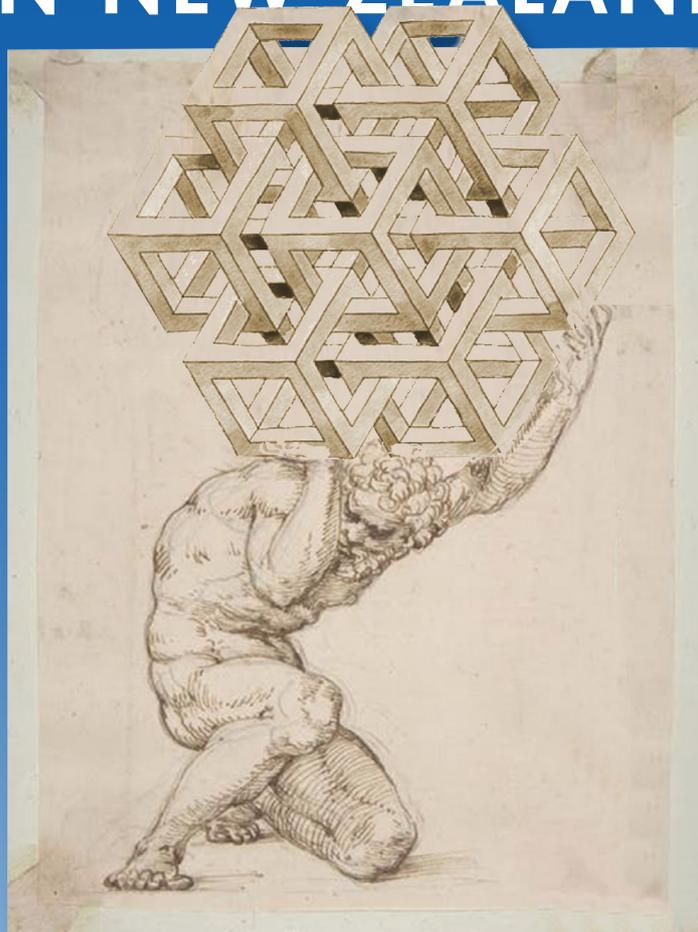


MANAGING MULTIPLE MYELOMA IN NEW ZEALAND



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THE WAY FORWARD

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Published by Myeloma New Zealand
Registered Charity No. CC53924
PO Box 25162
Wellington 6011
New Zealand

www.multiplemyeloma.org.nz

ISBN: 978-0-473-48522-1 - print
ISBN: 978-0-473-48523-8 - online/PDF

Cover design by Dennis Hearfield
Printed by City Print Communications

MANAGING MULTIPLE MYELOMA IN NEW ZEALAND: THE WAY FORWARD

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Myeloma New Zealand is a charitable trust established in 2016 to focus specifically on multiple myeloma and to improve the quality of life and survival of New Zealanders living with it.

We are primarily a patient advocacy organisation, that seeks to empower patients with information, research and support; to advocate with government to allow myeloma patients access to the remarkable treatments that are transforming lives and survival in other comparable countries; and to raise awareness and understanding among the general public of myeloma, one of our most common blood cancers.

HOPE

*Hope is the thing with feathers
That perches in the soul,
And sings the tune without the words,
And never stops at all.*

*And sweetest in the gale is heard;
And sore must be the storm
That could abash the little bird
That kept so many warm.*

- Emily Dickinson - 1830-1886

ACKNOWLEDGEMENTS

This report was commissioned by Myeloma New Zealand, to create more awareness and understanding of multiple myeloma as distinct from other blood cancers, and to estimate the burden of this disease in New Zealand in both personal and economic terms. The authors are grateful to Dr. Ken Romeril (CEO, Myeloma New Zealand) for initiating this study and providing clinical information, ongoing commentary and review; and to Dr. David Simpson (consultant haematologist, Waitemata District Health Board), Professors Nick Wilson and Mark Elwood for their insightful comments. We also thank Tania Crosbie for her expert editorial services and Catherine Isaac for her thoughtful and constructive input. We are especially grateful to the six individuals who have described their personal journeys with myeloma and four caregivers (of other individuals) for their stories. The lead author takes full responsibility for this report.

Approval to utilise the Integrated Data Infrastructure (IDI) was obtained from Statistics New Zealand, the Health and Disability Committee of the Ministry of Health and the University of Auckland Human Ethics Committee.

Funding was provided to Myeloma New Zealand by Janssen New Zealand. The sponsor had no input into the design, analyses or interpretation of this study.

FOREWORD



Ken Romeril
Chief Executive
Myeloma New Zealand

This report summarises the findings of a major new study, *The Burden of Multiple Myeloma: A Study of the Human and Economic Costs of Myeloma in New Zealand*, led by Assoc Professor Richard Milne and commissioned by Myeloma New Zealand. The report is a pioneering piece of work, bringing together and analysing for the first time all the available data in New Zealand on myeloma. It is an enormous achievement and a great credit to its authors, in particular, Richard Milne.

Because of the sheer volume of material in *The Burden of Multiple Myeloma*, we decided to summarise it as a separate publication, with a focus on the findings of the report that can help us chart the way forward in the treatment of myeloma.

As the report demonstrates, there have been great advances in the treatment of this complex disease in recent years, seen in particular in significant increases in survival. We are committed to working constructively with the Government to find workable, affordable ways to make more of these treatments available to New Zealanders.

There are also many potentially transformative treatments on the horizon, which, together with increasingly more accurate diagnostic techniques, are pointing to a brighter future and better quality of life for people living with myeloma. We have therefore begun this report with a review of the exciting new myeloma management strategies that are already in sight.

In addition to outlining these developments, the *Burden of Myeloma* highlights a number of ways in which we can do better for people with myeloma. These include in particular the need to ensure real equity of access to top quality care for patients, irrespective of where they live, and regardless of what they can afford to pay.

Addressing issues such as access to clinical trials, having adequate infusion facilities around the country, and the need for better collaboration among hospitals and researchers are important parts of this. Increasing our ability to move effective treatments up to the first line, and to tailor treatments to the individual's disease are also critical objectives.

The third report in our series, *Patients' Perspectives*, is a summary of a survey of myeloma patients and their carers. This provides valuable insights into what it is like to live with myeloma and what can be done to improve their journey and their quality of life.

Our message in publishing these three reports is one of hope and optimism: that in the not too distant future, myeloma patients will be living well, with a good quality of life, and their illness managed as a chronic disease, rather than a fatal one.

A handwritten signature in blue ink, appearing to read 'K. R. Romeril', with a long, sweeping underline.

Ken Romeril MBChB, FRACP, FRCPA
Chief Executive
Myeloma New Zealand
NZ Member of the International Myeloma Working Group

CONTENTS

HOPE.....	2
ACKNOWLEDGEMENTS.....	3
FOREWORD	4
CONTENTS.....	5
TABLE OF TABLES.....	7
TABLE OF FIGURES	7
I SCANNING THE HORIZON FOR NEW MYELOMA MANAGEMENT STRATEGIES ..	8
Molecular profiling.....	8
Testing for minimal residual disease (MRD)	8
Novel treatments and combinations	10
An overall transformation in myeloma treatment	12
II MULTIPLE MYELOMA.....	13
Diagnosis.....	13
Incidence and prevalence	16
Treatment.....	17
Stem cell transplant	18
Treatment for patients who are not eligible for stem cell transplant	18
Unfunded treatments	19
1. Named Patient Pharmaceutical Assessment (NPPA).....	22
2. Clinical trials.....	22
3. Private funding.....	22
4. Pharmaceutical supplier access programmes.....	22
III SURVIVAL OUTCOMES.....	23
IV UPTAKE AND IMPACT OF ASCT AND NEW THERAPIES AND COMBINATIONS ...	25
V QUALITY OF LIFE	26
VI COSTS OF MYELOMA.....	27
Costs to the healthcare system.....	27
Loss of personal income	27
Loss of tax revenue	28
VII CONCLUSIONS & RECOMMENDATIONS	29
Conclusions.....	29
Epidemiology & clinical management.....	29
Clinical data collection.....	30

Costs to government and families.....	30
Living with myeloma	31
Recommendations	33
1. Systems for collaboration, data collection and benchmarking to ensure equitable quality of care	33
2. Efficient delivery of medications.....	33
3. Facilitating access to compassionate-use programmes	33
4. Investment in more effective earlier lines of treatments.....	33
5. Supporting and facilitating the conducting of clinical trials in New Zealand	33
6. Improving support, information and advocacy for patients.....	34
7. Investing in research and facilitating collaboration among centres engaged in research	34
8. Introducing performance-based risk management and cost-effectiveness analyses	34
9. Research funding for New Zealand-specific economic evaluation of therapies to treat myeloma	34
10. Further research based on the findings of this report	35
VIII PATIENT & CARER STORIES.....	36
John	36
Briar	37
Samuel.....	38
Robert.....	39
Susan	40
Jim.....	41
Jessica.....	42
Tania.....	42
Ben.....	43
James.....	44
REFERENCES	47

TABLE OF TABLES

Table 1.	Registrations and annual incidence rates per 100,000 population in 2012-2016 by ethnic group.	16
Table 2.	Medications for treatment of myeloma.	17
Table 3.	12-month, 3-year, 5-year and median overall survival, by era, for all New Zealand.	23

TABLE OF FIGURES

Figure 1.	Minimal residual disease	9
Figure 2.	Tailored and response-adapted treatment strategy.....	9
Figure 3.	New therapeutic agents in myeloma	10
Figure 4.	The mechanism of actions of various classes of novel anti-myeloma treatment	11
Figure 5.	Images of the presence of myeloma outside the bone marrow	12
Figure 6.	Development & diagnosis of multiple myeloma	15
Figure 7.	Overall treatment strategies for multiple myeloma.....	20

I SCANNING THE HORIZON FOR NEW MYELOMA MANAGEMENT STRATEGIES

In view of the recent advances in the field of multiple myeloma (myeloma) treatment, management of this cancer is likely to undergo substantial changes in the coming years. Three key principles have started to emerge that are likely to shape the paradigm for the future management of myeloma: molecular profiling of the disease, testing for minimal residual disease (MRD) and targeted novel treatment combinations.

Molecular profiling

Molecular profiling refers to the analysis of DNA mutations and genetic rearrangements found in myeloma cells, some of which can be associated with inferior outcomes. The common current method in New Zealand (fluorescence in-situ hybridisation or FISH), cannot detect many of the newly discovered mutations, and can only evaluate one specific genetic abnormality at a time, making it costly if more extensive analysis is required. Researchers are therefore now looking at next generation sequencing (NGS), which can evaluate hundreds of mutations and rearrangements simultaneously. This is being developed internationally and locally and will probably be more cost effective than FISH. This array of analysis is likely to help optimisation and prioritisation of treatment in the future.

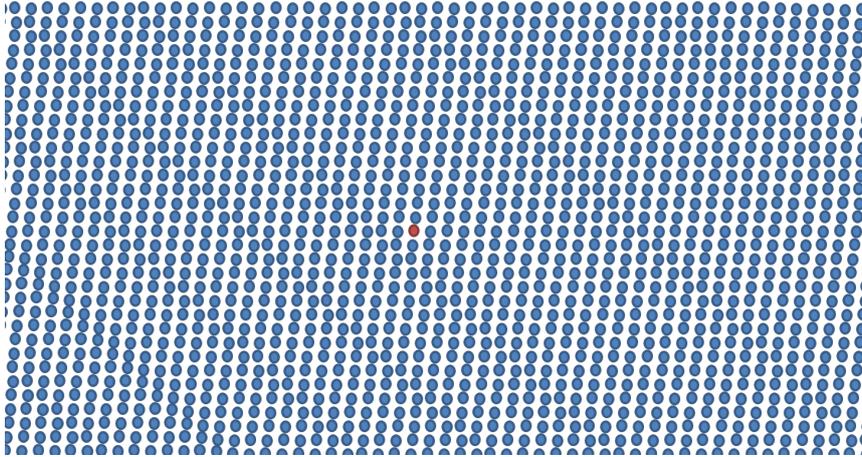
Advancement in NGS may also improve the ease of diagnosing myeloma, which generally requires a bone marrow biopsy. However, interest is emerging in 'liquid biopsy', where circulating tumour DNA is isolated from the peripheral blood and analysed without the need for tissue or bone marrow biopsy. When this technology has matured it could replace the need for bone marrow biopsy when used in conjunction with other assessment tools, such as imaging.

Molecular profiling would also help us better understand the pathophysiology of myeloma and pave the way for more targeted and tailored therapeutic treatments, as opposed to the current somewhat homogeneous approach. Ultimately this is likely to lead to better outcomes and (hopefully) more cost-effective management, as the costs of genetic testing comes down.

