Bone Marrow Transplant Services in New Zealand for Adults

Service Improvement Plan 2011

Citation: Ministry of Health. 2011. *Bone Marrow Transplant Services in New Zealand for Adults – Service Improvement Plan*. Wellington: Ministry of Health.

Published in September 2011 by the
Ministry of Health
PO Box 5013, Wellington, New Zealand

ISBN 978-0-478-37350-9 (online)
HP5415

This document is available on the Ministry of Health's website:
http://www.moh.govt.nz

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Executive Summary

Bone marrow transplants (BMTs) in New Zealand are provided by five District Health Boards (DHBs): Auckland, Waikato, MidCentral, Capital and Coast and Canterbury. Recently there has been significant growth in demand for BMT services, most evident at Auckland DHB.

This service improvement plan signifies the start of a process for increasing capacity and improving the delivery of BMT services in New Zealand. It has been developed to assist DHBs to plan for adult BMT services over the next three to five years.

The plan recommends that the current configuration of BMT services is continued in New Zealand; that is, that autologous BMT services continue to be provided at Auckland, Waikato, MidCentral, Capital and Coast and Canterbury DHBs and allogeneic BMT services at Auckland, Capital and Coast and Canterbury DHBs.

In addition, the plan identifies four main areas of service improvement:

- development of national clinical indications, consistent with international best practice
- addressing capacity issues – including physical resources and specialist staffing
- improving waiting times for BMT services
- international accreditation of BMT services and facilities.

The *Bone Marrow Transplant Services in New Zealand for Adults- Service Improvement Plan* has been developed by the Ministry of Health and the Haematology Work Group (HWG). The Cancer Treatment Advisory Group (CTAG) and Cancer Control Steering Group (CCSG) endorsed the plan with the proviso that if clinical indications or eligibility are reviewed and amended then the plan will need to be updated accordingly.

Recommendations

The Cancer Control Steering Group recommends that District Health Boards:

1. **agree** to model capacity requirements for their respective populations

2. **ensure** that they are able to respond to increased Bone Marrow Transplant volume growth appropriately

3. **provide** accurate Bone Marrow Transplant costing information to inform national pricing work

4. **continue** the current configuration of Bone Marrow Transplant services in New Zealand; that is:
   - provision of autologous Bone Marrow Transplant at Auckland, Waikato, MidCentral, Capital and Coast, and Canterbury District Health Boards
   - provision of allogeneic Bone Marrow Transplant at Auckland, Capital and Coast, and Canterbury District Health Boards

5. **note** that the Haematology Work Group has revised and updated the national clinical indications for Bone Marrow Transplants

6. **agree** to adopt the clinical indications to ensure nationally consistent access to Bone Marrow Transplant services

7. **note** that the haematology nursing workforce is at full capacity at the current level of demand for Bone Marrow Transplant services

8. **note** that the Health Workforce Information Programme will provide workforce forecast information and analysis to assist in Bone Marrow Transplant nursing workforce planning

9. **note** considerations outlined in this document applicable to patients readmitted via hospital emergency departments

10. **implement** the Bone Marrow Transplant waiting time criteria outlined in this document

11. **note** that the Haematology Work Group will monitor Bone Marrow Transplant waiting times

12. **note** that international accreditation of Bone Marrow Transplant services as set out by the Foundation for Accreditation of Cellular Therapy (FACT) is likely to be required in the near future, so that New Zealand services can participate in international BMT studies and gain access to international matched unrelated donor (MUD) donations.

Introduction

Purpose

This document provides:

- an overview of current BMT services in New Zealand, focusing on current issues of projected growth and demand
- advice for DHBs on planning for adult BMT services in New Zealand in the next three to five years
- advice for DHBs to ensure New Zealanders' access to BMT services is equitable and consistent with international best practice.

Authors

This document has been developed by the Ministry of Health and the HWG, a work group of the CTAG. The CTAG provides clinical advice to the CCSG, a joint DHB/ Ministry of Health governance group within the National Cancer Control Programme.

Endorsement

This document is endorsed by the CTAG and the CCSG.

Audience

This document has been developed for DHBs, to guide service planning. It is relevant to the following groups:

- DHB chief executive officers
- DHB clinicians
- DHB planners and funders
- regional cancer networks
- Ministry of Health officials.

Scope

This document covers the next three to five years.

Exclusions

This document covers BMT services for all people aged 16 years and over. It does not include paediatric BMT services: these are provided at Starship Children's Hospital as a national service.

Overview of Bone Marrow Transplants

What is a bone marrow transplant?

A BMT delivers healthy bone marrow stem cells to a patient, to replace existing marrow. This procedure is performed after the patient has received high-dose chemotherapy and/or radiotherapy, usually as treatment for their blood cancer.

BMT may be recommended for the treatment of:

- high-risk blood cancers such as acute and chronic leukaemia, lymphoma and multiple myeloma
- non-malignant disorders, including bone marrow failure and inherited immunodeficiency disorders.

Types of bone marrow transplant

There are two types of BMT, as follows.

1. *Autologous BMT*. For this procedure, stem cells are taken from a patient before he or she receives chemotherapy or radiation treatment. After very high doses of chemotherapy or radiation have been completed, the patient has their own stem cells reinfused.

2. *Allogeneic bone marrow transplant*. For this procedure, stem cells come from the bone marrow or blood of another person: a 'donor'. In most cases a donor must have the same tissue type as the patient; that is, they must be a 'fully matched donor'. Matching is determined by highly specialised blood testing known as tissue typing. There are four types of allogeneic donors, as follows.

    a. Matched sibling donor: a patient's brothers and sisters have the highest chance of providing a suitable match. There is about a one in four chance of a sibling's bone marrow matching the patient's.

    b. MUD: when patients do not have access to a fully matched sibling donor, an unrelated donor is found through data bases of registered volunteer unrelated donors maintained by New Zealand and international bone marrow registries. Generally MUD bone marrow provides a full match; if not, the transplant carries higher risks of graft versus host disease (GVHD) and poorer outcome.

    c. Unrelated umbilical cord blood (UCB) donor: for patients with hematologic malignancies lacking access to a matched sibling or MUD donor, unrelated UCB transplantation is an established alternative. There are now about 500,000 frozen UCB units held in banks around the world available for international exchange. UCB transplants have several advantages over MUD transplants: UCB units are promptly available; there is a potential reduction in chronic GVHD following transplant; and there is improved immune recovery, resulting in similar patient survival rates to MUD transplants. Greater human leukocyte antigen (HLA)-matching disparity is

acceptable for a UCB unit compared with one from a MUD donor, meaning that there is a greater pool of appropriate donors. However, the UCB cell dose is critical to the outcome of the transplant. Initial studies of UCB transplant were performed in younger children because of their lower body weight: they received a higher UCB cell dose per kilogram body weight. There are now well-established threshold cell doses for adult UCB transplant; higher cell dose units are available; and new transplant technologies, including the use of two UCB units, are available for successful transplant of adults. Many unrelated UCB transplants have been performed in children in New Zealand: Starship Children's Hospital has performed over 50. Uptake of adult BMT units has been much slower, but will certainly increase as a result of improved understanding.

d. Haplo-identical family member donor: an alternative strategy for patients without a matched allogeneic donor is use of a haplo-identical family member donor. This type of transplant requires a significant change to the transplant methodology, but may increase options for allogeneic BMT in patients without suitable matched allogeneic donors.

Both unrelated UCB and haplo-identical BMT increase the potential application of allogeneic BMT in patients previously ineligible for BMT because of a lack of appropriate donor. It is recommended that, in New Zealand, UCB and haplo-identical transplants be provided at a single centre, due to their high complexity and low volume compared with other BMT methods.

Method of transplant

For most patients, a bone marrow transplant follows high doses of chemotherapy, radiation treatment or both. Such a transplant is called an ablative (or myeloablative) transplant. It kills any cancer cells that might remain, and makes room in the bone marrow for new stem cells to grow. Radiotherapy treatment may require total body irradiation, which is a complex procedure and requires careful coordination and planning with the radiation oncology service.

Over the last 10 years, more patients have been receiving reduced doses of chemotherapy and radiation before their allogeneic transplant. The resulting transplant is called a reduced intensity conditioning (RIC) (non-myeloablative) or 'mini' transplant. Such procedures were first performed in New Zealand in 2001; there has since been a steady increase in their use.

Complications

All BMTs entail risk. In both autologous and allogeneic BMT, complications may arise before the new marrow grows in the patient, exposing the patient to serious infection, bleeding and complications involving the gut, mouth, kidneys and liver. During the immediate post-BMT period, patients are extremely unwell. Most suffer some vomiting, and frequently there is diarrhoea, from the BMT chemotherapy or from specific gut complications such as neutropenic colitis. Almost all patients develop high fevers from

blood-stream infections, requiring urgent intravenous fluids and antibiotics with close monitoring. Regular blood and platelet transfusion support is needed. Most patients lose weight (typically 10–15 kg). Allogeneic transplant patients require either enteral (naso-gastric) or intravenous feeding. Patients may also develop a syndrome of severe liver toxicity known as sinusoidal obstruction syndrome, for which intensive support and specific drugs are needed. Once the new bone marrow graft has grown and the patient's blood recovers (typically after 12–21 days), many of these complications begin to settle, and discharge may be planned for.[1] Patients are usually in hospital for two to four weeks following their BMT while they receive intensive supportive treatment.

