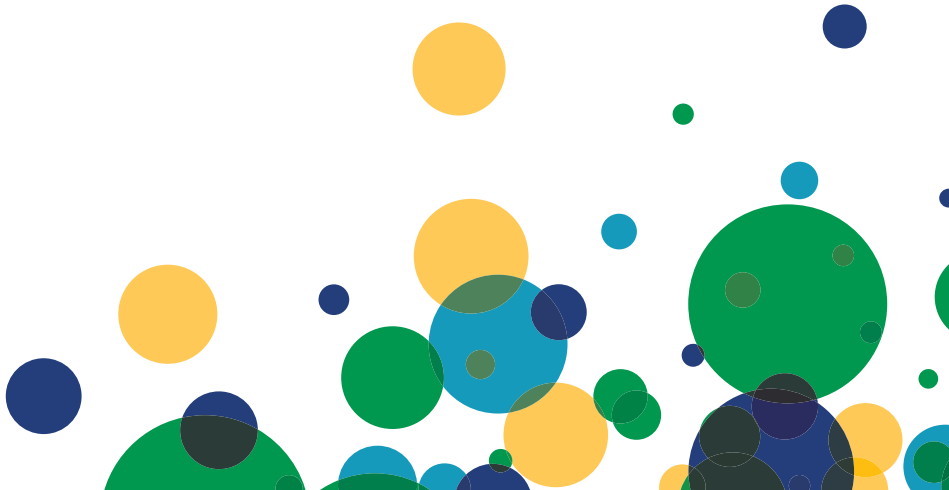
Now is the time to plan, to do the work, to lay the foundation, so we have the best therapies and technologies. We can deliver them to patients equally and our systems are ready and equipped to measure their value.

While there are also opportunities to consider prevention, risk and best care models within the cancer continuum, NOA is focused on a framework that builds a raft of evidence to support policy change, collaboration, and foundations for action for patients with cancer, today and tomorrow. We ultimately seek to give back life to cancer patients. This will inevitably return functioning, well balanced, healthy, and productive people from the health system, to their families, into the workforce and society.

NOA need not be the executors of the final steps of implementation under the 6 pillars of the framework. We will create roadmaps that highlight the potential gaps, risks, benefits, costs and economic returns.

The next ten years can focus on making Australia an attractive market for global investment for research and commercialisation within a thriving local industry. There are opportunities for growth and jobs as well as better outcomes and healthy lives for cancer patients.

Australia can be at the forefront of cancer treatment and outcomes in 2030. We invite you to support or join us to ensure that the work is done now to make this a reality.



> “The time to repair the roof is when the sun is shining.”
>
> JOHN F. KENNEDY
> FORMER U.S. PRESIDENT

APPENDIX

References

Table 3. The current state of AI for cancer care in 2020

[a] Grady (2019). A.I. Took a Test to Detect Lung Cancer. It Got an A. *New York Times*. https://www.nytimes.com/2019/05/20/health/cancer-artificial-intelligence-ct-scans.html

[b] Hale (2019). Atomwise inks 2 joint ventures in AI-based cancer drug development. *FierceBiotech.* https://www.fiercebiotech.com/medtech/atomwise-inks-two-joint-ventures-ai-based-cancer-drug-development

[c] Fortune Editors (2019). How Adding A.I. to Gene Sequencing Can Help Detect Cancer Early. Fortune. https://fortune.com/2019/11/07/ai-genomic-sequencing-detecting-cancer/

[d] Kent (2019). Artificial Intelligence Recognizes Cancer Cells in Pathology Slides. *Health IT Analytics*. https://healthitanalytics.com/news/artificial-intelligence-recognizes-cancer-cells-in-pathology-slides

[e] Sokol (2019). AI Brings Personalized Cancer Treatment to Cleveland Clinic. *Health IT Analytics*. https://healthitanalytics.com/news/ai-brings-personalized-cancer-treatment-to-cleveland-clinic

[f] Poudel et al. (2019). Heterocellular gene signatures reveal luminal-A breast cancer heterogeneity and differential therapeutic responses. npj Breast Cancer, 5(1). doi: 10.1038/s41523-019-0116-8

[g] Markopoulos (2010). Minimizing early relapse and maximizing treatment outcomes in hormone-sensitive postmenopausal breast cancer: efficacy review of AI trials. Cancer and Metastasis Reviews, 29(4), 581-594. doi: 10.1007/s10555-010-9248-x

[h] BiotechDispatch (2019). New study shows power of AI in matching patients to clinical trials. *BiotechDispatch*. https://biotechdispatch.com.au/news/new-study-shows-power-of-ai-in-matching-patients-to-clinical-trials