Testing for minimal residual disease (MRD)

The current evaluation of response to treatment based on bone marrow testing has been around for more than a decade but given the depth of response to novel treatment strategies, these tests are no longer sufficiently sensitive for determining treatment success. A deep response, where only a small number of residual cancer cells are present, is now referred to as minimal residual disease (MRD). Next generation flow cytometry and NGS are currently available to detect MRD in the bone marrow, and fluorodeoxyglucose positron emission tomography (F-FDG PET) can be used to detect MRD outside the bone marrow.

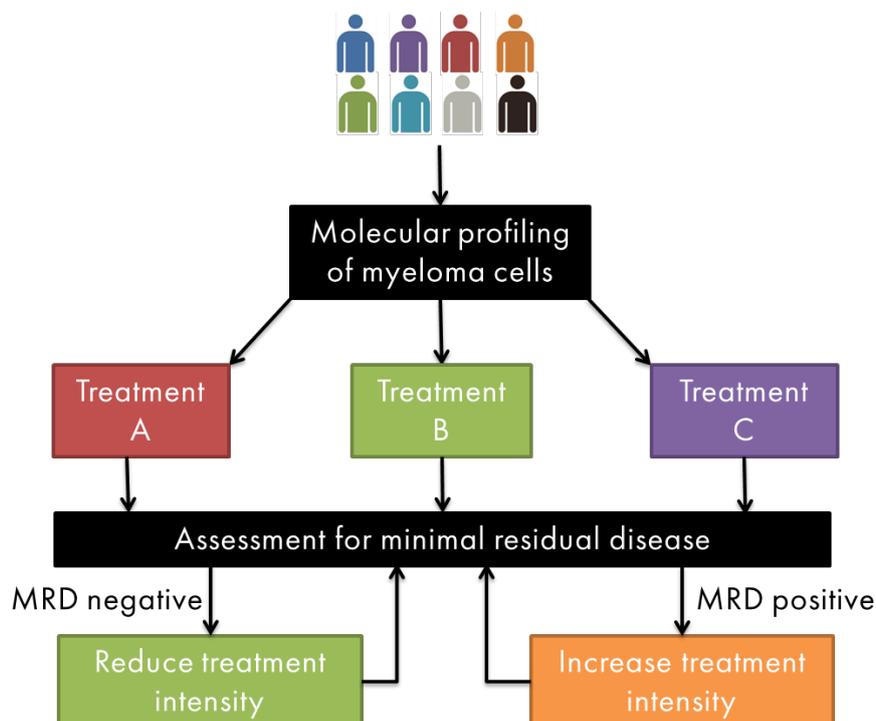
Figure 1. Minimal residual disease.



Current technology allows scientists to detect 1 myeloma cell among a sea of 100,000 to 1,000,000 cells. MRD status has significant prognostic value. Patients who are MRD negative after treatment, even those with high-risk disease, often experience a good long-term outcome compared to those who do not achieve MRD negativity.

This raises the possibility of having a response-adapted treatment plan based on MRD results, where patients who are MRD negative after initial treatment can forgo further treatment. Meanwhile, patients who failed to achieve MRD negativity, or progressed from MRD negative to positive, can receive intensification or re-initiation of treatment, respectively.

Figure 2. Tailored and response-adapted treatment strategy.



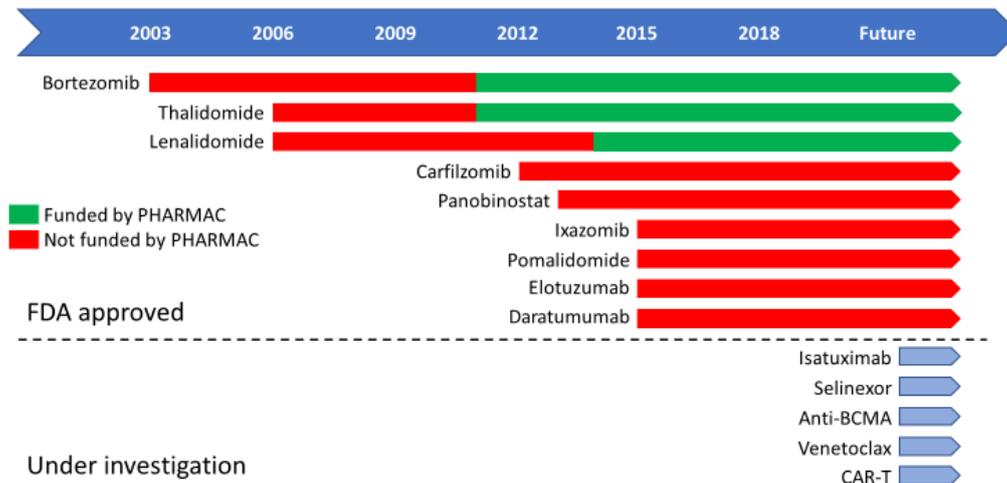
Patients with myeloma will have samples taken at diagnosis and time of relapse to determine the molecular profile of the myeloma cells. This result will guide clinicians to the most appropriate treatment regimen. After a period of treatment, patients will be evaluated for MRD. If they have shown a good response with no detectable MRD, then treatment intensity may be reduced. For patients who have remained positive for MRD, then treatment may be intensified. This process of assessment of MRD and adjustment of treatment intensity repeats throughout the treatment journey. This concept is currently being tested in clinical studies across the world. If proven feasible, such a strategy would be a very attractive and cost-effective option, as it would probably minimise unnecessary treatment and toxicities.

Novel treatments and combinations

Gone are the days when the only treatment option for myeloma is conventional chemotherapy. Multiple new classes of medications have been developed over the last two decades for the treatment of myeloma, and studies have consistently demonstrated a superior outcome when they are given in combinations. Although the ideal treatment strategy for myeloma remains to be determined, it is doubtful that an outright winner will ever be crowned, due to the heterogeneity of the disease and the better treatments being developed constantly.

What is certain, however, is that the current arsenal we have in New Zealand for the management of myeloma is lagging behind the rest of the world.

Figure 3. New therapeutic agents in myeloma.



The decision to fund bortezomib in 2011 has been serving our patients well, with many achieving good long-term outcomes. However, New Zealand still has relatively limited treatment options in frontline, for maintenance, and in particular for relapsed disease, and unless further investment/funding is put in place, we will see a widening gap in patient outcomes between New Zealand and other OECD countries.

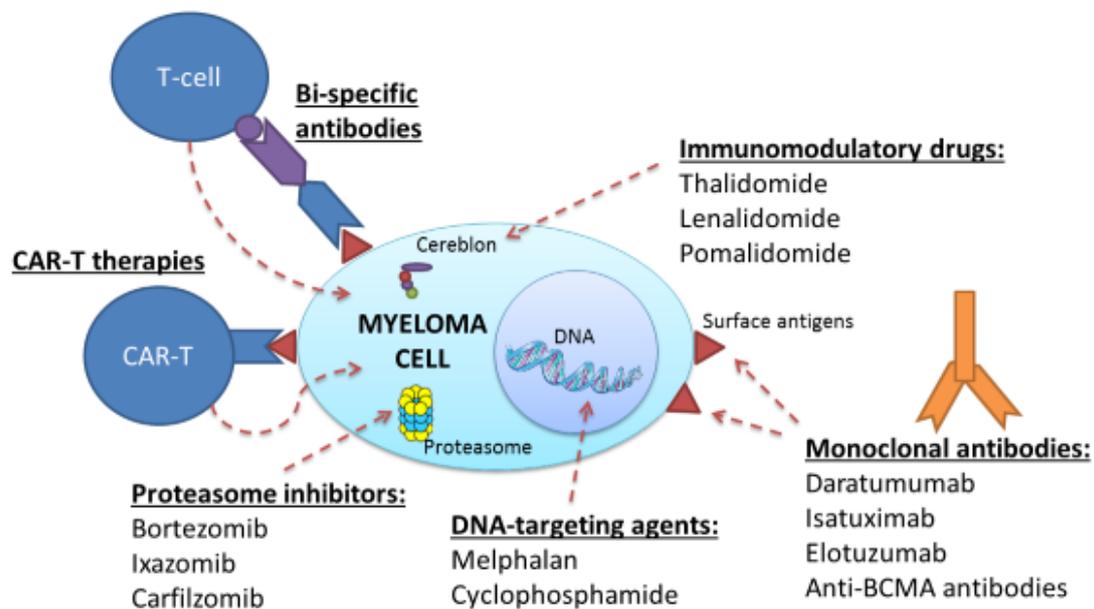
Combination treatment with proteasome inhibitors and immunomodulatory medication is likely to become the standard of care in the frontline setting. With these new combinations, we could

question the role of autologous stem cell transplant (ASCT) as a consolidation treatment, although this will remain an important tool. Meanwhile, one would expect newer classes of medication such as monoclonal antibodies to be used more heavily and earlier in the course of the disease. As newer treatments become more effective and better tolerated, the current standard of triplet therapy will probably be replaced by quadruplet regimens in the next 5 to 10 years as data from clinical studies mature.

In recent years, the idea of immunotherapy, where the patient's own immune system is manipulated to enhance tumour killing, has been gaining momentum. One of the most promising strategies is the use of chimeric antigen receptor (CAR) T cells, where the patient's own T-lymphocytes (immune cells) are harvested and modified to target a specific tumour cell type. Such cells would ideally remain within the patient over a long period of time and will provide long-term protection against the disease as a 'living drug'.

Following the recent success in the use of such therapy in acute lymphoblastic leukaemia and aggressive lymphomas, such technology is now being tested in myeloma as well, with promising results. Other forms of immunotherapy such as bispecific antibodies are also in development, with the aim of harnessing the power of the patient's immune system to achieve disease control.

Figure 4. The mechanism of actions of various classes of novel anti-myeloma treatment.



Immunomodulatory drugs primarily target cereblon, which leads to destruction of specific proteins and death of myeloma cells. Monoclonal antibodies bind to various specific antigens on the surface of the myeloma cells, tagging it for destruction. DNA-targeting agents cause damage in the DNA, which will lead to programmed cell death. Proteasome inhibitors block proteasomes, which leads to accumulation of toxic protein and subsequent death of the myeloma cells. CAR-T therapies work by modifying patient's own immune T-cells to specifically recognise and kill the myeloma cells. Bi-

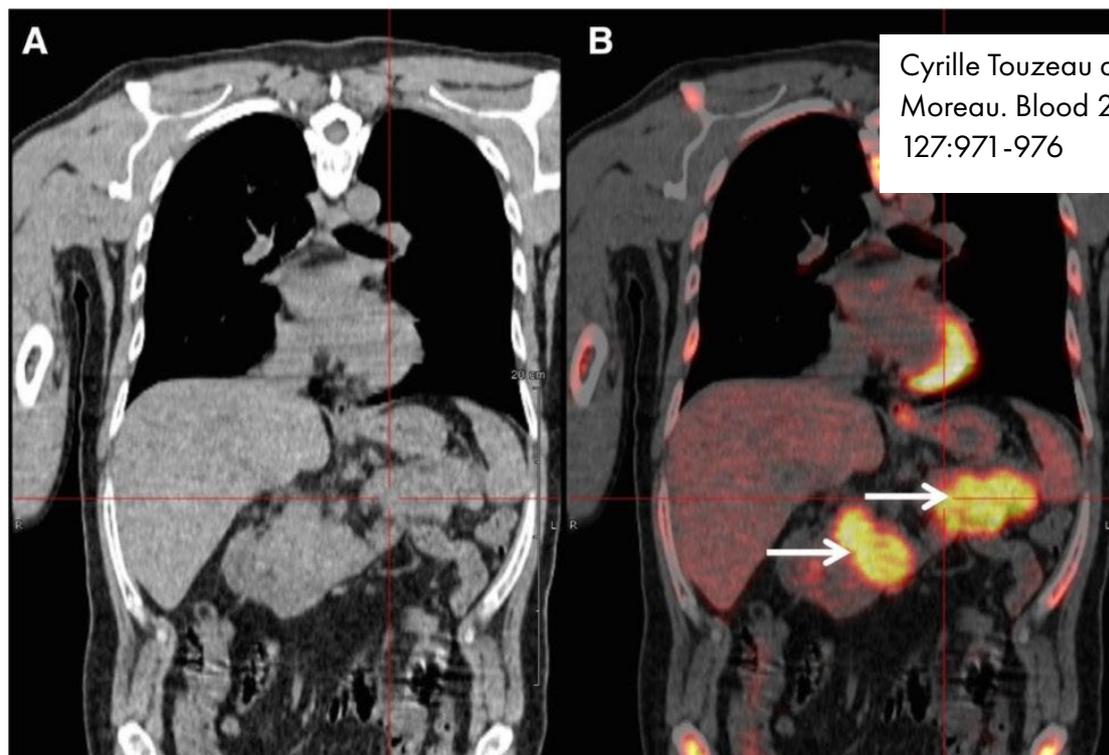
specific antibodies bring patient's immune T-cells in close proximity to the myeloma cell to facilitate direct killing of the myeloma cell.