Later, following marrow recovery, allogeneic transplant patients continue to be at risk of serious infections (especially viral and fungal) and immunological problems related to GVHD.

Overall, the risk of a patient dying from transplant complications is about 1 per cent for autologous and 15–20 per cent for allogeneic transplants. Additionally, the underlying cancer may relapse, despite the transplant.

Patient outcomes

Bone marrow transplants are performed as potentially curative therapy for patients under the age of 65–70 years, usually in the situation in which other standard treatment provides almost no option for cure. In general BMT provides a curative option in about 40–50 percent of transplants. A recent summary of the outcomes of both autologous and allogeneic BMT pertaining to selected diseases reported that a transplant can result in a five-year event-free survival of 50 percent or greater.[2] Survivors are very likely to be cured of their underlying malignancy following these transplants.

The most significant disease group in which BMT does not provide a recognised curative option is multiple myeloma (the major indication for autologous BMT in New Zealand and worldwide). However, several phase III studies have demonstrated unequivocal prolonged disease-free and overall survival in patients with multiple myeloma receiving autologous stem cell transplants compared to standard chemotherapy. All autologous transplants in New Zealand for multiple myeloma are performed in the same manner as in these trials. A recent review of outcomes for autologous BMT for multiple myeloma in Auckland demonstrated superior results to these international studies: a transplant-related mortality of less than 1 percent and a median survival of 6.6 years (78 months).

A small number of non-curative autologous transplants are performed for indolent lymphoma. BMTs are performed with curative intent for aggressive lymphoma.

1 Gluckman E. 2009. Ten years of cord blood transplantation: from bench to bedside. *British Journal of Haematology* 147: 192–9; Gluckman E, Rocha V. 2009. Improving outcomes of cord blood transplantation: HLA matching, cell dose and other graft and transplantation-related factors. *British Journal of Haematology* 147: 262–74.

2 See Copelan, EA. 2006. Hematopoietic stem-cell transplantation. *New England Journal of Medicine* 354: 1813–26. This article also provides a good overview of the theory of stem cell transplantation, preparative conditioning regimens, sources of stem cells, transplant outcomes and complications.

Patient outcomes: reduced intensity conditioning transplants

Patients are increasingly receiving RIC transplants for more indolent or slow growing cancers, particularly when they have other serious co-morbid conditions or are older (typically over 50 years of age). The non-relapse mortality of these transplants is approximately 15–20 percent at one to two years, with an expected overall survival rate of 40–80 percent, depending on the haematological malignancy.[3]

Age range

BMT is currently indicated particularly for younger patients, but can produce excellent outcomes for selected patients up to the age of 70. There is a higher risk of complications in older patients. As treatments and transplant techniques improve, the current upper age range may change.

Approval process

New Zealand BMT services are overseen by specific BMT advisory committees, which consider and approve each individual patient's BMT in advance of the procedure. This process provides very careful consideration and peer review, and ensures that transplants are only performed when there are clear indications in suitable candidates.

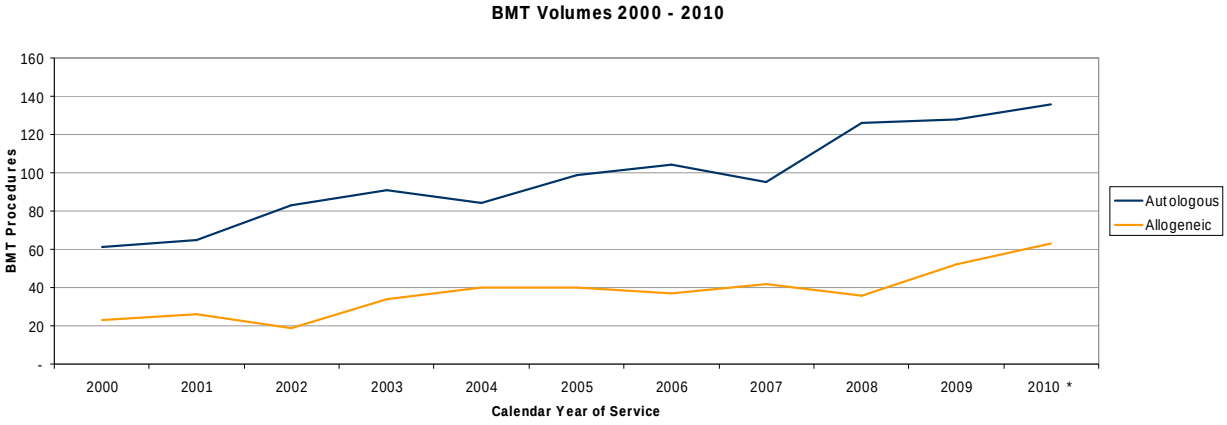
[3] Giralt S. 2005. Reduced-intensity conditioning regimens for hematologic malignancies: what have we learned over the last 10 years? *Hematology – The American Society of Hematology Program Book* 1: 384–9.

Rationale for a BMT Service Improvement Plan – Coping with Increased Demand

The current situation

BMTs are currently provided by five centres in New Zealand: Auckland, Waikato, MidCentral, Capital and Coast and Canterbury DHBs. The number of procedures performed is relatively small compared to other cancer treatment procedures (199 in 2010). Figure 1 below shows growth in BMT transplant activity over 2000–2010.

Figure 1: Total New Zealand BMT transplant activity 2000–2010



Growth in demand

Demand for BMT in New Zealand is growing due to a number of factors, including:

- the wider application of transplantation for haematological malignancies including multiple myeloma, lymphoma and selected acute myeloid leukaemia
- an increase in the population eligible for BMT, due to reduced toxicities (allowing older patients or those with more significant co-morbidities to undergo BMT) and a greater use of MUDs
- population growth.

Impact of growth in demand

The increase in BMT volumes has placed a large degree of stress on New Zealand's adult BMT units. Service delivery issues are occurring at all levels, and include:

- waiting times for BMT of up to 12 weeks
- the need to relocate patients and families to other treatment centres
- insufficient specialist nurses to staff BMT unit beds, educate and liaise with patients, undertake outpatient follow-up and manage staff education and quality control
- pressures on senior medical staff and resident staff

- insufficient inpatient beds
- difficulty in delivering transplants in a coordinated fashion with referring DHBs due to increased volumes, patient age range and the presence of comorbidities
- increasing requirements for data management and reporting to international bone marrow registries.

Analysis of international transplant rates

Data sources

It is difficult to obtain robust data on BMT activity in individual countries. Various international transplant registries collect data, including the Australasian Bone Marrow Transplant Registry, the American Bone Marrow Transplant Registry, the International Bone Marrow Transplant Registry and the European Bone Marrow Transplant Registry. However, data collected by these registries can be incomplete, because only some transplant services submit data.

Australasia has a very robust registry, requiring yearly reporting of all clinical BMT activity within Australia and New Zealand. British Columbia has a single transplant centre, at Vancouver General Hospital, and their data has been made available via personal communication (although it is also available on specific websites). United Kingdom transplant data is also available,[4] although accuracy, quality and completeness cannot be guaranteed.

Comparative analysis: Australia, New Zealand and British Columbia

While the recent growth in New Zealand BMT activity has closed the gap, New Zealand still has a lower intervention rate than Australia and British Columbia in both autologous and allogeneic transplants: particularly matched unrelated donor transplants.

Table 1 shows a comparison of adult New Zealand and international stem cell transplant rates (intervention rates), by transplant category (in patients older than 16 years), per 100,000 population in 2009.

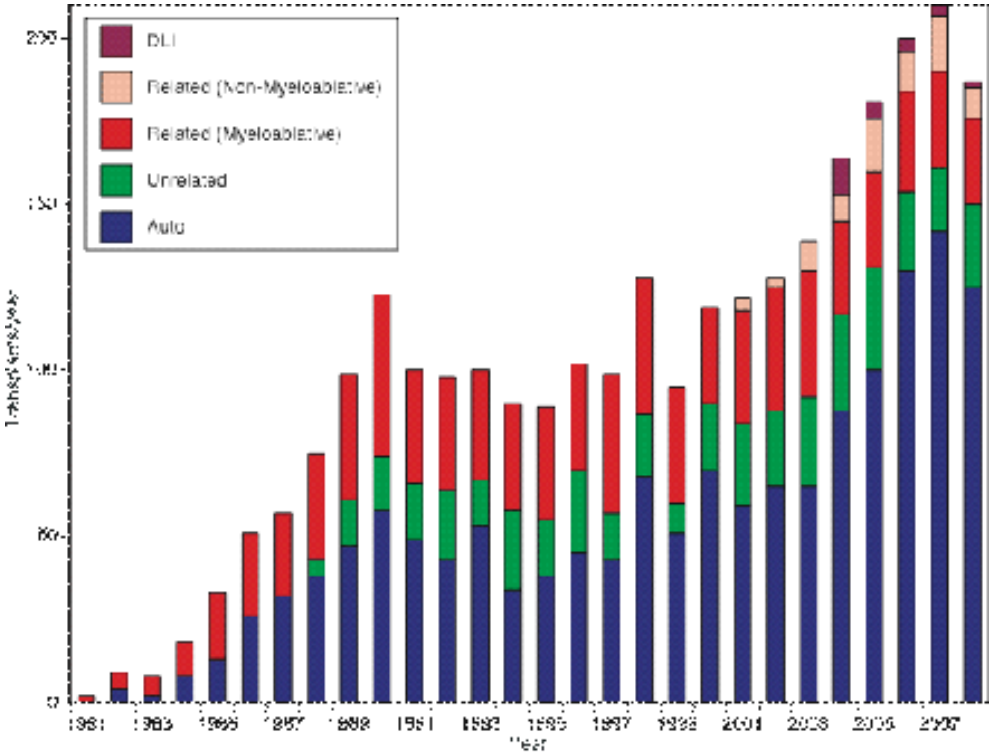
Table 1: 2009 transplant rates per 100,000 population

	New Zealand	Australia	British Columbia
Total	6.03	7.65	6.66
Autologous	4.29	5.40	4.33
Allogeneic (sib + mud)	1.74	2.25	2.33

[4] See www.bsbmt.org

Figure 2 shows data for British Columbia from 1981 until 2008, and clearly demonstrates a progressive increase in transplant activity over this time. Growth is particularly marked in rates of reduced intensity and autologous transplantation.