[i] Matheson (2018). Artificial intelligence model "learns" from patient data to make cancer treatment less toxic. *MIT News*. http://news.mit.edu/2018/artificial-intelligence-model-learns-patient-data-cancer-treatment-less-toxic-0810

[j] Devlin (2019). Hospital develops AI to identify patients likely to skip appointments. *The Guardian*. https://www.theguardian.com/society/2019/apr/12/hospital-develops-ai-to-identify-patients-likely-to-skip-appointments

[k] Morvan (2019). A dose of AI for pharma logistics optimization. *Pharma Manufacturing*. https://www.pharmamanufacturing.com/articles/2019/a-dose-of-ai-for-pharma-logistics-optimization/

[l] Hale (2019). ASCO: Concerto HealthAI uses real-world data to fill the research gap among patients excluded from NSCLC trials. *FierceBiotech*. https://www.fiercebiotech.com/medtech/asco-concerto-healthai-uses-real-world-data-to-fill-research-gap-among-autoimmune-patients

[m] Bhattacharya et al. (2019). AI Meets Exascale Computing: Advancing Cancer Research With Large-Scale High Performance Computing. *Frontiers in Oncology*, 9(984). doi: 10.3389/fonc.2019.00984

[n] Ives (2019). Research shows promising impact of systematic PROM collection in routine breast cancer care. *News Medical Life Sciences*. https://www.news-medical.net/news/20191021/Research-shows-promising-impact-of-systematic-PROM-collection-in-routine-breast-cancer-care.aspx

Terms

Acute lymphoblastic leukemia
A type of cancer of the blood and bone marrow that affects white blood cells.

Adjuvant therapies
Additional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biological therapy.

Agents
A substance that is made from a living organism or its products and is used in the prevention, diagnosis, or treatment of cancer and other diseases.

Agonists
A drug or substance that binds to a receptor inside a cell or on its surface and causes the same action as the substance that normally binds to the receptor.

Algorithms
A process or set of rules to be followed in calculations or other problem-solving operations, especially by a computer.

Allogeneic
Allogeneic stem cell transplantation involves transferring the stem cells from a healthy person (the donor; related or unrelated) to the patient's body after high-intensity chemotherapy or radiation.

Antigens
A toxin or other foreign substance which induces an immune response in the body, especially the production of antibodies.

Apheresis
A method for the collection of donor blood components or for the removal of parts of the blood that might contain disease-provoking elements.

Artificial Intelligence
The development of computer systems able to perform tasks normally requiring human intelligence, such as visual perception, speech recognition, decision-making, and translation between languages.

Autologous
An autologous stem cell transplant means that the patient is their own stem cell donor. These cells are collected in advance (while they are in remission) and returned to the patient at a later stage.

B-cells
A white blood cell not processed by the thymus gland, and responsible for producing antibodies.

Biological driver
Gene alterations which influence cancer development, occurring in oncogenes, tumor suppressors, and dual role genes.

Biomarker
A naturally occurring molecule, gene, or characteristic by which a particular pathological or physiological process, disease, etc. can be identified.

Biomarker
May be produced by the cancer tissue itself or by other cells in the body in response to cancer.

Brachytherapy
The treatment of cancer, especially prostate cancer, by the insertion of radioactive implants directly into the tissue.

Cancer
A disease caused by an uncontrolled division of abnormal cells in a part of the body.

Carbon atoms
The smallest component of an element having the chemical properties of the element.

CD19
A transmembrane protein that in humans is encoded by the gene CD19.

Cellular therapy
A therapy in which viable cells are injected, grafted or implanted into a patient in order to effectuate a medicinal effect.

Checkpoint inhibitors
Treatments that work by blocking checkpoint proteins from binding with their partner protein.

Checkpoint proteins
Any of various proteins that control progression of the cell cycle, especially those that limit replication of cells containing damaged DNA.

Chemotherapy
The use of drugs to destroy cancer cells.

Chimeric antigen receptor
A special receptor created in the laboratory that is designed to bind to certain proteins on cancer cells.

Chromosome
Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes.

Clinical pathway
Also known as care pathway, integrated care pathway, critical pathway, or care map, is one of the main tools used to manage the quality in healthcare concerning the standardisation of care processes.

Clinical trials
Research studies that involve people.

Comorbidities
The presence of one or more additional conditions often co-occurring with a primary condition. Comorbidity describes the effect of all other conditions an individual patient might have other than the primary condition of interest, and can be physiological or psychological.