An overall transformation in myeloma treatment

In addition to the three pivotal points outlined above, the management of myeloma has moved from giving just a finite duration of therapy to continuous treatment, similar to the management of some non-malignant diseases, such as diabetes and cardiovascular risk management. Many other aspects of the management of myeloma have already undergone significant changes in recent years. For example, whole body magnetic resonance imaging (MRI) is now used as part of the diagnostic work-up instead of skeletal survey with x-ray, and more potent bisphosphonates are now available to reduce the risk of fractures.

Figure 5 below shows how new imaging techniques, such as MRI and PET scans, allow better detection of myeloma disease in the body. Image A is from a CT scan showing the presence of myeloma, and B is from a PET scan that better highlights the same lesions for easier identification (as shown by the arrows.)

Figure 5 - Images of the presence of myeloma outside the bone marrow.



Together, these developments are likely to transform the treatment of myeloma in the coming years. While we are still some way away from curing myeloma, it is possible to foresee treating myeloma as a chronic disease rather than a fatal disease in the not-too-distant future.

Clinicians and patients are rightly encouraged by these developments, and as a nation we need to embrace them. With a raft of novel myeloma treatments already registered abroad, and others in late stages of development, our policymakers need to ensure New Zealanders living with myeloma

receive treatment in line with international best practice. Reducing the burden of this devastating disease is both essential and achievable.

II MULTIPLE MYELOMA

Multiple myeloma is a blood cancer that resides in the bone marrow. It affects multiple sites in the body where bone marrow is normally active in adults, including the spine, skull, pelvis, ribs, shoulders and hips. Sufferers of myeloma experience serious complications including bone and kidney disease, serious infections, and excessive levels of calcium which can lead to confusion, disorientation and weakness.

Although it is treatable, myeloma is not currently curable, and follows a remitting, relapsing course, requiring continued interventions aimed at destroying myeloma cells and controlling the symptoms and complications they give rise to. All myeloma patients eventually become unresponsive to treatment (refractory), or their disease returns (relapse). As myeloma relapses, periods of remission often become shorter and the disease becomes increasingly difficult to treat, with most patients eventually dying from the complications.

“Myeloma has a major impact on my independence, my ability to earn a wage to live, the ability to complete simple tasks such as vacuuming due to the pain I have, the reliance I have had to accept from my whanau & friends.”

The cause of myeloma is not fully understood, although it is believed to involve an interaction of both genetic and environmental factors. It develops when plasma cells, a type of white blood cell, undergo a cancerous change and become myeloma cells. As these cells multiply, they crowd the bone marrow and prevent it from making normal numbers of red cells, white cells and platelets, leading to anaemia and a higher risk of infections, bruising and bleeding.

Diagnosis

Myeloma is a very individual cancer, and patients present with a highly varied set of clinical signs and symptoms. Classic symptoms include calcium elevation (hypercalcaemia), renal impairment, anaemia and bone disease, collectively known as CRAB.

Other less common presentations of myeloma include recurrent infections, hyperviscosity (increased thickness of the blood), visual changes, headaches and dizziness. The way patients respond to treatment can also vary greatly.

These variations can be explained in part by the different features, types and subtypes of myeloma, involving factors that can influence the onset and speed of the progression of the disease. Detection of these, through analysis of the abnormal plasma cells, together with factors such as the stage of the disease, disease biology and gene mapping

“My wife and I both suspect she had MM long before she was given the blood tests that admitted her to hospital, ie she kept getting repeated urinary infections for which the GP gave antibiotics.”

through the use of fluorescent in situ hybridisation (known as FISH), can be used to identify patients with high-risk disease.

The effect the myeloma is having on the patient's body is assessed by using an international 'staging' system. Patients are classified into one of three risk stages, each with progressively worsening survival. The stage of myeloma is usually assessed at diagnosis and possibly again each time the disease relapses and is used for prognostic purposes. However, decisions regarding treatment depend on the presence of CRAB, the analyses described above, and MRI findings, rather than the stage of disease. The diagnostic criteria for myeloma were established by the International Myeloma Working Group (IMWG) in 2003 and updated in 2014.

“Even though the scans showed multiple fractures in my spine...at no time did anyone mention that it might be MM. The pain was so severe I could barely breathe... and two weeks before I was finally diagnosed I had pain so bad in the top of my right leg I couldn't walk. The ortho specialist admitted me to hospital with a suspected broken hip. After more x-rays and scans they found 2 spots on my pelvic bone, hence I was given a bone marrow biopsy, and then was told I had MM (stage 3). I have been left severely disabled and feel this could have been prevented if I was diagnosed sooner.”

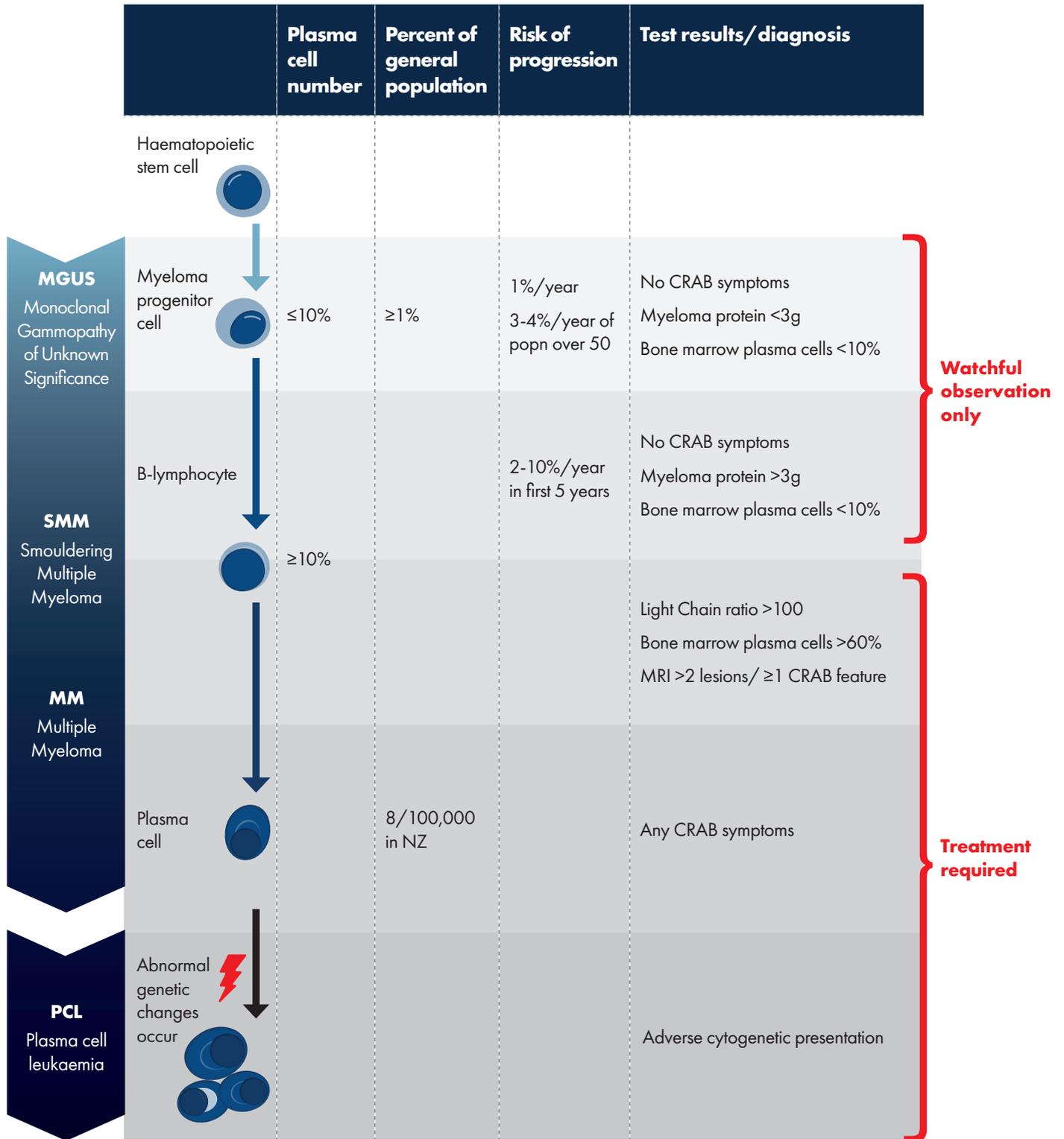
Myeloma is probably preceded by a pre-cancerous state known as monoclonal gammopathy of undetermined significance (MGUS), which may not have been detected. About 1% of MGUS patients will go on to be diagnosed with symptomatic myeloma each year. In between MGUS and myeloma is a state known as 'smouldering myeloma.' Patients in this state are monitored but generally do not receive treatment unless they have concerning signs such as abnormal bony lesions on MRI.

The rate of further progression from smouldering myeloma to symptomatic myeloma (or another blood cancer called amyloid light-chain (AL) amyloidosis) is approximately 10% per year for the first 5 years, reducing over the following years.

The development and diagnosis of myeloma is summarised in Figure 6.

“I have smouldering myeloma which has a real psychological effect – have it, but can't treat it. Like a ticking time bomb.”

Figure 6.
The development & diagnosis of multiple myeloma



Baseline investigations

- Blood tests
- Quantify myeloma protein (paraprotein)
- Imaging – MRI / CT / x-rays
- Bone marrow biopsy
- Cytogenetic analysis

CRAB: features of disease-related organ damage

- C:** Calcium elevation (hypercalcaemia) > 1.5/L or upper limit of normal
- R:** Renal dysfunction: serum creatinine >2mg/dl
- A:** Anaemia: haemoglobin <10g/dL
- B:** Bone disease: lytic lesions or osteoporosis

Reporting of myeloma to the New Zealand Cancer Registry (NZCR) in accordance with international guidelines is mandatory. However, it is possible that patients with smouldering myeloma who do not require treatment are classified as having myeloma, and this may explain why some patients in our study period did not receive the standard treatments.

In addition to the physical symptoms described above, many myeloma patients experience psychological distress, depression, anxiety and poor quality of life, in part associated with fear and uncertainty regarding the disease, treatments and their side effects, fear of relapse and an uncertain prognosis.

Incidence and prevalence

In New Zealand, myeloma is the second most common blood cancer (after non-Hodgkin’s lymphoma), with approximately 400 new cases reported each year, equivalent in the period 2012-2016 to 8.2 new cases per 100,000 population, or an age-standardised incidence rate of 5.19 per 100,000 population (Table 1).

Table 1. Registrations and annual incidence rates per 100,000 population in 2012-2016 by ethnic group.

	Māori	Pacific	Asian	Eur/Other	Total
Total					
Registrations	194	111	81	1478	1864
Annual crude incidence rate	5.53	7.59	2.93	9.86	8.20
Age std incidence rate (ASIR)*	7.19	10.13	3.51	5.05	5.19

New cases per 100,000 population; denominator: 2013 household census (non-residents excluded)

* Standardised to the WHO standard population

In the same period, age-standardised incidence rates were higher for Māori (7.2 per 100,000) and Pasifika peoples (10.1 per 100,000) than others. The age specific incidence rate was consistently higher for Māori/Pasifika than for all others, especially the elderly. The causes for the differences are unknown. In the same period, myeloma incidence was higher among men (58% of new cases).

Approximately 2500 New Zealand residents, 60% of whom are male, are currently living with myeloma (54 per 100,000 population) and there are about 180 deaths each year with myeloma as the underlying cause (4.0 per 100,000 population).

Considering Australia, Canada, the UK, USA, and Sweden, the age-standardised incidence of myeloma ranged from 5.6 in Canada to 9.3 per 100,000 in the UK. Worldwide, including in New Zealand, the incidence rate is rising but the death rate (mortality) in New Zealand remains relatively stable and these trends are likely to continue. Taken together, these observations are consistent with

improvements in clinical management. The median age at diagnosis was 70, although Māori and Pasifika were diagnosed at a younger age than other ethnicities (64 and 66 respectively).

Myeloma registrations in the period 2010 to 2016 were distributed unevenly around District Health Boards (DHBs), with the highest rates in the North Island. Some of the variation could be explained by different age structures, as older populations would be expected to have higher crude incidence rates.

“There is no support for families, nothing around the reality of what is in the future and dealing with issues around death. This has never even been addressed. It’s just left to the family to guess.”