Figure 2: British Columbia stem cell transplant activity (adults >16 years)[5]



Projected treatment rates for New Zealand

Treatment of malignant haematological disorders in New Zealand is based on accepted international practice. Services provided by New Zealand centres is in line with Australian treatment algorithms, and centres collaborate in several clinical and research societies, such as the Haematology Society of Australia and New Zealand (HSANZ), the Australasian Leukaemia and Lymphoma Group (ALLG) and the Bone Marrow Transplant Society of Australia and New Zealand (BMTSANZ).

Although there are some differences, issues such as population demographics, access to drug therapy and funding models for haematological malignancy treatment are comparable between Australia and New Zealand. For this reason, it is recommended that New Zealand plans are based on Australian rates.

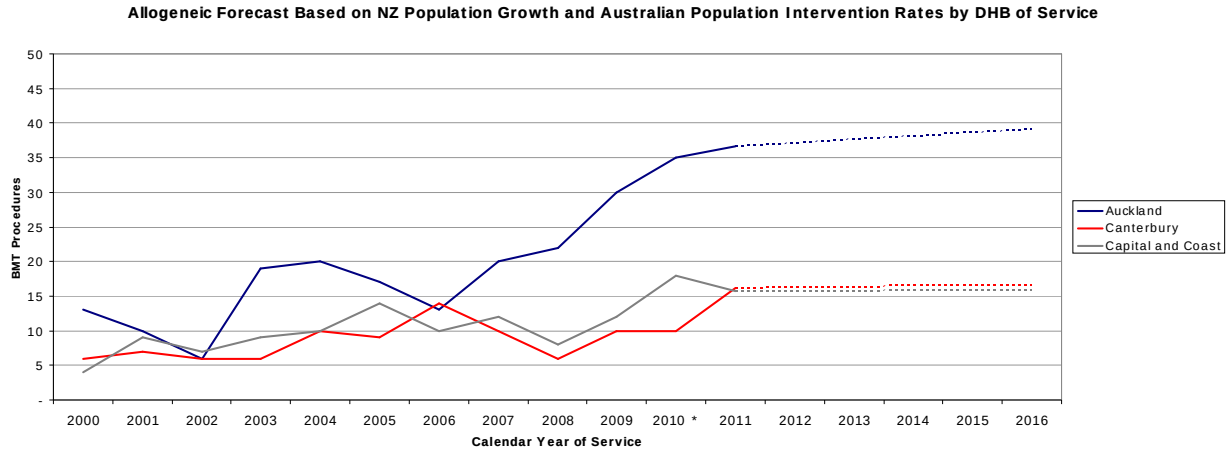
Projected transplant rates for New Zealand have been calculated using 2009 actual Australian transplant rates per 100,000 population and applied to forecast population volumes for each transplant centre. (Note that transplant populations are different for autologous and allogeneic BMT: see Appendix 1.)

[5] The total population of British Columbia is 4.3 million. Email from Dr Clayton Smith.

Projected allogeneic BMT volumes

Figure 3 shows historical and projected volume increases for the three provider DHBs for allogeneic BMT up to 2016, based on New Zealand population projections and 2009 Australian intervention rates.

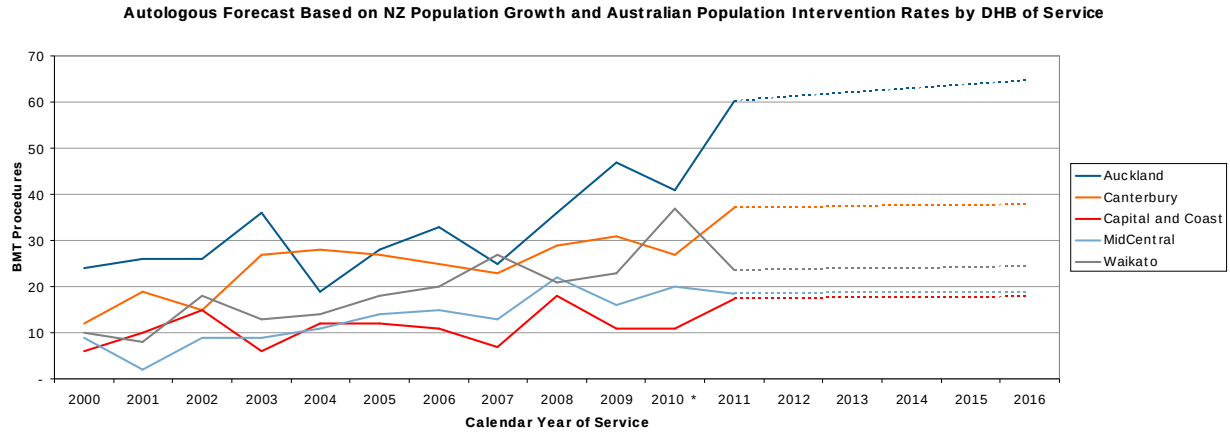
Figure 3: Projected rates of allogeneic BMT to 2016, by DHB provider



Projected autologous BMT volumes

Figure 4 shows historical and projected volume increases for the five provider DHBs for autologous BMT up to 2016, based on New Zealand population projections and 2009 Australian intervention rates.

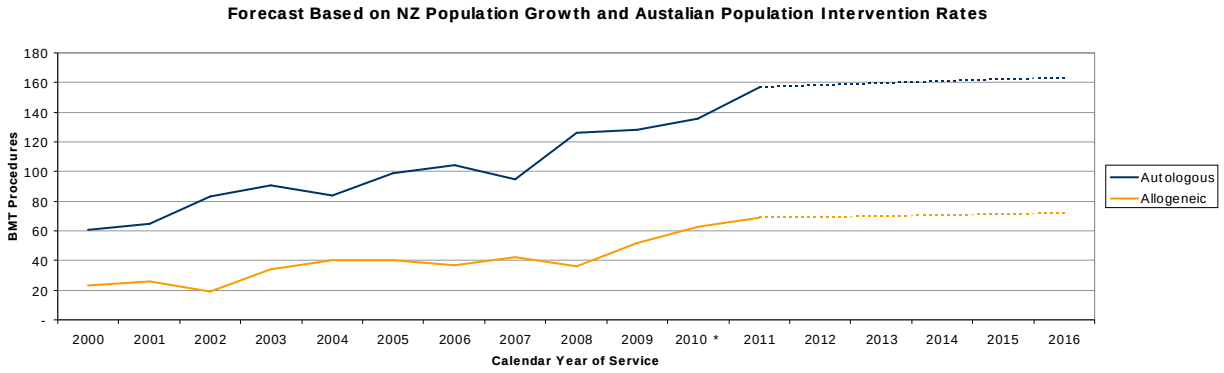
Figure 4: Projected rates of autologous BMT to 2016, by DHB provider



Note: Although the forecast modelling indicates a high rate of autologous BMT activity, the HWG anticipates that there will be comparatively greater growth in allogeneic BMT, due to the broader application of RIC transplants in an older patient group; increased availability of unrelated/alternative donors; greater use in treatment of acute leukaemia in first remission, according to improved disease risk stratification; and greater use in low-grade lymphoma and chronic lymphocytic leukaemia, where allogeneic BMT offers a curative treatment.

Figure 5 shows historical and projected total (autologous and allogeneic combined) volume increases for the five provider DHBs to 2016, based on New Zealand population projections and 2009 Australian intervention rates.

Figure 5: Projected rates of autologous and allogeneic BMT to 2016



Based on the planning assumption that New Zealand transplant rates match Australian rates per 100,000 population, an increase of approximately 25 transplants per annum on current activity can be expected. This growth will be limited to some extent by transplant capacity. Funders should take note of these projections. Although capacity is very limited nationwide, it may be possible to outsource occasional transplants to other New Zealand treatment centres when local capacity is unavailable.

Projected capacity implications

These data have varying implications for New Zealand centres. In particular, projections suggest that Auckland and Canterbury DHBs require additional treatment capacity.

Implications for resources

An increased intervention rate has direct implications for resources, including inpatient and outpatient facilities and staffing. All DHBs providing BMT need to plan an appropriate response to increased volumes.

Auckland DHB has completed a modelling exercise to calculate the number of transplant beds required to match Australian BMT rates (see Appendix 2). This analysis

demonstrates an immediate need for four transplant beds, with an additional need for approximately one bed every four to five years.

Other DHB providers should undertake similar research on likely future requirements.

Recommendations

The Cancer Control Steering Group recommends that provider District Health Boards:

- **agree** to model capacity requirements for their respective populations
- **ensure** that they are able to respond to increased Bone Marrow Transplant volume growth appropriately.