Comprehensive genomic profiling
A laboratory method that is used to learn about all the genes in a person or in a specific cell type, and the way those genes interact with each other and with the environment.

Conventional
Based on or in accordance with what is generally done or believed.

Custodianship
The caretaking responsibility for biospecimens that extends from collection through research use.

Cytotoxic
Toxic to living cells.

Dendritic cells
Specialised cells that are part of the immune system.

DNA
Deoxyribonucleic acid, a self-replicating material which is present in nearly all living organisms as the main constituent of chromosomes. It is the carrier of genetic information.

Dose
The amount of medicine taken.

Durability of effectiveness
A measure of clinical efficacy over a set period of time.

Early phase study
A study in which researchers test whether a new treatment is safe, what its side effects are, and the best dose of the new treatment.

Emerging therapy
New and developing treatment options, often targeted and specific, e.g. immunotherapy.

Enzyme
Proteins that aid digestion and are essential for the normal functioning and performance of the body.

Excise
Cut out surgically.

Exome sequencing
Also known as whole exome sequencing, is a genomic technique for sequencing all of the protein-coding regions of genes in a genome.

Exosomes
Small extracellular vesicles with a significant role in most processes associated with cancer.

Fusion
The process or result of joining two or more things together to form a single entity.

Gene
The microscopic units that determine how the body's cells grow and behave. Genes are found in every cell of the body and are inherited from both parents.

Genome
The complete set of genes or genetic material present in a cell or organism.

Genomic sequencing
Is figuring out the order of DNA nucleotides, or bases, in a genome.

Genomics
An interdisciplinary field of biology focusing on the structure, function, evolution, mapping, and editing of genomes. A genome is an organism's complete set of DNA, including all of its genes.

Heterogeneous
Diverse in character or content.

Heterozygosity
Refers to having inherited different forms of a particular gene from each parent.

High-throughput method
The automation of experiments such that large scale repetition becomes feasible.

Hormone therapy
The aim of hormone therapy is the slow or stop the growth of hormone receptor positive cells.

Hot spot
A place of significant activity, danger, or violence.

Hybrid
Hybrid tumors are very rare tumor entities which are composed of two different tumor types, each of which conforms to an exactly defined tumor category.

Imaging
The process of making a visual representation of something by scanning it with a detector or electromagnetic beam.

Imaging technology
Imaging technology is a way to let doctors see what's going on inside your body.

Immune response
The reaction of the cells and fluids of the body to the presence of a substance which is not recognized as a constituent of the body itself.

Immune system
The immune system protects the body against illness and infection that bacteria, viruses, fungi or parasites can cause.

Immuno-oncology
Immuno-oncology is the study and development of treatments that take advantage of the body's immune system to fight cancer.

Immunotherapy
Immunotherapy is a type of cancer treatment that helps your immune system fight cancer.

Incidence
The occurrence, rate, or frequency of a disease, crime, or other undesirable thing.

Incidental findings
An incidental finding might be a nodule or tumor.

Inoperable
Not able to be suitably operated on.

Intensive care
A department of a hospital in which patients who are dangerously ill are kept under constant observation.

Interferon-α/β receptor 1 (IFNAR1)
A chemical structure that receives signalling proteins generated by cells in response to viruses.

Intervention
A treatment, procedure, or other action taken to prevent or treat disease, or improve health in other ways.

Invasive
The cancer cells have broken out of the lobule where they began and have the potential to spread to the lymph nodes and other areas of the body.

Investigational targeted agents
Investigational targeted agents target a type of cancer treatment that targets proteins that control how cancer cells grow, divide, and spread.

Laparoscopic
A procedure that uses a laparoscope, inserted through the abdominal wall, to examine the inside of the abdomen.

Late-stage
A term used to describe cancer that is far along in its growth, and has spread to the lymph nodes or other places in the body.

Lymphoma
Types of cancer that begin in the lymphatic system (the various lymph glands around the body) when abnormal white blood cells grow. Lymphomas are the sixth most common form of cancer overall (excluding non-melanoma skin cancer).

Machine learning
The study of computer algorithms that improve automatically through experience. It is seen as a subset of artificial intelligence.

Markers
Tumor markers are substances found in higher-than-normal levels in the blood, urine, or tissues of some people with cancer. These substances, which are also called biomarkers, can be made by the tumor.

Mechanisms
A term used to describe how a drug or other substance produces an effect in the body.

Medicine
A drug or other preparation for the treatment or prevention of disease.

Melanoma
A form of cancer that begins in melanocytes (cells that make the pigment melanin). It may begin in a mole (skin melanoma), but can also begin in other pigmented tissues, such as in the eye or in the intestines.