Treatment

The goal of myeloma treatment is to prolong survival by achieving the best possible response while ensuring quality of life is maintained. Responses to treatment are monitored regularly, using a set of highly sensitive measures. Table 2 lists medications used in the treatment of myeloma in New Zealand as well as those available and used internationally but not currently funded here.

Table 2. Medications for the treatment of myeloma.

Chemotherapy drugs	Cyclophosphamide	Melphalan	Doxorubicin
Steroids	Dexamethasone	Prednisone	
Proteasome inhibitors (PIs)	Bortezomib (Velcade®)	Carfilzomib (Kyprolis®)*	Ixazomib (Ninlaro®)*
Immunomodulatory agents (IMiDs)	Thalidomide (Thalamid®)	Lenalidomide (Revlimid®)**	Pomalidomide (Pomalyst®)*
Monoclonal antibodies (Mabs)	Daratumumab (Darzalex®)****	Elotuzumab* (Empliciti®)	Isatuximab*
pan-HDAC inhibitor	Panobinostat (Farydac®)*		

Funded in NZ

*Not yet funded in NZ

**Funded in NZ for third-line/relapse only

****Currently available in NZ on compassionate access for third-line plus only

Patients diagnosed with symptomatic myeloma usually require immediate treatment and are generally grouped by their eligibility to undergo stem cell transplant. This can be an arduous treatment with challenging side effects and a long recovery period, and eligibility is therefore largely determined by the patient’s age and health status.

Stem cell transplant

This treatment entails giving high doses of chemotherapy (known as high dose therapy or HDT) to destroy myeloma cells, and then giving stem cells to the patient to 'rescue' the bone marrow. If the patient's own stem cells are given back to them, it is called an autologous stem cell transplantation (ASCT). This is by far the most common type of transplant used for myeloma.

"First SCT was a horrendous experience, with infections and fall onto toilet causing two spinal compression fractures. Discharged home after 5 weeks, on walking frame and weighing 40kg. A couple of days later admitted back in for a further 2 weeks. ...Not all bad news though – overall result was VGPR [very good partial response]. The second one was easy!"

Prior to the transplant, induction treatment is given to reduce the amount of myeloma in the bone marrow before stem cells are collected. Induction regimens vary but usually last several months, during which a combination of medications is given in cycles. These combinations usually include chemotherapy, a steroid and another novel agent such as a proteasome inhibitor (e.g. bortezomib) or an immunomodulatory agent (e.g. thalidomide or lenalidomide).

Induction treatment is followed by collecting the patient's own stem cells, before the HDT (melphalan) is given with the aim of destroying the remaining myeloma cells. The healthy stem cells are then returned to the patient's blood where they travel to the bone marrow and start to make new blood cells. After a period of recovery, a fixed period of chemotherapy may be given to consolidate the impact of the HDT and ASCT, although longer-term follow-up is needed to confirm evidence for consolidation treatment. Increasingly, maintenance therapy may be used where an agent such as thalidomide or lenalidomide may be given until the disease progresses.

Response rates to induction treatment followed by HDT and ASCT vary across regimens used and patient populations. The proteasome inhibitor-based combination of bortezomib, cyclophosphamide and dexamethasone has shown a complete response or near complete response rate of 39% following induction, rising to 70% following transplantation. For the combination of proteasome inhibitor carfilzomib with immunomodulatory agent lenalidomide plus steroid dexamethasone, it has been reported that 62% of patients achieved at least a near complete response in newly diagnosed myeloma after 17 months of follow-up.

Treatment for patients who are not eligible for stem cell transplant

Newly diagnosed patients in New Zealand who are ineligible for transplant typically receive several cycles of a bortezomib-based regimen. These first-line approaches are in line with international practice, although the option of an induction regimen that includes lenalidomide or carfilzomib, which is often used overseas, is not publicly funded in this setting in New Zealand.

At first relapse (second line) in New Zealand, patients are typically treated with thalidomide and dexamethasone, unless side effects compromise treatment. When patients relapse again (third line), they may receive treatment with lenalidomide and dexamethasone. Bortezomib is also funded for those patients with relapsed or refractory disease as long as they have not received funded bortezomib previously.

Unfunded treatments

Compared with international guidelines, the publicly funded options for relapsed myeloma patients in New Zealand are severely limited, and a high unmet need exists. Potential gains in health-related quality of life are greater with earlier lines of therapy than later in the course of the disease, suggesting that greater gains in quality of life and overall survival could be achieved by moving other novel agents, such as lenalidomide and monoclonal antibodies (if funded) up the treatment hierarchy.

“We downsized house six months after diagnosis to be debt free and in a financial position to be able to use the mortgage facility in a new lower-value home to pay for non-Pharmac funded drugs and overseas treatment.

This is frustrating as I have a very comprehensive insurance program including Southern Cross Medical Insurance (\$60K p.a. for Pharmac funded drugs and \$10K for Med Safe approved drugs) which falls well short of the cost of the latest available drugs. “

At the time of finalising this report, (May 2019), Pharmac, the national pharmaceutical management agency in New Zealand, was considering several new therapies for the treatment of myeloma, including three FDA-approved medicines: daratumumab and carfilzomib in relapsed disease, and lenalidomide earlier than the currently funded third-line setting.

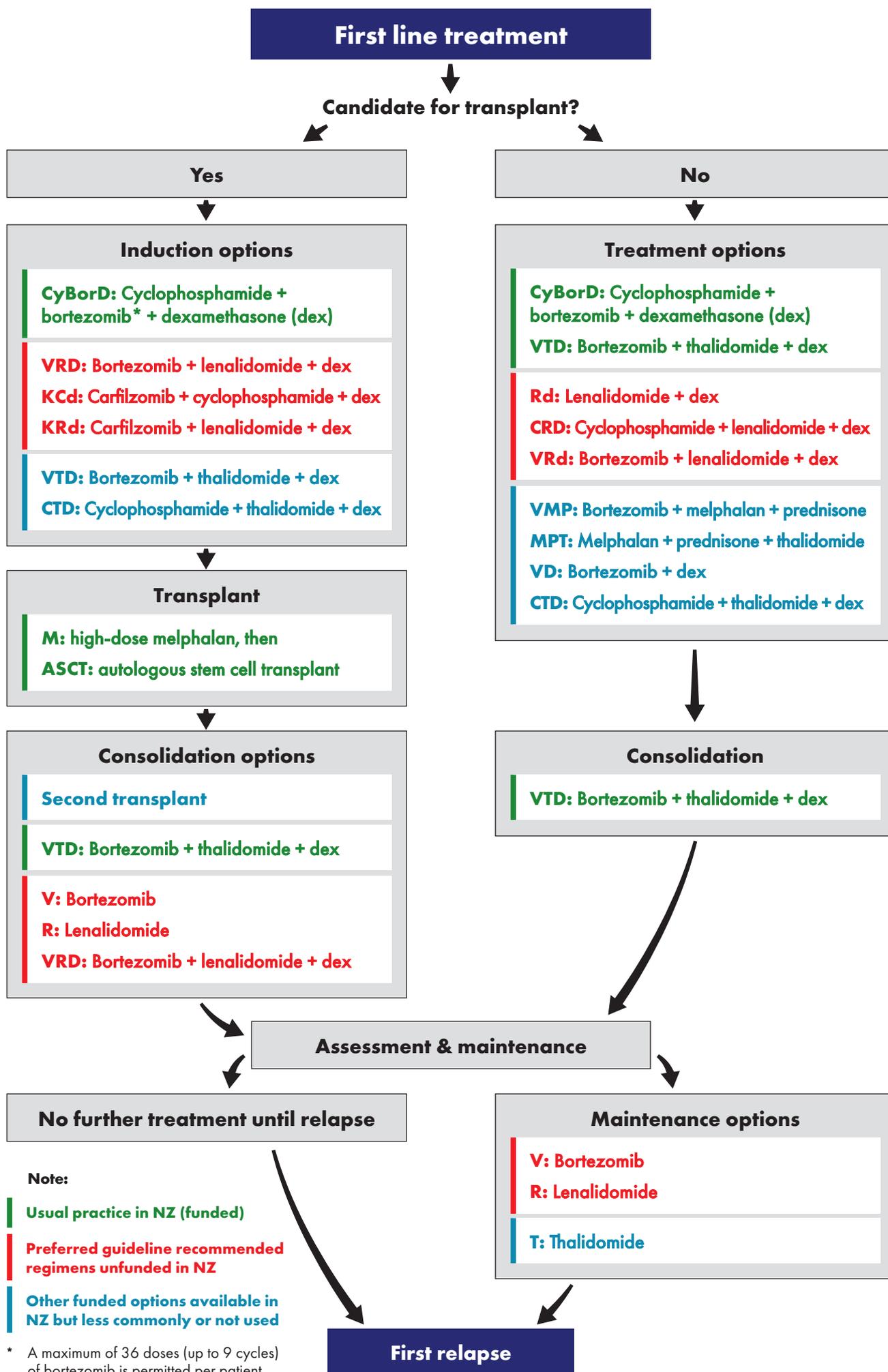
Daratumumab is currently provided free of charge on a case-by-case basis to New Zealand patients who have failed all available lines of therapy by the pharmaceutical supplier through a compassionate access programme. Carfilzomib has been available in New Zealand until recently on a compassionate access programme, but this has now closed.

Combination therapy with daratumumab + bortezomib + dexamethasone was approved in April 2019 by the National Health System in England and Wales for use after the first relapse.

Current New Zealand and international treatment regimens are shown in Figure 7.

Figure 7.

New Zealand & international myeloma treatment options & pathways



**First relapse
(2nd line treatment)**

If transplant eligible, consider second ASCT

First line treatment?

If prior bortezomib* or
carfilzomib treatment

If no prior bortezomib or **carfilzomib**
(or if patient received **first-line lenalidomide****)

Thalidomide-based treatment

CTD: Cyclophosphamide + thalidomide + dexamethasone (dex)
TD: Thalidomide + dex

or Lenalidomide/bortezomib/
carfilzomib-based treatment**

Rd: Lenalidomide + dex

CRD: Cyclophosphamide + lenalidomide + dex
DVD: Daratumumab*** + bortezomib + dex
DRD: Daratumumab + lenalidomide + dex
KRd: Carfilzomib + lenalidomide + dex
Kd: Carfilzomib + dex
PomD: Pomalidomide + dex
VD-Pano: Panobinostat + bortezomib + dex
Elo-Rd: Elotuzumab** + lenalidomide + dex
IRd: Ixazomib** + lenalidomide + dex
Vd: Bortezomib + dex
IsaLd: Isatuximab + lenalidomide + dex

Thalidomide-based treatment

TD: Thalidomide + dexamethasone (dex)
CTD: Cyclophosphamide + thalidomide + dex

or Bortezomib-based treatment

Vd: Bortezomib + dex
CyBorD: Cyclophosphamide + bortezomib + dex
VCD: Bortezomib + cyclophosphamide + dex

DVD: Daratumumab + bortezomib + dex
DRD: Daratumumab + lenalidomide + dex
VD-Pano: Bortezomib + dex + panobinostat
Elo-VD: Elotuzumab + bortezomib + dex

or Carfilzomib-based treatment

Kd: Carfilzomib + dex
KRd: Carfilzomib + lenalidomide + dex
KCd: Carfilzomib + cyclophosphamide + dex

**Second (3rd line) or
subsequent relapse**

Note:

Usual practice in NZ (funded)

Preferred guideline recommended regimens unfunded in NZ

Other funded options available in NZ but less commonly or not used

* A maximum of 36 doses (up to 9 cycles) of bortezomib is permitted per patient

** Lenalidomide is funded in NZ only at 3rd line, or at 2nd line if patient has a neuropathy

*** Daratumumab is currently available in NZ on compassionate access

**** B Cell Maturation Antigen

***** Bispecific T cell engager

***** Antibody drug conjugate

RD: Lenalidomide + dex

PomD: Pomalidomide + dex
DRD: Daratumumab + lenalidomide + dex
DVD: Daratumumab + bortezomib + dex
D: Daratumumab (single agent)
Isa-Ld: Isatuximab + lenalidomide + dex

Clinical trials, eg:
Anti-BCMA** Car-T cell therapy**
Anti-BCMA BiTE*****
Anti-BCMA ADC*****

Options for obtaining unfunded treatments in New Zealand are very limited. They include:

1. Named Patient Pharmaceutical Assessment (NPPA)

A patient's physician may opt to apply to Pharmac for an unfunded treatment for an individual patient who may have exceptional clinical circumstances.