Bone Marrow Transplant Services in New Zealand

Current service configuration

BMT is a specialised service delivered at five centres in New Zealand. The HWG agreed at its 24 February 2010 meeting that the number and location of these centres should not change. Autologous BMT services should continue to be delivered at Auckland, Waikato, MidCentral, Capital and Coast and Canterbury DHBs, and allogeneic BMT services should continue to be delivered at Auckland, Capital and Coast and Canterbury DHBs (due to their greater ability to provide concentrated expertise and achieve geographical coverage). Collectively, providers should consider performing highly complex adult allogeneic BMT (such as UCB and haplo-identical transplants) in a single BMT centre, to optimise treatment expertise and experience.

It is noted that the haematology service at Otago DHB provides some pre- and post-BMT care.

Auckland DHB is the largest transplant centre for both autologous and allogeneic transplants, serving total referral populations (older than 16 years) of about 1.2 million and 1.6 million respectively.

Appendix 1 records the referral population of each provider DHB.

Quality of current service configuration

The five autologous and three allogeneic BMT units currently:

- provide good geographical spread
- are located within centres offering comprehensive tertiary haematology services, including treatment of acute leukaemia and haematology malignancies requiring very intensive management over a long inpatient stay. The level of care required for treatment of acute leukaemia is similar to that for autologous BMT, but some procedures and resources are different. Stem cell collection and associated laboratory support requires major organisational resources. There is a clear synergy to be obtained by performing autologous BMT within services that provide comprehensive intensive haematology care. Tertiary haematology care is not provided by Waitemata or Counties Manukau DHBs
- have the necessary infrastructure to provide full tertiary level haematology care (although resourcing levels need further investigation), including inpatient haematology beds, outpatient services and nursing, registrar and specialist haematologist expertise
- have stable service delivery arrangements
- meet internationally recommended minimums. (FACT accreditation requires a minimum of 10 new patient allogeneic transplants per year.)

Allogeneic BMT is regarded as the most complex form of patient care in haematology; it requires highly experienced staff (medical, nursing, pharmacy and laboratory), management of complications and input from other specialty areas (for example renal and cardiological). Post-transplant care following discharge is also complex, and includes intensive clinical and specialist laboratory monitoring and potential readmission.

Funding model

Currently BMT is funded through DHBs as an inpatient (weighted inlier equivalent separation (WIES)) and outpatient (non-diagnosis related group (DRG)) service. This funding model entails certain challenges, as follows.

- There is the potential for increased costs per transplant, especially with MUD or sibling allogeneic BMT, in which there is an increased risk of complications.
- The model does not allow for real-time funding increases to meet the cost of improving services to international standards. Service costs feed into a national pricing framework, which entails a two-to-three-year delay for adjustment to national inter-district flow pricing.
- The process for financing major capital projects (such as provision of additional transplant beds) to accommodate the additional BMT load is complex. These projects have to be prioritised at a DHB level alongside other capital priorities.

However, Auckland DHB's 2008/2009 and 2009/2010 analysis of transplant activity found that the overall DHB revenue from BMT roughly approximated cost (see Appendix 3).

The CCSG does not recommend making any changes to the BMT funding model.

Cost of BMT

BMT is a relatively expensive treatment. A New Zealand-wide analysis of BMT costs has not been undertaken; however, the Auckland DHB study found that the average cost of an autologous, allogeneic and allogeneic MUD transplant is $45,800, $105,200 and $167,200 respectively (see Appendix 4). Transplant costs will vary across provider DHBs, dependent on models of care, transplant volumes and physical capacity investment.

Transplant costs include:

- preliminary investigations to demonstrate adequate pre-transplant patient organ function (including echocardiography and respiratory function tests)
- assessments to check that patients' underlying disorder is at an adequately stable stage for treatment (including bone marrow biopsies and sometimes CT scans)
- tissue 'typing', performed twice to confirm results

- donor search and assessment (for allogeneic transplants):
  - to carry out a search for a MUD, the New Zealand Bone Marrow Donor Registry (NZBMDR) electronically searches international registries (where full tissue-typing results are held on about 12 million potential volunteer donors)
  - donors need to be medically assessed, potentially including extensive viral serology to exclude potential infective risks
- harvesting of stem cells. For autologous BMT peripheral blood stem cells (PBSC) are harvested from the patient and frozen before the transplant chemotherapy. For sibling allogeneic BMT, marrow or PBSC are harvested at the transplant centre and infused fresh to the patient. For MUD transplants from overseas donors, fresh harvested cells are couriered to New Zealand, attended by a staff member from the transplant centre in New Zealand to ensure absolute security in cell transport. For international cord blood donations, cryopreserved cord blood units are flown to New Zealand in a frozen state
- inpatient hospital stays: typically three to four weeks for autologous transplant and four to six weeks for allogeneic transplant
- intensive outpatient follow-up, particularly for allogeneic transplants, during which patients re-establish adequate oral intake and are reviewed for specific transplant complications such as infection, veno-occlusive disease of the liver and (for allogeneic transplant) GVHD.

International bone marrow donor searches are expensive: approximately NZ$5,000 per search. Procurement of unrelated stem cells is more expensive: NZ$5,000–NZ$39,000.[6] Cord blood units cost NZ$25,000–NZ$57,000 each, and two cord blood units are needed for most adults. It is anticipated that volumes of adult UCB transplants will increase in the near future.

Cost benefit analysis

A cost benefit analysis has not been undertaken in preparing this document, but it is widely accepted that for some blood disorders BMT significantly limits the number of required cycles of standard chemotherapy treatment. This means that the cost of transplantation is offset against repeated cycles of chemotherapy.

This is often the case in the treatment of both acute myeloid and acute lymphoblastic leukaemia. Newly diagnosed patients with acute myeloid leukaemia are typically treated with four or five intensive courses of chemotherapy over four to six months. Patients who will receive an allogeneic transplant may only receive two cycles of intensive chemotherapy before the procedure. For acute lymphoblastic leukaemia, treatment involves intensive chemotherapy for approximately 12 months, followed by 18–24 months of maintenance low-dose chemotherapy. Allogeneic transplant may be applied relatively early in the course of treatment, abbreviating the treatment course with significant cost offset. The costs of supportive care, transfusions, palliation and

[6] The German donor registry is most frequently used, because it provides full typing and demographics for donors in the registry, and donors are frequently available. The total cost of donor assessment and procurement of stem cells through the German registry is about NZ$19,000 per procedure.

anti-cancer drugs need to be considered in the case of those patients who do not have a donor.

Future service configuration needs

BMT is generally provided as an inpatient service. However, some aspects of autologous BMT may be delivered via a carefully planned outpatient service, for patients who meet strict criteria. It is established practice in some centres overseas to perform all or part of autologous BMT as an outpatient service.

Outpatient BMT requires considerable resources, including:

- daily outpatient visits
- accommodation for patients who reside some distance from the BMT centre
- community visits from experienced BMT nurses
- the capacity to review and admit patients to an optimal ward situation if significant complications occur.

Outpatients require a constant caregiver (often a partner or parent), who will be unable to work over the course of treatment, entailing significant personal financial cost. Patients need to be well motivated and reliable, and need to live close to the base hospital, or there needs to be suitable funded accommodation near to the hospital for the patient and caregiver.

Outpatient BMT is an option for individual BMT services to consider; it will be more appropriate for some units than others. New Zealand has adopted this practice to a degree: Wellington has a well-established outpatient BMT service, and Auckland may adopt this approach with selected patients (see Appendix 5).

A successful outpatient BMT service needs to be resourced with suitable outpatient and inpatient facilities and appropriate staffing (medical, nursing, social and psychological) support. Outpatient BMT will only be appropriate for a proportion of autologous and very low intensity RIC allogeneic transplant patients.

Recommendations

The CCSG recommends that DHBs:

- **provide** accurate annual Bone Marrow Transplant costing information to inform national pricing
- **continue** the current configuration of Bone Marrow Transplant services in New Zealand; that is:
  1. provision of autologous Bone Marrow Transplant at Auckland, Waikato, MidCentral, Capital and Coast and Canterbury District Health Boards
  2. provision of allogeneic Bone Marrow Transplant at Auckland, Capital and Coast, and Canterbury District Health Boards.

Service Improvement Areas

The following areas have been identified as priorities in terms of increasing capacity and improving the delivery of BMT services in New Zealand.

1. Development of national clinical indications for BMT

The HWG has revised and updated national clinical indications, in line with international best practice. These indications are based on those developed by the European Group for Blood and Marrow Transplantation (EBMT),[7] with adjustments for some indications for which New Zealand does not perform BMTs (for example breast cancer).

The EBMT guidelines are also recognised and supported by HSANZ, ALLG and BMTSANZ.

The recommended 2010 New Zealand national clinical indications for BMT are:

- acute myeloid leukaemia
- myelodysplastic syndrome
- acute lymphoblastic leukaemia
- multiple myeloma
- non-Hodgkin lymphoma, including indolent, mantle cell and aggressive subtypes
- Hodgkin lymphoma
- chronic lymphocytic leukaemia
- myelofibrosis
- aplastic anaemia.

A small number of BMTs are performed for other rare indications, comprising less than 10 percent of BMT activity.

These clinical indications are supported by the CTAG and the CCSG.

For a full detailed list of national clinical indications for BMT see Appendices 6, 7 and 8.