Metabolic
Relating to anabolism (the buildup of substances) and catabolism (the breakdown of substances) within the body.

Metastatic
Cancer that has spread to a different body part from where it started.

Microenvironment
The cells, molecules, and structures (such as blood vessels) that surround and support other cells and tissues.

Microsatellite instability
A unique molecular alteration and hyper-mutable phenotype, which is the result of a defective DNA mismatch repair (MMR).

Modality
A method of treatment for example, surgery and chemotherapy are treatment modalities.

Modified
Transform (a structure) from its original anatomical form during development or evolution.

Molecular imaging
Broadly described as imaging techniques used to detect molecular signature at the cellular and gene expression levels.

Molecule
The smallest particle of a substance that has all of the physical and chemical properties of that substance. Molecules are made up of one or more atoms.

Morphology
Refers to the histological classification of the cancer tissue and a description of the course of development that a tumour is likely to take: benign or malignant.

Next generation sequencing
A DNA sequencing technology which has revolutionised genomic research. Using NGS an entire human genome can be sequenced within a single day.

Nuclear medicine
A medical speciality that involves giving a patient a small amount of radioactive medication, called a radiopharmaceutical to look at and to treat diseases.

Oncolytic virus
A virus that preferentially infects and kills cancer cells.

Outcomes
Are measurable changes in health, function or quality of life that result from care.

Palliative treatments
Designed to relieve symptoms, and improve quality of life. It can be used at any stage of an illness if there are troubling symptoms.

Panel test
A genomic test that looks at a curated set of genes known to be associated with the development of a condition or a collection of clinical symptoms under investigation.

Phenotype
Refers to the observable physical properties of an organism; these include the organism's appearance, development, and behavior.

Personalised medicine
Uses specific information about a person's tumor to help make a diagnosis, plan treatment, find out how well treatment is working, or make a prognosis.

Pharmacovigilance
The practice of monitoring the effects of medical drugs after they have been licensed for use, especially in order to identify and evaluate previously unreported adverse reactions.

Photon beam
Consists of numerous photons which pass from the target, through beam modifying devices, and into the patient or phantom.

Pipelines
The drugs or compounds that a company has under development or is testing.

Preventative
To promote health and well-being and prevent disease, disability and death.

Prognosis
The likely outcome or course of a disease; the chance of recovery or recurrence.

Prognostic
Relating to or serving to predict the likely course of a medical condition.

Precision surgery
Surgery to target tumor cells in precision image-guided surgery.

Proteins
Proteins have specific functions and act as messengers for the cell. Each gene must have the correct instructions for making its protein.

Proteomic
Proteomics is a fast and powerful discipline aimed at the study of the whole proteome or the sum of all proteins from an organism, tissue, cell or biofluid.

Proton beam
A type of particle therapy that uses a beam of protons to irradiate diseased tissue, most often to treat cancer.

Radiation therapy
A cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumors; also called radio therapy.

Radioisotopes
An unstable form of a chemical element that releases radiation as it breaks down and becomes more stable. In medicine, they are used in imaging tests and in treatment.

Radiomics
Radiomics is a method that extracts a large number of features from radiographic medical images using data-characterisation algorithms.

Reconstructive
Surgery that is done to reshape or rebuild (reconstruct) a part of the body changed by previous surgery.

Registration
Prescription and over-the-counter medicines which meet Australian standards of quality, safety and efficacy receive registration with the Therapeutic Goods Administration.

Regulatory agencies
Commonly set up to enforce standards and safety, or to oversee use of public goods and regulate commerce.

Re-infused
To return (as blood or lymphocytes) to the body by infusion after having been previously withdrawn.

Relapse
The return of a disease or the signs and symptoms of a disease after a period of improvement.

Remission
All signs and symptoms of cancer have disappeared, although cancer still may be in the body.

Repository
A place that holds data, makes data available to use, and organises data in a logical manner.

Residule
Cancer cells that remain after attempts to remove the cancer have been made.

Response
An indicator of therapeutic efficacy.

RNA
Ribonucleic acid is a polymeric molecule essential in various biological roles in coding, decoding, regulation and expression of genes.

Sanger method
Also known as the “chain termination method”, is a method for determining the nucleotide sequence of DNA.

Stakeholders
An individual, group or organization who is impacted by the outcome of a project.

Stem cell transplantation
Also known as bone marrow transplant. This treatment may be recommended for people with blood cancers such as leukaemia, myeloma,or lymphoma.

Subpopulation
A group of patients with a common diagnosis or other feature.