2. Clinical trials

Some pharmaceutical suppliers run clinical trials that make medicines available prior to Medsafe registration, subject to very specific patient criteria and strict protocols. These may only be available at 1 or 2 sites. Late stage clinical trials of medicines that have been registered by Medsafe but are not yet funded by Pharmac may also be considered.

3. Private funding

Patients and their families may consider paying privately for unfunded myeloma treatments directly from their retail pharmacies with a prescription from their specialist. Some health insurers provide subsidies for unfunded medicines, although the shortfall is often substantial.

4. Pharmaceutical supplier access programmes

There are two types of programmes:

- Shared cost programmes, whereby unfunded medicines are made available by the supplier at a discount. Any medicine funded privately by the patient, either fully or in part, cannot be administered on DHB sites, so the patient must find a private facility for this; and
- Compassionate, early access or patient familiarisation programmes, whereby a pharmaceutical supplier may open a programme providing an unfunded medicine free of charge for specific patient populations. Sometimes these programmes cannot be taken up by all DHBs, due to lack of facilities or staff. For example, in the carfilzomib and daratumumab programmes, the treatment requires long infusions, initially on a weekly basis, and some centres are reluctant to offer it to patients because of lack of infusion chair time and nursing staff. Once a medicine is funded, however, it must be made available by all DHBs.

III SURVIVAL OUTCOMES

Survival statistics for myeloma are grim but improving, with long-term survival lengthening significantly with the availability of newer anti-myeloma therapies.

Over the period 2004 to 2016, both all-cause survival and cause-specific survival increased. Across all ages combined, 5-year survival increased from 36% to 45% when comparing patients who registered in the period 2004 to 2007 to the period 2012 to 2016. Likewise, 28% of patients aged 70 or over who were diagnosed in 2012 to 2016 survived for more than 5 years, compared to 18% of those who were diagnosed in 2004 to 2007.

Table 3. 12-month, 3-year, 5-year and median overall survival, by era, for all New Zealand

Era	# Patients	Mean survival			Median survival (months)		
		12 months	36 months	60 months	Median	-95%CI	+95%CI
<i>All ages</i>							
2004-2007	934	73%	49%	36%	34.8	31.4	39.3
2008-2011	1124	75%	52%	40%	38.1	33.9	43.2
2012-2016	1864	81%	62%	45%	50.7	48.5	57.3
<i>Age ≤ 70y</i>							
2004-2007	461	84%	68%	54%	65.2	59.1	73.1
2008-2011	546	87%	70%	58%	73.0	65.7	80.2
2012-2016	931	90%	78%	62%	NE	NE	NE
<i>Age > 70y</i>							
2004-2007	473	63%	31%	18%	17.7	15.2	20.8
2008-2011	578	63%	34%	22%	21.9	18.4	24.3
2012-2016	933	71%	45%	28%	28.6	24.4	33.6

NE, non-estimable

Five-year overall survival for all patients who were registered in New Zealand in 2012 to 2016 was 45% and median survival was 51.2 months. Five-year overall survival was the same for men and women. Survival was strongly age specific, with younger individuals surviving longer than older.

Overall survival was worse for younger Māori/Pasifika peoples than for other ethnicities, however cause-specific survival did not differ between Māori/Pasifika and others in that age group, suggesting that the ethnic difference can be attributed to factors other than genetics or management of myeloma.

Overall survival at 3 years and 5 years as well as median survival was better for patients living in the Northern region than elsewhere. Overall survival was best for individuals living in least deprived regions of the country (deciles 1 to 4). Five-year survival varied from 40.5% to 50% and median survival varied from 43.8 to 60.9 months.

For comparison, 5-year relative survival ranged from 42% in Canada to 52.4% in the USA. A previous comparison between New Zealand and Australia based on patients diagnosed in the period 2006-2010 showed no statistically significant difference in 5-year relative survival rates between the countries.

Multivariate analysis showed that in New Zealand overall survival depends primarily on age, socioeconomic status, geographic location, and uptake of ASCT and novel pharmaceutical therapies.

“When I was diagnosed [in 1997], I told my wife that if I could just hang on for a few years I was confident new treatments would come through. ...So far, I have been right.

Through an extraordinary set of circumstances - too long and complex to explain here - the ugly old drug thalidomide had been shown to be effective with myeloma.... In my case, I was hyper-sensitive to it and the myeloma was under control for around 14 years. Two years ago, it was on the march again, alongside two major health problems – and treatment for the myeloma had to be abandoned, resulting in its inextricable rise month after month.... Fortunately, and as I had hoped, new myeloma drugs have been developed over the past twenty years. I’m now on Velcade and dexamethasone, a combination which has suppressed the myeloma to almost non-detectable levels.

Of course, the future of any cancer is always uncertain, but I still believe it won’t kill me, not least because there are yet more new drugs on the horizon and one or another of them will do the trick!”

(from Samuel’s story – see Section VIII)

IV UPTAKE AND IMPACT OF ASCT AND NEW THERAPIES AND COMBINATIONS

Uptake of bortezomib-containing drug regimens was independent of ethnicity and higher for Northern region than other regions. Uptake of ASCT was lower for Māori/ Pasifika and slightly lower in Central cancer network region than elsewhere. ASCT was only rarely given to patients over 70 years of age because of its toxicity.

Lenalidomide-containing regimens were funded as third line therapy in September 2014. Prior to funding it was made available through a compassionate access programme and a clinical trial. Up to October 2018 lenalidomide had been given to 846 New Zealand patients.

Over 20% of patients up to 70 years of age, comprising 36% of all patients, received neither of the two most effective funded first-line therapies (bortezomib and ASCT) and many others received considerably fewer than the funded 36 doses of bortezomib. This could have been because of unwillingness to undergo the therapy, comorbidities, not requiring treatment due to only having smouldering myeloma, limited access to infusion facilities and/or lack of alternative less toxic first-line therapies. Additionally, in 2012-2016, there was regional variation in the time taken from registration to utilisation of ASCT. These two disparities both deserve explanation and remedy.

ASCT and bortezomib individually and together were associated with improved overall survival. There was a clear improvement in both overall survival and cause-specific survival after 1 May 2011 when bortezomib was funded, especially for patients over 70 years of age. The improvement in survival was larger for those patients who did not also receive ASCT.

Multivariate analysis showed that younger age at registration, higher socioeconomic status, and being domiciled in the Northern cancer region were independently associated with better survival.

There is great opportunity to improve New Zealand survival statistics further, thanks to a surge in research and the development of innovative myeloma treatments over the past couple of decades. However, funding is not keeping up with Australia and elsewhere because of the different funding models and processes that determine if, when, and how these treatments can be used in New Zealand. (Access to Medicines Report 2018, IQVIA)

“Most horrendous part of the treatment. Ten days after the SCT I was hospitalised with infection for 5 days. I only got around 15 months remission from my SCT. I would most probably have a completely different view of the SCT if I was still in remission as a result of it.”

“I was delighted to be able to have a transplant after successful treatment with Velcade. Although I was pretty sick afterwards (as expected), it kept the myeloma at bay for 7 years. I was back at work after 3 months and felt great.”

V QUALITY OF LIFE

Quality of life was not studied formally for this report, but it includes a number of patient and carer stories that provide insights, sometimes harrowing, on reduced health-related quality of life (HRQoL). The report is also accompanied by the results of a survey of patients and carers that sheds significant light on this issue.

It is clear from these that myeloma carries a high burden of symptoms and reduced quality of life, which varies with the course of the disease. Fatigue, pain, physical weakness, depression and other mental health issues, and loss of independence and 'self' are common.

Many other aspects of living with myeloma impact heavily on quality of life. These can include long delays in getting diagnosed resulting in some cases in years of debilitating pain, severe impacts and side effects of treatments, increased costs and loss of income, and the ongoing fear and uncertainty of living with an incurable disease.

Only a few formal studies on HRQoL are available, and a review of these demonstrates that extensive physical, emotional, and social challenges can be experienced by patients throughout their illness trajectories, even in periods of remission.

Osteolytic lesions develop in nearly 90% of myeloma patients, and these are frequently complicated by skeletal-related events such as severe bone pain, pathologic fractures, vertebral collapse, calcium elevation (hypercalcaemia), and spinal cord compression. These have a negative effect on patients' quality of life and affect their long-term outcomes, including survival.

Large and medium HRQoL improvements occur during first-line treatments, but no clinically beneficial change or deteriorations in scores of global QoL or fatigue were reported during treatment of relapse.

A Global Burden of Disease study reported that myeloma caused 2.1 million disability adjusted life years globally in 2016 but the contribution of New Zealand to the total was not reported.

“My partner’s diagnosis has quite radically changed our lives. From having active lives diving, boating, fishing etc, and with very good salaries, we sold everything and moved cities to be close to family for support. [My partner] had 2 years of no work and I took a \$15,000 annual salary drop in a new job, and my career has limited options here. We must plan everything around his ability to cope with pain and lethargy.”

“Multiple myeloma has turned me from a fit, active retired person into an old man.”

VI COSTS OF MYELOMA

Multiple myeloma is characterised by intense use of healthcare resources for cancer treatment, adverse effects of treatment, management of disease symptoms, imaging, pharmacotherapies, comorbidities, loss of income by affected families, increases in taxpayer-funded benefits and loss of tax revenue to the government. While some of these costs are borne by patients and their families, in New Zealand, most fall on the taxpayer-funded public healthcare system.

To calculate the costs of myeloma to the healthcare system, the well-established 'excess' or 'attributable' cost approach was used, using the Integrated Data Infrastructure (IDI). First, the expected health system cost in 2016 of a New Zealand resident without a diagnosis of myeloma, by sex and 5-year age group, was calculated. This was then subtracted from the health system costs of myeloma patients in the same sex and age groups. Loss of personal income was calculated in a similar way, and loss of income tax revenue for the Government was estimated for each individual from Inland Revenue Department tax tables.

Costs to the healthcare system

In 2016, the healthcare system incurred costs of approximately \$46.3 million on New Zealanders with myeloma, over and above what was spent on a same-sized group of the general population when matched for age group and sex.

Some of the costlier treatments for multiple myeloma include: therapy with novel medicines including bortezomib and lenalidomide; stem cell transplant; radiotherapy; surgery; intravenous bisphosphonates, and diagnostics such as MRI and FISH chromosomal analysis.

The largest expenditure attributable to myeloma in 2016 was for pharmaceuticals (\$30.3 million). However, pharmaceutical costs could be greatly overestimated because of confidential rebates paid by the pharmaceutical industry to Pharmac.

Compared to the general population matched for age and sex, myeloma patients also had higher average costs for hospital admissions (\$10.65 million), outpatient hospital visits (\$4.41 million), laboratory testing (\$0.66 million), emergency department visits (\$0.30 million) and other miscellaneous items. Laboratory costs are probably under-estimated, and primary care costs of myeloma patients have been assumed (conservatively) to be similar to those of the general population. This is because myeloma is largely managed by specialists and we did not have convincing information on primary care visits or costs.

Loss of personal income

Most men and women under 65 years of age have paid employment in addition to financial and social responsibilities. Many over 65 years of age also have full-time or part-time work. Because individuals with myeloma usually have to scale down their workload or retire from the workforce, a diagnosis of myeloma signals substantial loss of income to the family, increases to taxpayer-funded welfare benefits, and loss of tax revenue to the government.

Compared to the age/sex matched general population, in 2016 individuals with myeloma received lower incomes on average by approximately \$20,000 and \$10,000 for middle-aged men and women and \$9000 and \$6000 for men and women aged 65 or upwards. Income lost by caregivers would add to this burden but was not quantified.

Loss of tax revenue

Income tax revenue lost by the Government in 2016 was estimated at \$2.31m for men and \$1.01m for women, a total of \$3.31m. Welfare benefits would increase this cost to government but were not calculated because of incomplete records.

“At the time my husband and I owned a business. We had to sell the business at a huge financial impact which put us under enormous pressure in addition to finding out he was seriously ill.”

“I am in partnership with my own business which had to be closed for 5 months.”

VII CONCLUSIONS & RECOMMENDATIONS

Myeloma is a highly individual cancer, including how the disease progresses and responds to treatment. Getting the best possible outcome for each individual's unique circumstances and reducing the overall burden of myeloma in New Zealand will require a unique approach.

This report recommends moves to hasten the public funding for proven innovations, remove existing restrictions on the available treatments and ultimately give blood cancer specialists the clinical choice to utilise their expertise and the proven treatments as the international evidence base indicates. This will become increasingly important as medical treatments become tailored to the individual characteristics of each patient based on genetic analysis ('precision medicine'). The current focus on cost must be balanced with the high quality of the outcomes delivered by new biologic therapies in particular. It should be noted that no new myeloma treatments have been funded in New Zealand in the past five years.