Recommendations

The Cancer Control Steering Group recommends that District Health Boards:

- **note** that the Haematology Work Group has revised and updated national clinical indications for Bone Marrow Transplants

[7] Ljungman P, Bregni M, Brune M, et al. 2009. *Allogeneic and Autologous Transplantation for Haematological Diseases, Solid Tumours and Immune Disorders: Current Practice in Europe*. Stockholm: European Group for Blood and Marrow Transplantation.

- **agree** to adopt clinical indications to ensure nationally consistent access.

2. Addressing capacity issues

Workforce requirements

BMT is a very complex treatment, requiring high levels of coordination between inpatient and outpatient care entailing frequent patient movement. Staff need to be well trained, demonstrate defined competencies and receive adequate continuing medical education; in this way, the workforce will be kept up to date on the typically rapid changes in the field of BMT.

BMT staffing requires a dedicated multidisciplinary team of many diverse professionals. Staffing of a BMT service will vary depending on the type of transplants performed, the focus of the unit on either inpatient or outpatient care and the varying role of BMT nurse specialists.

Table 2 suggests workforce requirements for BMT services, based on numbers of BMT patients within New Zealand.[8] No published international papers currently identify best practice staffing levels, and staffing levels are not specified in the FACT accreditation recommendations.

Table 2: BMT workforce requirements

Staff title	Ratio of staff member full-time equivalent to BMT patients (average for allogeneic and autologous BMT)
BMT nurse	1 per 2–3 inpatients
BMT nurse specialist	1 per 30 transplants/year
BMT registrar (covering both in- and outpatients)	1 per 50 transplants/year
BMT clerical support	1 per 100 transplants/year
Psychologist/ psychiatrist support	0.2 per 100 transplants/year
BMT outpatient nurse	1 per 100 transplants/year
FACT project manager	0.5 per year per unit
BMT registry reporter	1 per 70 transplants/year
Pharmacist/social worker/dietician	
Physiotherapist	
BMT programme director	
BMT haematologist	provide 24/7 cover

[8] Information provided by Dr Tim Hawkins, chair HWG, haematologist Auckland City Hospital.

Although individual DHBs should undertake further analysis, current workforce numbers for BMT appear to be lower than they should be. In particular, there appears to be lack of a skilled haematology nursing workforce.

The Ministry of Health has contracted the Health Workforce Information Programme (HWIP) to provide workforce forecast information and analysis, to assist in planning for the future needs of the BMT nursing workforce.

BMT unit design

There is limited information available on the design of BMT services. The FACT provides some guidance on design of inpatient and outpatient services, which designers of New Zealand BMT units should take into consideration.

Inpatient service requirements

The FACT states that, to optimise patient management, allogeneic and autologous inpatient care should be accommodated together in the same unit or immediately adjacent units.

High-efficiency particulate air (HEPA) filtration and positive pressure rooms are essential requirements for allogeneic BMT because of the infection risk, but are not an absolute requirement for autologous stem cell transplants.

Outpatient service requirements

Outpatient units should ideally either be separate but adjacent to BMT inpatient units, or included within but separate to the general haematology outpatient unit, to help prevent opportunistic infection.

BMT services must have the ability to arrange immediate admission to an appropriate area of the hospital. The FACT states that 'Emergency Department may be an acceptable place for assessment when other outpatient facilities are unavailable but patients should not be exposed to the risk of infectious disease transmission, including respiratory spread'. In New Zealand, this is a very important issue. New Zealand emergency departments and acute assessment and planning units are very busy, and would be inappropriate for management of acute BMT patients because of the risk of opportunistic infection and potential delays in access to experienced nursing and medical care.

Whenever possible, unless a patient is critically unwell, patients should be transferred to an inpatient BMT unit immediately after triage. This has important implications for capacity in terms of BMT inpatient bed numbers. Bed number modelling (occupancy factor) needs to acknowledge the need for inpatient BMT beds post-triage in individual hospital business cases for BMT service specifications.

Recommendations

The Cancer Control Steering Group recommends that District Health Boards:

- **note** that the haematology nursing workforce is at full capacity at the current level of demand for Bone Marrow Transplant services
- **note** that the Health Workforce Information Programme will provide workforce forecast information and analysis to assist in Bone Marrow Transplant nursing workforce planning
- **note** considerations outlined in this document applicable to patients readmitted via hospital emergency departments.

3. Improving waiting times

There are currently no published standards for acceptable waiting times for the initiation of BMT. However, with the exception of patients with multiple myeloma and indolent lymphoma, BMT provides a curative treatment for patients under the age of 65–70 years; it is accepted that short wait times are critical to optimising curative potential.

The HWG has developed waiting times criteria based on accepted best practice and consistent with radiation and medical oncology wait times, as outlined in Table 3.

Table 3: Waiting time criteria for BMT

Description	Waiting time
From receipt of referral for BMT to first medical review with BMT team	Four weeks
Commencement of transplant chemotherapy and/or radiotherapy conditioning treatment prior to autologous stem cell transplant	Within four to six weeks of stem cell collection (depending on disease subtype)
Commencement of transplant chemotherapy and/or radiotherapy conditioning treatment prior to allogeneic sibling, MUD or cord blood stem cell transplant	Within four weeks of deemed optimal time for the transplant, in coordination with stem cell donor availability

Recommendations

The Cancer Control Steering group recommends that District Health Boards:

- **implement** the Bone Marrow Transplant waiting time criteria outlined in this document
- **note** that Haematology Work Group will monitor Bone Marrow Transplant waiting times.

4. International accreditation of BMT services

Current quality and safety standards

Quality and safety standards for BMT services in New Zealand are mainly under the governance of individual haematology departments and individual hospital quality management programmes.[9] In many New Zealand BMT centres, the New Zealand Blood Service is responsible for stem cell collection and cryopreservation. (At Capital and Coast DHB these activities are performed under Medsafe accreditation.)

Nursing and medical continuing education is provided internally, but includes national and international meetings and research participation.

All New Zealand BMT centres report transplant outcomes to the Australasian Bone Marrow Transplant Recipient Registry; they also report on allogeneic programmes to the International Bone Marrow Transplant Registry based in the United States.

The NZBMDR lists approximately 8000 potential donors willing to donate cells from their bone marrow to patients worldwide. The NZBMDR was accredited by the World Marrow Donor Association (WMDA) in May 2006, having provided sufficient documentation to demonstrate its commitment to following WMDA standards.

FACT accreditation

It is likely that in the near future New Zealand BMT centres will need to obtain FACT accreditation. This will allow each BMT centre access to stem cells from international unrelated donors or cord blood, and to participate in international research studies. The majority of transplant centres in Europe and the United States have FACT accreditation; one centre in Australia is accredited. The combined paediatric and adult BMT service at Auckland City Hospital received full FACT accreditation in July 2010, after 18 months of preparation. This is the second accredited BMT service in Australasia.

Transplant programmes that have been accredited by the FACT have demonstrated compliance with the current FACT Cellular Therapy Standards, designed to provide minimum guidelines for programmes, facilities and individuals performing BMT or providing BMT support services. They define clinical program standards, including minimum yearly transplant numbers, unit design, personnel requirements, quality management, policies and procedures and data management, including compulsory reporting to BMT registries. Similar rigorous standards are defined for stem cell collection and processing, including clear lines of communication and quality management between the clinical and laboratory components of a service.[10]

[9] Excepting Auckland DHB, which has FACT accreditation.

[10] The FACT standards are published on www.factwebsite.org

Financial implications of FACT accreditation

FACT-accredited facilities are inspected once in three years. The accreditation process costs about US$25,000.

Recommendation

The Cancer Control Steering Group recommends that District Health Boards:

- **note** that international accreditation of Bone Marrow Transplant services as set out by the FACT is likely to be required in the near future so that New Zealand services can participate in international BMT studies and gain access to international MUD donations.

Next Steps

The development of a national service plan for BMT is just the start of the process for increasing capacity and improving the delivery of BMT services. Table 4 outlines a proposed implementation process.

Table 4: Proposed implementation process for New Zealand BMT services

	Action required	**Responsibility**	**Timeframe**
1	Circulate BMT indications to BMT centres (Auckland, Waikato, MidCentral, Capital and Coast and Canterbury DHBs)	HWG	2011/2012
2	Investigate impact of BMT volume growth and gaps in service capacity	Provider DHBs	2011/2012
3	Review current and future BMT specialist staffing requirements, with a particular focus on Auckland DHB (in line with capacity planning)	Provider DHBs	2011/2012
4	Achieve or maintain international accreditation to reach agreed minimum recommended standards, as set out by the FACT	Provider DHBs	Ongoing
5	Establish reporting and monitoring systems for BMT waiting times	HWG and provider DHBs	2011/2012
6	Review clinical indications for BMT	HWG	Ongoing

Appendix 1: Referral populations to each BMT centre for autologous or allogeneic transplants

2009 total population

Referring DHB	Population	BMT service provider DHB and total referral population	
		Autologous BMT	Allogeneic BMT
Northland Auckland Waitemata Counties Manukau	156,400 450,480 529,420 482,560	Auckland 1,618,860	Auckland 2,291,430
Waikato Bay of Plenty Lakes	360,270 209,400 102,900	Waikato 672,570	
Tairawhiti Taranaki Hawke's Bay MidCentral Whanganui	45,890 107,620 154,130 166,820 63,205	Mid Central 537,665	Capital and Coast 1,006,730
Hutt Capital and Coast Wairarapa	142,460 286,860 39,745	Capital and Coast 469,065	
Nelson Marlborough West Coast Canterbury South Canterbury Southern	136,645 32,105 499,520 55,370 296,965	Canterbury 1,020,605	Canterbury 1,020,605

Source: Statistics New Zealand population projections, September 2009.