Surrogate test
In clinical trials, an indicator or sign used in place of another to tell if a treatment works. Surrogate endpoints include a shrinking tumor or lower biomarker levels.

Surveillance
A treatment plan that involves closely watching a patient’s condition but not giving any treatment unless there are changes in test results that show the condition is getting worse.

T cells
So called because they are predominantly produced in the thymus; white blood cells that play a central role in the immune response.

Targeted therapy
A therapy which zeros in on some of the changes that make cancer cells different from normal cells and leave normal, healthy cells alone.

Tele trials
An innovative approach to enhancing and improving clinical trial infrastructure to extend clinical trials into rural, regional and remote areas.

Therapeutic radionuclides
A type of radiation therapy in which a radionuclide (a radioactive chemical) is linked to a cell-targeting molecule, such as a monoclonal antibody, and injected into the body.

Therapy
A therapy or medical treatment is the attempted remediation of a health problem, usually following a diagnosis

Tissue-engineered products
Derived from living cells or tissues, with the final product containing viable or non-viable cells.

Toll-like receptors
A class of proteins that play a key role in the innate immune system.

Tumour agnostic
A drug treatment that is used to treat any kind of cancer, regardless of where in the body it started or the type of tissue from which it developed.

Tumour mutation burden (TMB)
The total number of mutations (changes) found in the DNA of cancer cells; a predictive biomarker

Tumours
An abnormal mass of tissue that forms when cells grow and divide more than they should or do not die when they should.

Vaccine
A product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease.

Validity
Refers to how accurately a method measures what it is intended to measure.

Vector
Refers to an organism that transmits a disease, parasite, or genetic information from one species to another.

Viable
Capable or possible.

Glossary

A protein receptor that functions as an immune checkpoint and downregulates immune responses (CTLA-4)

Activated B Cell like (ABC)

Acute lymphoblastic leukaemia (ALL)

Artificial Intelligence (AI)

Australian alliance for AI in healthcare (AAAAiH)

Australian Clinical Trials Alliance (ACTA)

Bacillus calmette–guérin (BCG)

Based on BCL6 fusions and NOTCH2 mutations (BN2)

Based on EZH2 mutations and BCL2 Translocations (EZB)

Based on NOTCH1 Mutation (N1)

Based on the co-occurrence of MYD88L265P and CD79B mutations (MCD)

Breast Cancer Type 1 susceptibility protein (BRAC1)

Centres of excellence (CoEs)

Chimeric antigen receptor (CAR)

Chronic lymphocytic leukaemia (CLL)

Circulating tumour DNA (ctDNA)

Clinical Oncology Society of Australia (COSA)

Cluster of differentiation 19 (CD19)

Comprehensive genomic profiling (CGP)

Deoxyribonucleic acid (DNA)

Diffuse large B-cell lymphoma (DLBCL)

General Practitioner (GP)

Germinal Center B Cell like subgroups (GCB)

Health technology assessment (HTA)

Immun-oncology (IO)

Interferon -α/β receptor 1 (IFNAR1)

Lymphoma and Related Diseases Registry (LaRDR)

Magnetic resonance imaging (MRI)

Medical Benefits Schedule (MBS)

Medical Services Advisory Committee (MSAC)

Medullary Thyroid Cancer (MTC)

Molecular Screening and Therapeutics (MoST) clinical trials

Multidisciplinary Molecular Tumour Advisory Boards (MTBs)

Multidisciplinary molecular tumour advisory boards (MTBs)

Multiple myeloma (MM)

Myeloma and Related Diseases Registry (MRDR)

National Blood Agreement (NBA)

National Health and Medical Research Council (NHMRC)

National Medicines Policy (NMP)

Next generation sequencing (NGS)

Non-Government Organisations (NGO)

Patient reported outcomes (PROMs)

Pharmaceutical Benefits Advisory Committee (PBAC)

Pharmaceutical Benefits Scheme (PBS)

Positron emission tomography (PET)

Programmed cell death protein (PD-1)

Programmed death-ligand 1 (PD-L1)

Ribonucleic acid (RNA)

Stem Cell Treatment (STC)

T cell receptor (TCR)

The Australian Alliance for AI in healthcare (AAAAiH)

Therapeutic Goods Administration (TGA)

Toll-like receptors (TLR)

TUMOUR MUTATION BURDEN (TMB)

US Food and Drug Administration (FDA)

Whole exome sequencing (WES)

Whole genome sequencing (WGS)

If you would like to speak with us about joining NOA or to discuss the content of the report or the proposed *Australian Cancer Futures Framework*, please contact:

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