Our study, taken together with the findings of the survey of patients, also leads us to draw a number of more detailed conclusions and also reveals issues that warrant further investigation, as follows.

Conclusions

Epidemiology & clinical management

1. Myeloma incidence rates have increased since 2004, and these rates will continue to increase as the population ages.
2. Overall survival improved substantially for myeloma patients registered in 2012-2016 compared to earlier periods. Our study gives confidence that this was due to developments in the management of myeloma, including funding of bortezomib, ASCT and lenalidomide.
3. Patients who are 65 to 69 years of age at registration have relatively low uptake of ASCT. The reasons for this require further study. We note, for example, that in countries such as the US, ASCT is considered up to the age of 75, depending on individual fitness.
4. Overall, 36% of patients who registered in 2012-2015 received neither bortezomib nor ASCT therapy in the period 2012-2016. Some of these would have had serious comorbidities and others would have had 'smouldering myeloma' which did not require treatment during this period. Others could have declined treatment because of limited first-line treatment options, or limited access to infusion facilities. Moving infusions or subcutaneous injections into primary care or the home setting could improve adherence to bortezomib treatment and would also reduce the cost burden of outpatient visits.
5. An important finding is that most patients receive a suboptimal (less than the funded) dose of bortezomib, which could be driven by disease progression or by toxicity. This suggests a need for different management strategies and/or more choice in first-line therapies.

6. Socioeconomic deprivation is associated with lower uptake of ASCT following bortezomib, and is also an independent prognostic factor for overall survival, suggesting that poorer survival is associated with both poverty and poorer uptake of ASCT.
7. Māori, Pacific and Asian people were less likely than others to receive both therapies. The same ethnic groups were more likely to receive neither therapy. This should be further investigated.
8. Further research is needed to determine barriers to access. For example, could distance from treatment centres be a barrier? Lack of chairs in day wards could also be an issue.
9. Investment in dedicated myeloma nurses has also occurred during this time period, and this is likely to have led to improved uptake of chemotherapy, adherence, and promptness of provision. An evaluation of their contribution in this regard would be useful, to determine whether and how further investment could build on these benefits.

Clinical data collection

1. The Myeloma and Related Diseases Registry (MRDR) established at Monash University is an important resource for New Zealand clinicians and researchers, and can be used to supplement the NZCR, which contains little clinical data. While improving the quality of NZCR data remains a high priority, until such time as that is achieved clinicians and hospitals should be encouraged to enrol in the MRDR.

Costs to government and families

1. Compared to the general population matched for age and sex, in 2016 the annual healthcare cost per myeloma patient varied from about \$11,000 for elderly women to \$36,000 for young men, (population mean \$25,500). Improved therapies could provide cost savings to the government through benefits such as earlier return to work and improved productivity by both patients and caregivers, and recovery of tax revenue lost through absenteeism and early retirement.
2. As noted in the report, our costing of pharmaceuticals is based on list price (i.e. excluding confidential rebates), meaning the total cost of pharmaceuticals will be overestimated to an unknown extent.
3. Analyses of income and income tax in this report are limited by the incompleteness and inaccuracy of the IDI. However, compared to the general population matched for age and sex, in 2016 the disparity in income between myeloma patients and the general population matched for age and sex varied from about \$4,000 for older women to \$15,000 for young men. Loss of income by informal caregivers will increase this burden on families to an unknown extent.
4. Cost savings could be made in areas such as making more use of primary care, increasing allied health input, and achieving efficiencies in palliative care.

Living with myeloma

As part of this burden of disease study, Myeloma New Zealand conducted a survey of patients in September 2018 (see www.multiplemyeloma.org.nz) to gain their insights into the personal, psychosocial and financial costs of myeloma for New Zealanders living with this disease. The findings of this study have been published separately as part of this suite of reports, titled *Managing Multiple Myeloma in New Zealand: Patients' Perspectives*. The following is a summary of the survey's findings.

1. Myeloma has an immense impact on patients and their carers, both in everyday life and on their overall future. They have to come to terms with a shorter life expectancy and the reality of no known cure. Most patients experience fatigue on a daily basis, many are anxious and/or in pain every day, and many suffer from depression due to their illness.
2. Many describe heightened stress levels, falling self-esteem and confidence, feeling out of control and a loss of 'self' and personal identity and a heavy impact on their intimate relationships.
3. The most difficult challenges of living with myeloma are: fear and uncertainty; mental health issues, including sometimes terrifying mood swings and personality changes; loss of physical abilities, independence and income; coping with harsh medical treatments and procedures, and severe and debilitating side effects, and lack of preparation and emotional support for the 'journey'. For a few, however, myeloma has changed their perspective on life and taken them away from the 'treadmill of work'.
4. Time taken to diagnose myeloma is a significant issue. While most myeloma patients were diagnosed relatively quickly, many within three months, others described long episodes of GPs misunderstanding their symptoms, some being treated for flu or anaemia, with pain relief for back pain, and antibiotics for recurring infections, before eventually being diagnosed with myeloma.
5. A sizeable number of patients had suffered years of misdiagnoses and potentially preventable, debilitating pain, and felt the disease is not well enough understood, especially by GPs, but also by specialists. Quite a few had to move to another GP or make multiple trips to ED to get the correct diagnosis.
6. Going through a stem cell transplant was in many cases a harrowing experience for both patients and carers, although views were often coloured by whether or not the transplant was successful and the length of remission it provided. Severe nausea, fatigue, lethargy and diarrhoea, isolation due to the risk of infection, continuing compromised immunity and the very long road to recovery were among the worst aspects of the treatment.
7. The care and support of medical staff and their own family members, and being well prepared and fully informed were important factors in getting through the ordeal. The presence and support of dedicated myeloma nurses was highly valued.
8. The financial impact of a myeloma diagnosis is very significant. Over a quarter have had to leave full-time work, many having to stop working or retire early. While employers were generally supportive of the need for employees to take time out, patients and carers who had their own businesses or were self-employed were hard hit.

9. Almost a quarter of patients/carers have missed over 200 days of work since their diagnosis, significantly affecting income and increasing stress levels.
10. Insurance premiums and the costs of private specialists are the major contributors to the increase in patients' costs due to myeloma diagnosis. Alternative treatments, medications, and travel and accommodation are also significant costs. The average amount a patient or caregiver has spent annually in relation to myeloma is approximately \$7,600 and the estimated average loss in income of a myeloma patient since their diagnosis is over \$100,000.
11. Most patients/carers are satisfied with the overall level of care, although fewer are happy with the quality of treatment available in New Zealand, with almost a third feeling it is average or of low quality. There is a great need for simpler, more comprehensible information about tests and treatment pathways, more advice about what to expect as the disease progresses, and a guide to all the support services that are available.
12. Many want more information on research, treatments and clinical trials. Over half of patients or caregivers have at least some level of doubt about their understanding of their condition.
13. Some patients felt they were rushed into treatment after diagnosis, before having time to fully understand what was going to happen and the likely side effects. Patients and caregivers highly rate the level of support they receive from their family, their specialist and their haematology nurse.
14. Many patients have tried alternative or complementary therapies, and some found them helpful in managing symptoms, mental health, energy levels or reducing pain. Many felt just 'doing something' helps, but others were unsure of any benefit. Some patients still just felt very lost, tired and in need of more support and advice.
15. The majority of comments on what patients want concerned the need to advocate with government for funding new treatments. Improved myeloma therapies would ease the burden of the disease for patients, both in terms of reducing the costs they bear in relation to it and, more importantly, in improvements in quality of life and survival.
16. More seminars around the country from experts on an array of subjects would be welcome. Topics should include latest international research, advances in treatment, the various phases of myeloma, training for carers, pain levels and management, mental health issues, as well as question and answer sessions (preferably online), and the opportunity to meet and talk with other myeloma patients and carers.

Recommendations

1. Systems for collaboration, data collection and benchmarking to ensure equitable quality of care

The current New Zealand Cancer Registry (NZCR) lacks important clinical information and needs to enable better and more accurate data capture, to make it a more useful tool for ongoing comparison and monitoring of outcome. In addition, or at least until such time as the NZCR has been made more robust, clinicians should be resourced to participate in the Monash registry.

2. Efficient delivery of medications

Medication is a major cost and needs to be delivered efficiently so that the patient receives the full benefit of the treatment. Initiatives such as district nurse administration, partnering with local general practice and providing equipment for patient self-administering at home should be considered.

3. Facilitating access to compassionate-use programmes

Some medications available in other countries but not currently funded by Pharmac are available to patients via compassionate-use programmes set up by pharmaceutical companies. However, some centres are unable to make full use of these programmes due to lack of infusion chair time and nursing staff. Resolving these capacity issues is likely to lead to better treatment options for the patients at a fraction of the cost

4. Investment in more effective earlier lines of treatments

As the duration of remission is likely to be the longest during first remission and second remission, investment into better access of novel therapeutic agents in earlier lines of treatment is most likely to lead to better quality of life and less time off work, delay the need for residential care, and improve life-expectancy.

5. Supporting and facilitating the conducting of clinical trials in New Zealand

Another way to improve access to medicine for patients is to work collaboratively with pharmaceutical companies in the formatting and conducting of clinical trials. New Zealand is well positioned for conducting clinical trials due to our small geographic size with relatively dense population in major centres, high quality clinicians and first-world healthcare systems. There should also be equitable access to clinical trials across New Zealand, including support with travel costs if required. Ensuring all eligible patients are offered participation in clinical trials may also lead to better clinical data on effectiveness.

6. Improving support, information and advocacy for patients

Patients and carers need better preparation and support throughout the treatment process, particularly when undergoing difficult procedures such as ASCT. This includes access to counselling and mental health support, ways to connect with other patients and support groups, and training for caregivers, particularly in coping with patients' depression and mental health issues.

They also need more, better information, presented in a way that is easy to understand, and at the right time. They want information including seminars and expert talks about: the disease and its many treatments; survival rates; new treatments; clinical trials and research; and compassionate access programmes.

Patients want Myeloma NZ and other related patient groups to actively advocate to government to fund new treatments and facilitate the opening of more clinical trials and access programmes.

They also see better education of GPs and medical professionals to improve understanding of myeloma as critical. Upskilling doctors at the frontline should lead to earlier tests and earlier diagnoses.

Patients and carers would also like to see greater public understanding and awareness of myeloma.

7. Investing in research and facilitating collaboration among centres engaged in research

Although great work is being done in local hospitals and universities, this is often done in isolation without additional funding or support from the government. Direct investment into these stakeholders and facilitation of collaboration between centres would allow streamlining of research and reduce overlap.

8. Introducing performance-based risk management and cost-effectiveness analyses

In addition to ongoing price negotiations, performance-based risk management of pharmaceutical therapy could be introduced. It might also be possible to divest from some treatments with minimal real-world benefits across the disease spectrum in order to focus on those medicines with larger proven gains. Ongoing improvements in patient selection, and increasing use of generics, are likely to be important in the future.

9. Research funding for New Zealand-specific economic evaluation of therapies to treat myeloma

This should include ASCT, novel pharmacotherapies and cancer care management using real world evidence as distinct from clinical trials, as shown in this report. There is also a need for methodologically comparable studies across all major cancers, especially those that are particularly costly and/or have high prevalence.

10. Further research based on the findings of this report

The following issues identified in this study require further investigation:

- small but meaningful differences in survival for patients living in different cancer regions: further study could identify the cause for these differences, and facilitate best management practice in all regions
- the large proportion (36%) of patients who registered in 2012-2015 who received neither bortezomib nor ASCT therapy in the period 2012-2016: potential reasons for this finding are outlined above, but the issue is significant and worthy of further investigation
- the association of poorer survival both with poverty and poorer uptake of ASCT
- the causes for the higher age-standardised incidence rate in Māori and Pasifika peoples
- the finding that most patients receive a suboptimal dose of bortezomib
- barriers to access, such as distance from treatment centres and availability of chairs in day wards, and
- the relatively low uptake of ASCT by patients who are 65 to 69 years of age at registration, given that in countries such as the US, ASCT is considered up to the age of 75, depending on individual fitness.

VIII PATIENT & CARER STORIES

Names and identifiers have been changed.

John

In 2004 I was a consultant working in Auckland, in my mid-40s. After a few strange symptoms, I was lucky enough to find a rheumatologist who was able to diagnose sarcoidosis. Unbeknown to me, those who have sarcoidosis have a higher risk of developing Myeloma.

Within 18 months the symptoms of sarcoidosis receded, however a final blood test by the specialist showed something unusual, so I was transferred down the corridor at North Shore Hospital to see the haematologist where I was diagnosed with Smouldering Myeloma in late 2005. Regular monitoring with four-monthly blood tests followed.