Appendix 2: Auckland DHB bone marrow transplant modelling

Auckland DHB completed a modelling exercise to calculate the number of transplant beds required based on Australian BMT rates (per 100,000 population). This analysis demonstrates an immediate need for an additional two transplant beds, an additional five by 2015, and thereafter a new bed every four to five years. Findings are set out below.

BMT modelling for National Haematology Working Group – ADHB provider

Type of transplant	2010 Northern region BMT volumes (actual)	Plus BMT outsourced to other New Zealand centres	Total 2010 Northern region demand	Inpatient LOS (days) based on 24-month average	Allowance for readmission (days)	Total LOS assumption for capacity planning	BMT bed day requirement (365 days pa)	BMT bed requirement (365 days pa)	Allow for 85% occupancy
Allogeneic (sibling + MUD)	35		35.00	31.41	7.00	38	1,344.19	4	4.33
Autologous	41	7.00	48.00	20.26	0.50	21	996.27	3	3.21
Total	76	7	83.00				2,340.46	6.41	7.54

Type of transplant	2011 Northern region BMT volumes (forecast)	Inpatient LOS (days) based on 24-month average	Allowance for readmission (days)	Total LOS assumption for capacity planning	BMT bed day requirement (365 days pa)	BMT bed requirement (365 days pa)	Allow for 85% occupancy
Allogeneic (sibling + MUD)	37	31.41	7.00	38	1,409.29	4	4.54
Autologous	60	20.26	0.50	21	1,250.85	3	4.03
Total	97				2,660.14	7.29	8.57

Immediate requirement for 9 transplant beds

Type of transplant	2012 Northern region BMT volumes (forecast)	Inpatient LOS (days) based on 24-month average	Allowance for readmission (days)	Total LOS assumption for capacity planning	BMT bed day requirement (365 days pa)	BMT bed requirement (365 days pa)	Allow for 85% occupancy
Allogeneic (sibling + MUD)	37	31.41	7.00	38	1,427.03	4	4.60
Autologous	61	20.26	0.50	21	1,269.21	3	4.09
Total	98				2,696.23	7.39	8.69

Type of transplant	2013 Northern region BMT volumes (forecast)	Inpatient LOS (days) based on 24-month average	Allowance for readmission (days)	Total LOS assumption for capacity planning	BMT bed day requirement (365 days pa)	BMT bed requirement (365 days pa)	Allow for 85% occupancy
Allogeneic (sibling + MUD)	38	31.41	7.00	38	1,446.66	4	4.66
Autologous	62	20.26	0.50	21	1,289.06	4	4.15
Total	100				2,735.72	7.50	8.82

Type of transplant	2014 Northern region BMT volumes (forecast)	Inpatient LOS (days) based on 24-month average	Allowance for readmission (days)	Total LOS assumption for capacity planning	BMT bed day requirement (365 days pa)	BMT bed requirement (365 days pa)	Allow for 85% occupancy
Allogeneic (sibling + MUD)	38	31.41	7.00	38	1,464.21	4	4.72
Autologous	63	20.26	0.50	21	1,307.39	4	4.21
Total	101				2,771.60	7.59	8.93

Type of transplant	2015 Northern region BMT volumes (forecast)	Inpatient LOS (days) based on 24-month average	Allowance for readmission (days)	Total LOS assumption for capacity planning	BMT bed day requirement (365 days pa)	BMT bed requirement (365 days pa)	Allow for 85% occupancy
Allogeneic (sibling + MUD)	39	31.41	7.00	38	1,482.03	4	4.78
Autologous	64	20.26	0.50	21	1,325.79	4	4.27
Total	102				2,807.83	7.69	9.05

Requirement for 10 transplant beds by 2016/17

Type of transplant	2016 Northern region BMT volumes (forecast)	Inpatient LOS (days) based on 24-month average	Allowance for readmission (days)	Total LOS assumption for capacity planning	BMT bed day requirement (365 days pa)	BMT bed requirement (365 days pa)	Allow for 85% occupancy
Allogeneic (sibling + MUD)	39	31.41	7.00	38	1,498.09	4	4.83
Autologous	65	20.26	0.50	21	1,342.58	4	4.33
Total	104				2,840.67	7.78	9.16

ADHB current transplant beds : 5 Hepa filtered + 2 inpatient beds used for auto.

Note: 2010 BMT volumes include adjustment for BMT volumes outsourced to other New Zealand centres due to capacity constraints.

Note: 2011–2016 forecast BMT volumes assume all delivered locally, at Australian rates per 100,000 population.

Updated April 2011 to incorporate recent modelling incorporating New Zealand population projections and Australian transplant rates.

Appendix 3: Auckland DHB's transplant cost versus revenue analysis

The following analysis, undertaken by Auckland DHB, demonstrates total inpatient and outpatient costs associated with BMT in comparison with revenue streams generated through national pricing and MUD programme funding.

BMT activity cost vs revenue for year 0808 and 0910

		IP/OP data								
		Inpatient			Outpatient			Total sum of cost	Total sum of revenue	Total sum of variance
Disch F year	BMT type	Sum of cost	Sum of revenue	Sum of variance	Sum of cost	Sum of revenue	Sum of variance			
0708	Auto			$–	$156,253	$172,177	$15,924	$156,253	$172,177	$15,924
	Allo	$5,966	$6,919	$953	$88,472	$98,110	$9,638	$94,438	$105,029	$10,591
	MUD			$–	$28,551	$18,690	-$9,861	$28,551	$18,690	$9,861
0708 total		$5,966	$6,919	$953	$273,275	$288,976	$15,701	$279,241	$295,896	$16,654
0809	Auto	$1,232,610	$2,178,651	$946,041	$714,255	$559,090	-$155,166	$1,946,865	$2,737,741	$790,876
	Allo	$1,186,139	$1,441,298	$255,159	$466,192	$363,945	-$102,247	$1,652,331	$1,805,242	$152,912
	MUD	$950,512	$1,065,721	$115,209	$807,627	$276,866	-$530,761	$1,758,139	$1,342,587	-$415,552
0809 total		**$3,369,260**	**$4,685,669**	**$1,316,409**	**$1,988,074**	**$1,199,901**	**-$788,174**	**$5,357,335**	**$5,885,570**	**$528,235**
0910	Auto	$1,395,478	$1,903,231	$507,754	$581,411	$537,914	-$43,497	$1,976,889	$2,441,145	$464,256
	Allo	$1,458,693	$1,768,768	$310,076	$649,806	$544,092	-$105,714	$2,108,499	$2,312,860	$204,362
	MUD	$764,192	$821,259	$57,067	$555,315	$316,024	-$239,292	$1,319,507	$1,137,282	-$182,225
0910 total		**$3,618,363**	**$4,493,258**	**$874,896**	**$1,786,532**	**$1,398,029**	**-$388,503**	**$5,404,895**	**$5,891,287**	**$486,393**
1011	Auto	$12,283	$7,181	-$5,101	$24,891	$26,059	$1,167	$37,174	$33,240	-$3,934
	Allo	$21,313	$18,487	-$2,826	$81,352	$60,460	-$20,892	$102,665	$78,947	-$23,717
	MUD			$–	$1,882	$1,804	-$77	$1,882	$1,804	-$77
1011 total		$33,596	$25,669	-$7,927	$108,125	$88,323	-$19,802	$141,721	$113,992	-$27,729

Note: Based on BMT procedure date in FY08/09 and FY09/10. 08/09 and 09/10 transplants have activity in FY08/08 and FY10/11 is due to the date range set (see below).

Author: Leo Tang

Ref No: 6149

BMT type based on procedure costs – 1370607; 1370608 = Auto 1370600; 1370606 = Allo; 1370610 = MUD.

WIES funded inpatients admission include: BMT procedure admission and other BMT related admissions (admitted 10 days before BMT next admissions and 90 days after previous BMT discharge).

Non-DRG events: occurred 180 days on each side of BMT admission and discharge from Haematology CBU.

Revenue include: MUD donor searching Fee Programme fund allocated to MUD activities pro rata.

PCT revenue to reflect PCT wash-up.

Appendix 4: Auckland DHB's study of BMT costs

Auckland DHB undertook a study of the costs incurred in BMT transplant activity in 2008/2009 and 2009/2010. The following table sets out findings.

Average cost/transplant

DischFYear	BMT type	Total cost	Number of transplants	Average cost
2008/09	Auto	$2,103,118	40	$52,578
	Allo	$1,746,769	14	$124,769
	MUD	$1,786,689	11	$162,426
2008/09 total		$5,636,576	65	$86,717
2009/10	Auto	$2,014,063	44	$45,774
	Allo	$2,211,163	21	$105,293
	MUD	$1,321,389	8	$165,174
2009/10 total		$5,546,615	73	$75,981

Note: 0708 events are rolled up to 0809 as they are relevant to transplants in 0809.
1011 events are rolled up to 0910 as they are relevant to transplants in 0910.

The study notes that, as would be anticipated with low-volume, high-complexity cases, there are large variations in individual transplant costs. For example, a small number of cases develop very complex medical problems and therefore accrue high transplant-related costs.

Appendix 5: Models of care – ambulatory vs inpatient autologous transplants

Dr Peter Ganly (unpublished paper)

Traditionally patients receiving treatment with allogeneic or autologous haematopoietic stem cell transplants have spent most of their time as inpatients in hospital. More recently it has been shown that it is not necessary for patients to spend their entire transplant journey in hospital, and indeed there may be improved quality of life and no excess risk if a patient spends some or most of their treatment at their home – so-called 'outpatient transplants'.

The transplant treatment starts with the recipient being 'conditioned' using chemotherapy with or without radiotherapy, and then haematopoietic stem cells are infused. Post-infusion the patient recovers from the effects of the conditioning and requires supportive therapy, which may include prophylaxis against infection, treatment of infection, blood transfusion support, analgesia and fluid and nutritional support. In the longer term, particularly following allogeneic transplant, the patient may need treatment for adverse effects of transplantation, such as graft versus host disease.

Transplants are not all equal. Some conditioning programmes involve several treatments a day for many days, and the patient requires a lot of supportive therapy to manage with these. Other conditioning programmes are simpler and may only involve a single brief IV infusion, or repeated brief injections which do not cause immediate symptoms. The actual infusion of stem cells ('transplant') is usually straightforward. Post-infusion, depending on the programme, it can be predicted which patients will feel well for some days, and which will be likely to need support to cope with side effects present immediately after the conditioning. A week or so after infusion, most patients will have severe suppression of blood formation and be at high risk of infection, such that the majority will require treatment with intravenous antibiotics for a period at this stage. The risk of infection varies, being greatest in those who have the intensive immunosuppression associated with an allograft. For these it may be valuable to try to reduce the risk by keeping the patient in a low pathogen environment provided by HEPA filtered air and isolation, rather than at home, but for other transplant patients, isolation in such an environment is not necessary.[1] The longer-term consequences (three or more weeks after the stem cell infusion) apply almost exclusively to those having an allograft. The management of these may require in-patient based treatment but are outside the scope of 'outpatient transplants' and are not discussed further here.

In practice, the most complex patients are those who have allografts following very intensive conditioning (myeloablative allografts). Other patients, typically older, have 'reduced intensity conditioning' prior to their allografts, and in the short term are less complex, particularly those whose reduced intensity conditioning does not suppress blood formation so much. The majority of patients, however, have autografts, and most of these have myeloma or lymphoma. The conditioning for these may be quite simple (myeloma) or longer but still relatively uncomplicated to deliver (lymphoma). Their recovery is relatively predictable, occurring over two to three weeks, and for much of

the time they may feel reasonably well. The contrast between allograft and autograft management is illustrated by the procedural related mortality (the deaths caused by the treatment in the first hundred days), which may be as high as 20 percent for some sorts of allografts, but would be much lower than 5 percent for autograft patients.

Many centres have devised programmes for patients receiving transplants which aim to keep the patient at home for as much of the transplant course as possible. Although some home-based approaches for myeloablative allograft have been described,[2,3] in practice the overwhelming experience is in those having autografts and some reduced intensity allografts.[4–6] It is important to emphasise that the programmes have not been set up in an unplanned way, but that patients have been carefully selected and a scrupulous infrastructure exists.

A typical approach is first to select a patient who is to have the procedure which is least complicated and most predictable (an autograft for myeloma).[5] This happens to be the commonest indication for transplant in New Zealand and worldwide, so is likely to have the greatest impact on inpatient resources. To be selected that patient must live within 60 minutes from the transplant centre, and must live in a suitable home with mains water and sanitation (the home is inspected). No pets are accepted in the home. Sheets need to be laundered three times weekly. The patient must have a full-time carer present throughout the entire transplant course for which they are in hospital. The patient and the carer must be fully educated by a dedicated team of nurses. The conditioning and reinfusion of stem cells takes place in hospital, since 24-hour continuous fluid regimens are employed. The patient may then be discharged to the home service. This may consist of a number of nurses who are able to visit the patient each day at their homes for investigations, review and treatments. The nurses need to have their transport, and not have other duties which prevent them delivering this service. The dedicated outpatient doctor then contacts the patient each day for telephone review. Criteria are set around what treatments can be administered at home, and under what circumstances patients must be admitted to hospital. Typically patients are admitted if they require more than two visits per day from nurses, or if the patient is unstable or requires treatment with intravenous antibiotics. Some centres are able to support patients at home with intravenous antibiotics for limited times. If the patient is to be readmitted there must be a high likelihood that they can be admitted to a specialised transplant unit bed, since if they are admitted to the wrong area of a hospital they may be severely disadvantaged.

These programmes can and do work if they are delivered in this way. They can be shown to be safe, use less hospital inpatient beds and may be preferred by patients.[5] Depending on the funding model, they may be cost-saving – for example a patient's insurance may only fund a planned limited number of days in hospital (some procedures, some insurers in United States); alternatively in Brazil a hospital may only be reimbursed if the patient spends a minimum of 11 days in hospital, so all patients are discharged on day 12.[7] Outpatient transplant requires significant commitments on the part of the patients and their families – representing a major shift in the fiscal and non-fiscal burden from health care providers to patients.[6]

The impact of an outpatient programme is limited to what proportion of patients can use it. Only a proportion of patients who receive these simpler types of transplant meet criteria of living close to hospital, and having suitable carers and homes.[8] Many who do are readmitted for much of their transplant course, such that only a small part of the 'out-patient transplant' is spent as an outpatient. Overall these programmes seem to reduce transplant costs, but analysis of this is often not detailed, and it is accepted that much of the cost reduction is due to cost shifting to other parts of the health care service and to the patient and carer. The outpatient programmes are intensive and often more complex for staff than having the patient in hospital anyway. Some centres which have instituted such programmes, particularly in the days when many patients were being given autografts for breast cancer, have abandoned them as insufficiently applicable to their patients and overly complex. Thus only four of five academic centres in Chicago have ambulatory care programmes; previously they all did.[7]

One economic model prepared by Akehurst (unpublished, European Bone Marrow Transplant meeting, Florence, 2008) from the University of Sheffield for the National Health Service examined how to accommodate rising BMT demand within finite capacity. It was simplified by only considering myeloma autografts. It did not consider costs but only extra BMT unit capacity generated. The model indicated the scale of increased patient treatment that might be possible, given a particular level of facilities, and identified achievable key factors that affected this. Various assumptions were made, such as the size of the BMT unit (10 beds), occupancy (95 percent), the length of stay of hospitalised patients (22 days), to conclude 114 patients could be treated in a year under normal inpatient conditions. They then modelled an outpatient procedure, considering the percentage of patients treatable as out patients (50 percent), the risk of infection and the frequency of patient disease presentations requiring admission (0.21) and an 'acceptable' risk of 10 percent that a specialist patient bed would not be available for admission to show that in the same facility 183 (or 70 extra) patients could be treated per year. The most sensitive variables were the risk of hospitalisation and the percentage of patients to which this approach was applicable, changes in these reducing or increasing the treatable numbers very noticeably – for example if risk of readmission is 75 percent it reduced the number of patients treatable to only 50 extra per year. If the 'acceptable' risk of not having a hospital bed available is as low as only 2 percent of occasions, then an ambulatory care system can only treat 33 extra patients per year. The New Zealand centres have very much smaller transplant units – typically only one to three patients are having transplants for myeloma at any one time – so presumably this model needs to be reduced three- to ten-fold.

No centre in New Zealand has set up a dedicated outpatient transplant service. All centres to a greater or lesser extent get patients out of hospital for parts of their transplant course if it is deemed safe to do so. This is informal: no homes have been inspected, and no visiting outpatient nurses exist. Instead the onus is on the patient to be well enough to visit the hospital, where they have investigations, are reviewed by doctors and nurses regularly, and receive day treatments as necessary. For some centres it has been easier to put the patient 'on leave' when they go home, rather than discharge them, since if they are discharged there may be great difficulty in being able to readmit them if necessary to a transplant bed. The Wellington centre has done the most work in planning and delivering 'outpatient transplants'. They follow a typical

model,[6] and their patients have all been receiving autografts for myeloma or lymphoma. Patients are admitted for their conditioning and stem cell infusion. Patients must live within 30 minutes of the hospital, and have a responsible and sensible support person with them continuously at home. Patients are reviewed daily on the day ward by a doctor, and all are readmitted if they develop infections. The Wellington centre has managed all allografts and more complex autografts as inpatients. The Christchurch approach is similar; some patients with less complex RIC allografts have also been managed in this way. Where appropriate and possible, this may also occur with patients receiving such treatment in all other centres (Auckland, Palmerston North and Hamilton). It has not been applied to children where they are treated (Auckland Starship, Christchurch).

The most successful outpatient transplant experiences have been from large cities with extensive practices of patients who receive autografts for myeloma and lymphoma. New Zealand centres treat relatively small numbers of patients with many different types of disease, so that at one time in any one centre only a few are receiving autografts for myeloma or lymphoma. Furthermore only a minority of patients live close to the transplant centres. (In the South Island, for instance, only a third of the transplant population lives in the same city as the transplant centre.)

In conclusion, it is recognised that a proportion of fit patients receiving the simpler autografts can safely spend much of their post-autograft transplant course as outpatients, if carefully selected. The proportion will vary with the geography of the transplant centre and its catchment area. Careful preparation is required; it should not be driven by cost savings – which may be small or non-existent – but rather to improve the patient experience, if they are motivated and prepared. In the relatively small units which are in place in New Zealand it is unlikely to make a dramatic impact on transplant capacity or cost of transplant procedures.