In 2009, blood tests showed that the blood condition had changed from 'smouldering' to progressive Myeloma. One prognosis I was given was 24 months, due to the presence of an aggressive clone. Luckily a brand-new drug called bortezomib (Velcade®) was available for my induction chemotherapy, albeit unfunded. So, I borrowed \$20,000 and proceeded to have induction chemo towards the end of 2009.

Since 2009, I seem to have either been in treatment, or recovering from treatment. I have had at least four cycles of chemo for Myeloma, and induction chemo for autologous and allogeneic stem cell transplants, followed by Donor Lymphocyte Infusions. I have become resistant to all the front-line drugs that Pharmac provides, so my options are limited to clinical trials or private supply. I have also had to have gruelling chemotherapy for Acute Myeloid Leukaemia (AML), another fatal blood cancer, caused by the treatment for Myeloma, due to highly unusual circumstances.

It has been almost impossible to carry out any work, especially given the highly specialised nature of the consultancy services I provide, and the fact that 'chemo brain' is real!

My family life and social connections are under stress, as someone frequently on high doses of steroids is not pleasant to live with. My bone marrow has been compromised by all the chemotherapy, and the consequent lowered immunity limits my social activities and friendship maintenance. I have had shingles and have been hospitalised through emergency admissions numerous times for neutropenic fevers and respiratory tract infections.

I am currently undergoing intensive chemotherapy for myeloma over nine months, and the results thus far have been very good, although not the complete remission I was hoping for. Hopefully the treatment will buy me a little breathing space where I am treatment free, and new drugs become available.

Finally, even though I have two fatal blood cancers, I feel very lucky. My appreciation of every day, my awareness of the good things moment by moment, is far heightened over the distant time when I was working full time. I have survived far longer than predicted, and the AML is currently in remission.

Briar

How the Multiple Myeloma has affected me and my family

Numb: On 20th September 2016 my GP told me my bloods indicated Multiple Myeloma. Further tests were required. Two days later it was confirmed. My partner, of 30 years, and I went numb. We didn't even know what Multiple Myeloma was.

Sad: We had little sleep for three days and just held each other and cried. Research told us it was incurable, and we felt a tsunami of sadness for so many reasons.

Acceptance: We quickly accepted the diagnoses and went into total research mode needing to know everything there is to know about this cancer. The more we found out the **sadder** we felt. We have fought many things during our lives but never a fight I would ultimately lose regardless of the intensity of our fight. Our lives were changed forever and the sooner we accepted this the better.

Financial Loss: Chemotherapy starts and our weekly drive from our distant residence to North Shore Hospital in Auckland dominated our week. We run a home accommodation business and had to reduce bookings and ultimately close it for 5 months. The costs remained the same – but little to no income. This, along with the cost of travel, hit us badly. I was declined any type of government benefit. Early superannuation due to my partner being a superannuant was declined, as it is means tested. For the first time in 40 years I had to be financially reliant on someone else – **humiliating**. The financial losses got worse as treatment progressed to and through Stem Cell Transplant – mine went terribly wrong and my recovery was long and slow.

Unsafe: No matter where I went, I felt so unsafe. Fear of catching any infection overtook me. I wore a mask in theatres, public transport, meetings etc. I could no longer 'meet and greet' guests arriving to our business. This put a huge load on my partner.

Buck up: A few months after diagnosis everything changed, and I went into fight mode. I dug deep and found every survival gene within me.

Stem Cell Transplant: Could anything go more wrong. Ending up in critical care and on life support was a nightmare of the worse kind imaginable. Family were gathered; accommodation and air fares had to be thought through. How valuable are friends. However, the psychological scars from this horrendous experience were to last for months and months. Months of sobbing every day and physical weakness leaving me unable to be left alone. I was terrified of darkness and of life itself. The **psychologist** made available to us was invaluable and a huge part of my recovery.

My partner: She is resentful of the massive aging effect it has had on her yet totally dedicated as a caregiver she never faulted but has paid a huge price. Some home help would have been worth diamonds.

My daughter: How Myeloma has affected her family "It has changed our perception of you. We always knew you were tough, but this has really highlighted how super strong and brave and positive you are. It increases our respect because it's very impressive how your attitude has been so positive. It's given me a great example for my own children to be positive. We've always thought of you as so young, so having a mortality scare makes us all realise your role as grandmother and, I guess, matriarch is more recognised".

Summary: What a ghastly experience SCT was. I want to live, and I want a respectful death. I am a fighter for medicinal cannabis and euthanasia. Whoever said, 'an attitude is a bad thing'. That's how I got through to today. I love life and, damn it, I'll live it to the end.

A GIFT: Given I am 65 now, in some ways I consider this cancer a gift. I have had time to access what is and isn't important. No more mucking around. Catching up with people and putting things to rest OR thanking them for their role in my life.

I am living with cancer – not dying of it.

Samuel

21 Years Visiting Riddiford St

The first indication of the cancer occurred while I was doing the Tongariro Crossing in 1997. I had some pain in my groin, which I convinced myself was muscular. It occurred on and off over the following months, but I still believed I had pulled a muscle, or something similar.

It was not until I was referred by a physiotherapist to a sports medicine doctor that it was discovered I had a somewhat rare plasmacytoma on my pelvis, in effect a single myeloma tumour. Plasmacytomas can be killed stone dead by radiation and mine was blasted away over Christmas and New Year of 1997/1998.

So, at my 50th birthday in February I was able to tell the family I was cancer free – provided it had not metastasised. The radiologist had told me the chances were 50/50 - he was right, but I got the wrong 50! By November 1998 the myeloma was back.

My treatment - three types of chemotherapy over the following 12 months - was a failure. With the proportion of myeloma cells in my bone marrow rising to dangerous heights, the question arose as to whether I should have an autologous bone marrow transplant. The transplant was a huge success and I went into remission for almost 18 months.

It is from this point onwards that I think my myeloma story is most interesting. When I was diagnosed, I told my wife that if I could just hang on for a few years I was confident new treatments would come through. For reasons I cannot explain, I did not even remotely think that the cancer would kill me.

So far, I have been right. Through an extraordinary set of circumstances - too long and complex to explain here - the ugly old drug thalidomide had been shown to be effective first with leprosy, then with multiple myeloma. After causing severe deformities in 12,000 babies, the morning sickness drug was offering hope to myeloma patients around the world.

In my case, I was hyper-sensitive to it and the myeloma was under control for around 14 years. Over that time, I experienced virtually no side-effects, living a perfectly normal life ... tramping, mountain biking, travelling overseas and enjoying an active cultural life here in Wellington.

It's a cliché but fair to say that all good things do come to an end. In my case, that happened about two years ago. The myeloma was on the march again just as I was about to encounter two major health problems – an urgent need to replace a calcified aortic valve, followed some months later by two days on a life support machine then four weeks in hospital suffering from septicaemia.

Over this period, treatment for the myeloma had to be abandoned, resulting in its inexorable rise month after month.

Fortunately, ... and as I had hoped ... new myeloma drugs have been developed over the past twenty years. I'm now on Velcade and dexamethasone, a combination which has suppressed the myeloma to almost non-detectible levels.

Of course, the future of any cancer is always uncertain, but I still believe it won't kill me, not least because there are yet more new drugs on the horizon and one or another of them will do the trick! I must also pay tribute to the wonderful professionalism, care and compassion of the Wellington Blood and Cancer Centre team.

Robert

I was diagnosed with IgG Multiple Myeloma in March 2009 at the age of 46 years 8 months. Initial diagnosis was via my GP who took a blood test because I had a summer cold that wouldn't clear. Two days later I was in Auckland Hospital. My haematologist wanted me to start chemotherapy the following day, but when I asked him about having children, he delayed treatment so that sperm could be captured prior to treatment. This put us on the expensive path of IVF, and three cycles later we were pregnant and had a son in March 2011. At that point in time I was working for a large infrastructure company as a Performance Excellence Advisor.

After induction treatment I underwent an Autologous Stem Cell Transplant at the end of July 2009. I was told that this had an impact on the body like open heart surgery, and not to expect to return to work for 13 plus weeks. Unfortunately, I had a job to consider and so pushed my recovery with a return in 6 weeks. Fortunately, none of my employers wanted me to reimburse the company for the time off. A case of "there but for the grace of God go I". In January 2012 I was made redundant and until June 2015 was only able to get employment in short term contracts, mostly with organisations I already had relationships with. During this period, I was constantly seeking full time employment, but most online applications required statements about health and (despite being informed by the Human Rights Commission that this was only required when discussing employment contract terms) it is impossible to bypass these questions. In some ways this was somewhat of a godsend as I was participating in the Endeavour trial which required attendance at a clinic at least 3 days per week, although the side effects were minimal.

Eventually in June 2015 I was employed by a Not for Profit agency, firstly as a contractor, then 0.8 FTE, then as General Manager (0.8 FTE followed by 0.6FTE) and currently as a contractor doing the jobs of the GM. This unusual set of circumstances surrounding my employment is to show what people in my position are prepared to put up with to stay in some form of employment. This is particularly pertinent, considering that I have at least 10 years until retirement and need to ensure that my family and I are in a position financially that allows me to retire. I was told when diagnosed that most people diagnosed with myeloma are 65 or over. This means they have a totally different perspective on life. Up until mid-2016 I had not experienced the cancer itself, but more the side effects of chemotherapy.

In about August 2016, three events seemed to coincide: the treatments stopped working, the next option meant a referral to North Shore Hospital, and my address changed to Titirangi which changed my hospital from Auckland to North Shore. This change means a further 30 minutes' drive

over what it would take me to drive to Auckland hospital. In addition, depending on the time of appointments, I cannot guarantee making them on time in Auckland's rush hour traffic. Currently I find myself after 10 years of treatment at a point where despite the continued efficacy of the chemo prescribed, my body is becoming less tolerant and resilient to them. Regrettably this is coinciding with a requirement to seek new employment, but not knowing what to tell a prospective employer about my health status.

Being at this point on the cancer continuum, i.e. the survivorship stage, I have found several omissions in people's perspectives on cancer. Firstly, there is a belief that if you are not on chemotherapy, are possibly in remission and look OK, then there is nothing wrong with you. This is a fallacy, as there is a likely degenerative effect of all drugs taken. Secondly, survivorship is a very personal perspective of the patient and his or her context, and as such is difficult for support agencies to deal with because there is no silver bullet for all patients. This is probably why Diagnosis, Treatment, Palliative Care, and Education have all been put on a path of continuous improvement, but survivorship has been ignored.

Susan

When I was first diagnosed with Multiple Myeloma 6 years ago, I had never heard of the disease and knew nothing about it. It was discovered only when I damaged my spine hauling a heavy suitcase in (of all places) Paris. It seems that a good number of cases are diagnosed because of a fracture or something similar. Things moved very fast, with my GP sending me off to Haematology at North Shore Hospital and treatment beginning without delay. At first this was Velcade (bortezomib), Cyclophosphamide and Dexamethasone for 6 cycles after which I underwent a stem cell transplant at Auckland City Hospital. This went well and a few months later I completed a further 3 cycles of the above. I didn't have too many problems with the Velcade treatment, very little nausea and perhaps one or two days after each treatment when I just felt generally tired and unwell. In fact, fatigue has been the main problem with all treatments, some more so than others.

After the Velcade cycles I was in remission until November 2016 when I began Lenalidomide/Dexamethasone treatment. This was continued until October 2017, but it seemed to be less effective after a break while I had back surgery. Since then I have been on Carfilzomib/Dexamethasone which has been effective for the myeloma. I have, however, had some problems with shortage of breath, which seems to be linked to the drug. Other than that, the main problem is the fatigue which seems to be present regardless of the treatment. The myeloma seems to have taken over our lives over the past 6 years, especially the last few months, with twice a week infusion at the hospital plus the usual clinic visits, blood and various other tests and so on. It is fortunate that my husband and I are pretty much retired. I am not sure how we would handle the appointments if either of us were working full time not to mention the fatigue which, at times, is very draining.

I cannot stress strongly enough how important it is to have a support person whenever possible for all these procedures. I don't think my husband has missed one of the many appointments I have had over these 6 years. What is significant is that when I was undergoing the stem cell transplant at Auckland Hospital the specialist haematologist was not optimistic about the survival rate for myeloma patients. I did, in fact, wonder if it was worth going ahead with the transplant but now, 5 years later, it has all been worthwhile. I have also found great support with the 'Leukaemia and

Blood Cancer' (LBC) meetings and forums. Initially I was not keen to attend ("my name is and I am an alcoholic" phobia) but it wasn't like that at all. I can safely say that at every meeting you learn something useful and the support has been invaluable. The same can be said for Haematology Day Stay at North Shore Hospital. The staff have always been helpful and supportive, and we appreciate everything they do.