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Appendix 6: Indications for adult allogeneic bone marrow transplant in New Zealand

This list provides indications for the majority of adult BMTs that are performed in New Zealand. A small number of BMTs are performed for other rare indications, comprising less than 10 percent of BMT activity.

A decision to perform BMT on an individual patient is based upon:

- an improved outcome following BMT compared with non-transplant therapy, recognising that transplant may be part of a combined modality approach. Potential benefits include cure, improved survival or a better quality of life
- an assessment of the potential benefits compared with risks. This assessment may change with time, and is dependent upon many factors, including patient disease; disease stage and risk; age and co-morbidity; goals of therapy; treatment options and availability; cost; and patient and physician preference.

The decision to perform BMT in New Zealand is made after due consideration in relation to evidence, international standards, peer review at local BMT advisory committees, patient counselling and consent and availability of health care resources. All BMT units in New Zealand are authorised to perform such procedures and report their data to regional and international transplant registries for ongoing audit of effectiveness.

Myeloablative allogeneic BMT – up to 55 years of age

The age level for this procedure may increase with the introduction of certain transplant regimens which can be applied more safely in older patients.

RIC allogeneic BMT – up to 65 years of age

There is no age differentiation between HLA identical sibling and 8/8 allellic high resolution MUD, depending on patient assessment/comorbidity index.

All potential donor sources should be considered unless otherwise stated.

Acute myeloid leukaemia (AML)	Adverse risk in CR1 Adverse karyotype or molecular profile Therapy-related AML Antecedent haematological disorder Slow response to induction chemotherapy Primary refractory disease
	Any risk group in CR2 Previously treated AML managed with successful reinduction chemotherapy
	Acute promyelocytic leukaemia (APML) – relapsed disease Morphological CR2 with persisting molecular positivity

Acute lymphoblastic leukaemia (ALL)	Transplant in CR1 Consider in any adult with ALL aged >25 years with available HLA identical sibling donor (ablative conditioning age <40 years; RIC age >40 years) High risk ALL and available MUD donor (ablative conditioning age <40 years; RIC age >40 years) Acute biphenotypic leukaemia Any risk group in CR2 Previously treated ALL managed with successful reinduction chemotherapy
Myelodysplastic syndrome	Consider allogeneic BMT in patients with: • IPSS intermediate-2 / high risk score • adverse cytogenetic profile • clonal evolution • increased blast count • red blood cell or platelet transfusion dependence
Aplastic anaemia	Very severe/severe disease at first presentation Patients < 40 years with HLA identical sibling donor Consider allogeneic BMT in patients failing adequate trial of immunosuppression Patients >40 years with HLA identical sibling donor Patients with suitable matched unrelated donor
Chronic myeloid leukaemia	Patients in first chronic phase failing tyrosine kinase inhibitor therapy Patients with prior advanced stage disease obtaining disease control with tyrosine kinase inhibitor therapy
Myelofibrosis	Consider allogeneic BMT in patients with: • poor risk assessment based on blood count and cytogenetics • significant red cell transfusion requirement
Chronic lymphocytic leukaemia	Consider RIC allogeneic BMT in: • early stage disease with poor risk features (for example 17p deletion) • fludarabine refractory patients (non-response / relapse within 6–12 months of therapy) • young patients with multiple relapsed disease following prior fludarabine-based therapy
Multiple myeloma	Consider RIC allogeneic BMT in patients with poor risk disease (t(4;14), deletion 13q by G-banding, deletion 17p, complex karyotype) in first response as part of tandem autologous/allogeneic approach
Indolent lymphoma	Consider allogeneic BMT in patients with advanced stage but chemosensitive lymphoma in second or later disease response
Mantle cell lymphoma	Consider RIC allogeneic BMT in patients with advanced stage disease in second response

Hodgkin lymphoma	Consider RIC allogeneic BMT in relapsed disease ≥ six months following prior autologous BMT with good stable partial remission to salvage chemotherapy
Aggressive lymphoma	T / NK cell lymphomas in CR1 Consider allogeneic BMT for chemosensitive aggressive disease
	Relapsed T / NK cell lymphomas and large B cell lymphoma Consider allogeneic BMT for carefully selected patients with stable relapsed chemosensitive disease

Appendix 7: Indications for adult autologous bone marrow transplant in New Zealand

This list provides indications for the majority of adult BMT performed in New Zealand. A small number of BMTs are performed for other rare indications, comprising less than 10 percent of BMT activity.

Autologous BMT – up to 70 years of age

AML	Specific AML groups in CR2 APML in molecular CR2
ALL	Recent studies demonstrate no advantage of autologous BMT compared with chemotherapy
Multiple myeloma	De novo myeloma Standard of care following initial chemotherapy – chemosensitive disease Primary refractory disease Proven place of single or double BMT depending on myeloma response
	Relapsed myeloma Consider second autologous BMT if treatment-free interval of at least three years after first BMT Autologous BMT on first relapse if BMT not performed as part of initial myeloma treatment
AL amyloid	Perform BMT in carefully selected patients with limited organ involvement
Severe autoimmune diseases	Consider in carefully selected patients on a case-by-case basis
Hodgkin lymphoma	Standard of care in primary refractory or relapsed lymphoma demonstrating some chemosensitivity
Aggressive lymphoma	Consider in very poor risk chemosensitive large B cell or poor risk T/NK cell lymphoma at presentation
	Consider in primary refractory large B cell lymphoma with demonstrated stable chemosensitivity
	Standard of care in chemosensitive relapsed large B cell lymphoma
Indolent lymphoma	Consider in chemosensitive relapsed indolent B cell lymphoma
Mantle cell lymphoma	Recommended in de novo chemosensitive mantle cell lymphoma
	Consider in chemosensitive relapse (CR2)
Germ cell tumours	Standard of care for chemosensitive relapsed germ cell tumour

Appendix 8: Summary table of indications for BMT procedures, 2010

Key:

Allo	Allogeneic	Auto	Autologous	R	BMT recommended	D	Developmental
ACP	Accepted clinical practice	NR	Not recommended	Sib	Sibling		

		Allo Sib (or suitably matched family donor)	**RIC Allo**	**Allo MUD**	**Auto**
Age limit		**55**	**65**	**50 RIC 65**	**65–70**
Disease					
AML	CR1 (intermediate/high risk)	R	R	R	ACP
	Early first relapse	R	ACP	R	NR
	CR2	R	R	R	ACP
	Primary resistant leukaemia	ACP	NR	ACP	NR
	Resistant relapse	NR	NR	NR	NR
Adult ALL	L3 (Burkitt's) CR1	NR	NR	NR	NR
	Sensitive relapse	R	NR	R	ACP
	Ph^+ ALL CR1	R	ACP	R	NR
	CR2	R	ACP	R	NR
	Ph^- ALL CR1	R	ACP	R	NR
	CR2	R	ACP	R	NR
	Primary resistant leukaemia	NR	NR	NR	NR
	Resistant relapse	NR	NR	NR	NR
CML	First chronic phase, failing TKI	R	R	R	NR
	>First chronic or Accl phase	R	ACP	R	NR
	Blast crisis	NR	NR	NR	NR
CLL	Chemosensitive and • poor risk first presentation (eg, 17p del) • or fludarabine refractory • or advanced stage CLL	ACP	R	ACP	ACP
	Poor risk CLL in CR, or good PR	–	–	–	D
Myeloma	Primary responsive (single or double transplant)	D	ACP	D	R
	Primary refractory	D	ACP	D	R
	Sensitive relapse (no initial transplant or long first remission to transplant)	NR	ACP	NR	R
Al amyloid	Limited disease, good risk	D	D	D	ACP
MDS	Good risk (eg RA, RAEB)	R	R	R	NR
	Poor risk (chemosensitive)	R	R	R	D

		Allo Sib (or suitably matched family donor)	RIC Allo	Allo MUD	Auto
Severe aplastic anaemia	De novo, age < 40	R	–	NR	NR
	Relapsed, refractory to immunosupp	R	–	R	NR
	Red cell aplasia	R	ACP	ACP	NR
	β Thalassaemia major and severe variants	R	–	ACP	NR
	Sickle cell disease	R	–	ACP	NR
Severe autoimmune disease		D	D	NR	ACP
Hodgkin lymphoma	Poor prognosis CR1	NR	NR	NR	NR
	Primary refractory	NR	ACP	ACP	R
	Chemosensitive relapse	NR	ACP	ACP	R
Age limit		**55**	**65**	**45 RIC 65**	**65**
Disease					
Lymphoma	Lymphoblastic (adults) – CR1	ACP	ACP	ACP	ACP
	Chemosensitive relapse	R	ACP	R	ACP
	Burkitt's Chemosensitive relapse	ACP	ACP	ACP	R
	Aggressive poor risk – CR1	NR	NR	NR	ACP
	Primary refractory	NR	NR	NR	R
	Chemosensitive relapse	ACP	ACP	D	ACP
	Indolent	ACP	ACP	ACP	ACP
	Mantle De Novo – CR/PR	NR	ACP	NR	ACP
	Chemosensitive relapse	R	R	ACP	ACP
Myelofibrosis	Progressive or high risk	R	R	R	NR
Adult solid tumours	Germ cell tumours – relapse	NR	NR	NR	ACP