Jim

I was jogging in early 2001 when a sharp pain in my hip left me barely able to walk. The GP diagnosed a groin strain, and the physio recommended a set of exercises that seemed to be improving things, until a winter ski crash had me hobbling again. An X-ray confirmed that my hip had been weakened by multiple myeloma. As an aside, before seeing the specialist who confirmed the diagnosis, I showed the X-Ray to a surgeon friend. He examined the dark smudges on the image and said quietly "this needs to be investigated". Some years later he told me that what he was really thinking was "Jim won't be with us much longer".

Which brings me to survival. When I was diagnosed, multiple myeloma was generally considered to have a 3-4 year median survival, which of course sounds scary. But the distribution is skewed, with a long tail of people who survive much longer than the median. If you're otherwise healthy, you've got a good chance of being in that long tail. Biologist Stephen Jay Gould wrote an excellent essay explaining this: "The median isn't the message" <https://www.cancerguide.org/median_not_msg.html>.

In 2002 I had a relatively uneventful stem cell transplant, and was symptom free through to 2007, when lesions appeared in my chest and spine. Since then the journey has been an approximately 2 year cycle: (1) relapse (2) have radiotherapy and chemotherapy (3) achieve stability (4) repeat.

I've been fortunate that when I've relapsed, there has generally been a new and effective treatment available, either through Pharmac funding, or through a drug trial or compassionate access. It's only one of the most recent drugs, Pomalidomide, that we've had to self-fund. I'm grateful to the medical staff who have navigated the often byzantine drug regulations to achieve this.

The flexibility of my work as a university lecturer, and tolerant colleagues, meant that I had a satisfying career until I retired in 2014.

The biggest impact of multiple myeloma has been on recreation. I had to give up running and skiing, and scale back tramping trips - although I walked the Routeburn track in 2014. But I've kept up cycling, more recently with the assistance of an electric bike. When I thought that my legs might not be up to carrying me for long distances, I took up sea kayaking. Thanks to travel insurance that recognises pre-existing conditions, I've been able to continue overseas travel, most recently a family bike ride down the Rhine river, although I have to be careful of fatigue.

Cycling has been a big part of my life - as well as recreation, it has been my main transport around town. I've been able to bike to the majority of my hospital appointments, and I think the fitness engendered by cycling has helped me survive the rigours of treatment.

My myeloma journey has been a "good" one, if such a thing is possible. For this I have to thank my ever supportive partner, as well as the medical staff. I'm aware that had things been slightly different - if the stem cell transplant hadn't lasted as long, for example - the journey would have been rockier.

Jessica

The words “Multiple Myeloma” changed every aspect of my life. I still remember the day I first heard those words vividly, a beautiful Sunday morning in the middle of summer. I was 29, carefree, putting in offers on what we hoped would be our very first home, planning on expanding our family. In the blink of an eye that day my entire world fell apart. Becoming a caregiver to my husband hadn't featured in my dreams of the immediate future. My biggest dream now is our daughter growing up with her father. It still seems such a foreign dream for someone my age to hold onto so ferociously.

My rock, the strongest man I knew was in immense pain. The most attentive and playful father could no longer pick up or play with his baby due to numerous fractures. The main provider for our family could no longer work. The confident man I fell in love with began to suffer from anxiety and didn't want to be left alone. My comedian, the most beautiful, brightest soul I have ever met stopped smiling, stopped laughing. Thank goodness I've got him back for the most part, but I think it's a carer's love and energy that feeds their patient, so I run on empty.

It's hard to pinpoint words to describe the impact Myeloma has had on our family and particularly myself as a caregiver, yet not one area of my life remains untouched. The option of having more children being taken away due to treatment was one thing we both particularly struggled with. It was just one more choice, and part of our future that had been taken away by this disease. This is the one and only aspect that we found lacked a lot of early discussion, possibly as majority of people diagnosed with Multiple Myeloma tend to be older.

Practically, it's incredibly difficult being a carer and juggling a young child. Providing my husband with the best care and as much love as possible, whilst keeping our baby's life consistent. Minimising any negative impact to ensure a happy, loving, fun filled childhood that every child deserves. There aren't enough hours in the day to do both to what I feel is the standard they deserve whilst working to put food on the table. Guilt is a regular feature in my mind now days.

Financially we have lost everything we worked for. It took over a month to even get a WINZ appointment booked. We have encountered many costs since diagnosis and although most treatments are funded, sometimes there are better treatments available which unfortunately aren't funded in certain circumstances.

I'm a positive and strong person but this illness is a hideous beast and takes its toll on all within its reach. Emotionally I'm completely drained. I'm a mum, a wife, the provider, some days I'm a nurse, a counsellor, the pharmacist, his advocate, the protector, I'm terrified, I'm wiser and much older than my years.

Tania

My husband was diagnosed with myeloma a few years ago at the age of 45. At the time our two sons were aged 7 and 4. Like most of the population we knew very little about this nasty disease, but we became fast learners.

Within a year and a half my husband had undergone high dose steroid treatment, radiation therapy, induction therapy, high dose chemotherapy with autologous stem cell transplant and some

follow-up chemotherapy when he was well enough after the transplant. Overall the process of treatment and recovery took him away from full-time employment for about 2 and half years.

The memories of this crazy time are a little bit blurry now, but some things stand out. The support of our family and community. The meals, the school and kindy pick-ups and the much-needed hugs. Our 7-year-old correcting me with 'don't you mean plasmacytoma' when I referred to a tumour as a 'lump'. Those young ears and minds don't miss a thing. The kindness and understanding of employers. The uncertainty and fear for our future. The incredible people that serve our hospitals.

The anxiety of relapse is never far away, but we do our best to focus on raising our family and getting on with life.

People often think if you have cancer, you're either cured or you're dying. We have so much hope in new treatments that I try to think of it as living as best you can with cancer. I try to think of it as a chronic illness rather than a terminal one.

Ben

My wife's initial diagnosis (4.5yrs ago) was very traumatic – having gone to AE with muscles spasms in shoulders - only to be told a few hours later that it was a broken neck caused by multiple myeloma (which we had never heard of before). Our life (and I believe our children's lives) changed from that point on. We had been planning to travel to Australia the next week to visit our daughter and I had just started a new job following major heart surgery. The holiday was cancelled, close family had to be told, then friends, and special arrangements had to be made so I could work remotely - all very stressful whilst navigating an unfamiliar medical landscape.

The initial shock lasted a few months while we came to understand what multiple myeloma was, but the complexities of the disease, the science and various treatment protocols took much longer to absorb, and we continue now to try and keep pace with recent developments. It is always changing.

The longer-term impact has meant my wife had to give up her job as a practising psychotherapist, and I have taken early retirement to spend more time with her while she is well. My daughter came back from abroad with her partner and settled in Auckland...and my son separated from his wife (which may have been due in part to the added stresses of his mother's condition). I started drinking more heavily than I had done in the past. Fortunately, money was not an issue since we had been prudent and planned well for retirement during our 35 years of marriage

However, there have been positives. I finally recognised I had a drinking problem and joined AA and have now been sober for 2.5 yrs. I am closer and more emotionally available to my wife now more than ever. We were always close to our children, but now I think we are more honest as a family. We can cut through all the noise & busyness of life in general and make decisions more easily. We know and appreciate what's important and tend not to put things off, rather do things now & live in the moment, plus we have become more spiritually aware, and we don't take too much for granted.

Saying all that – it is still very difficult to live with multiple myeloma. The emotional roller coaster has very high and low dips. Our understanding and compassion are often stretched and after 3.5yrs in a treatment-free, very good partial remission, my wife relapsed and following several

months back on chemo-therapy, she is soon to undergo her 2nd stem cell transplant. The stress and worry returns, and with it a sense of again facing the unknown.

Our life currently, orbits around doctor's appointments, blood tests and hospital visits. We are firmly back in the hospital system. The different treatments 2nd time around have caused new and more severe side effects, but we are hopeful that she will again make a good recovery and whilst it probably won't be a drug free remission this time – we understand that the maintenance regime is better tolerated.

We live in hope that a cure for this terrible disease will not only be found (in the not too distant future) but will also be readily available and accessible for those of us who live in New Zealand and who need it.

James

Because we were reasonably well-off financially, and had a family of adult children, the practical and financial burdens of myeloma were not too severe, but the emotional roller coaster was huge.

1. *Diagnosis*

"MGUS with a high probability of multiple myeloma"

Lethargy and quite a few unusual pains including rib pain led my wife to the GP initially, and IgA readings from a blood test produced this diagnosis. It was 2002 and she was aged 56. We were about to meet our children overseas involving a three-month journey. Her reaction to being told a bone marrow biopsy was needed to confirm whether or not she had myeloma, was: "Well, we are going overseas and if I've got myeloma, I would rather not know until we come home."

I accepted this was the right decision for my wife, but I was in the agonising situation of not knowing for nearly five months, during which time I did a great deal of research and reading about the disease, concluding that the future was bleak.

On our return we undertook the bone marrow biopsy with the result being a negative diagnosis of myeloma. The relief, particularly for me, was quite extraordinary. My wife put it out of her mind.

"Likely active multiple myeloma with spinal lesions"

Seven years later my wife developed significant back discomfort and, after several visits to her GP, a young relieving GP picked up on the MGUS diagnosis and sent us immediately to a haematologist in Dunedin. She was then admitted to public hospital with the above diagnosis confirmed from blood tests, a scan and a bone marrow biopsy.

After much discussion we decided that a stem cell transplant was her best hope of life extension, and immediate radiotherapy to deal with her spinal lesions was undertaken. My wife's attitude and reaction to this was amazing. She often said "I'm not going to concern myself about this. They know what they're doing, I'm in their hands." I was devastated and wanted to know all of the implications and possible treatments.

Immediately after the radiotherapy we drove home, a three-hour drive from Dunedin. Later that evening her legs became completely paralysed. She had no wish to return to hospital on Easter Thursday, so we battled through the night trying to manage her pain and paralysis. Fortunately, a

GP friend who was in town came around at 8.00am with an immediate diagnosis of post-radiation swelling around the spinal cord, which would likely dissipate by the afternoon, and it did.

2. *Pre-stem cell transplant chemotherapy*

This was a terrible five months, with nausea, hair loss, weight loss, total lethargy, and multiple side effects from nerve damage, steroid induced changes, and infections. We were told only 16% of patients get any benefit from this gruelling treatment.

3. *Stem cell transplant*

A seven-week spell in Christchurch Public Hospital included a successful stem cell harvest, bone marrow destruction, a near death experience, extreme illness which required supervision from ICU staff, and slow recovery.

4. *Remission*

The next 18 months was a time of hope and we restored our lives to reasonable normality. We planned to go to India to get Velcade which wasn't funded in NZ.

5. *Relapse*

After that brief reprieve, pain returned, and a scan showed many new lesions. I was devastated, while my wife switched into practical mode, getting things into order. We went to Hanmer Springs for a break, then told all three of our children, a hideous task.

When it came to considering further treatment, we discovered she had contracted an avian strain of tuberculosis, which made further treatment impracticable. She developed shingles during this time and gradually declined.

6. *Death*

My wife was 64 when she died a harrowing death in a local hospital. She managed a trip to Australia with our whole family including a newborn granddaughter four weeks before she died. She was extraordinarily courageous, caring more for her husband and family than herself. Her pain was reasonably well-managed, but we had one long Sunday night after a GP had left her vomiting and in much pain without providing the relief she needed. Next day she was fitted with a morphine pump. A long trip in an ambulance to Dunedin for more radiotherapy which she didn't want was a mistake. It was traumatic, made her ill and did not prolong her life.

7. *Grief*

About three weeks after my wife's death I went into a terrible decline, overwhelmed by the loss. I went to my GP who, without attempting to talk to me, just handed me a script for sleeping pills and a therapist's business card. I changed to a more sensitive GP and was put on an anti-anxiety drug, which did not remove my grief but took the sharp edge away and made me feel back in control.

8. *What we needed to know*

- possible side effects from spinal radiotherapy
- likely outcome from oral cortisone – the possibility of post dosage depression
- infection risk and essential protection – a check list of essential post stem cell transplant vaccinations including shingles. (My wife suffered a shingles episode which left her in pain until she died).
- high infection risk places to avoid. We went to the Hanmer Hot Pools which is probably where she picked up her avian TB infection. We should not have done that.
- If you can't get help from your GP when you hit rock bottom, where else can you turn?

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© Myeloma New Zealand 2019
Published by Myeloma New Zealand
Registered Charity No. CC53924
PO Box 25162
Wellington 6011
New Zealand
www.multiplemyeloma.org.nz

ISBN: 978-0-473-48522-1 - print
ISBN: 978-0-473-48523-8 - online/PDF