The cost of Cure: managing the long term conseqences of curative therapy for haematological malignancy

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Learning outcomes:

1. Increased knowledge of the complications and late effects of curative therapy for haematological malignancy.
2. Developed an approach to the assessment and management of common consequences of treatment of haematological malignancy.

Haematological malignancy

1. Collectively represent 5th most commonly diagnosed cancer type
2. Represent 10% of all cancers diagnosed annually in Australia
3. NHL is the most common blood cancer of adulthood whilst ALL is the most common childhood cancer of any type and 2nd most common cancer of adolescence and young adulthood, 2nd only to melanoma.

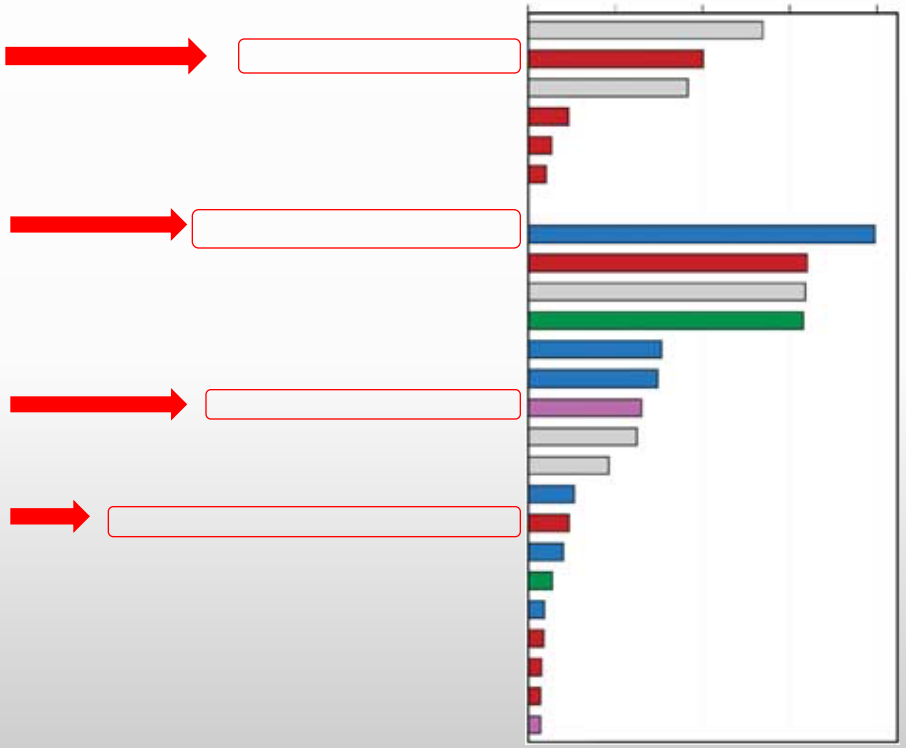
Haematological malignancy

4. With the aging population, increasing population adjusted incidence of many of these malignancies and the improved survival and cure rates with modern therapies, the prevalence of survivors of blood cancer will to continue to rise.

5. The holistic management of such survivors, often with many co-existing co-morbidities and frequent late effects of therapy is currently limited globally.

6. Shared care approaches integrating care between GP's, specialist cancer centres and community based rehabilitation and support programs will be essential in the future for this growing demographic.

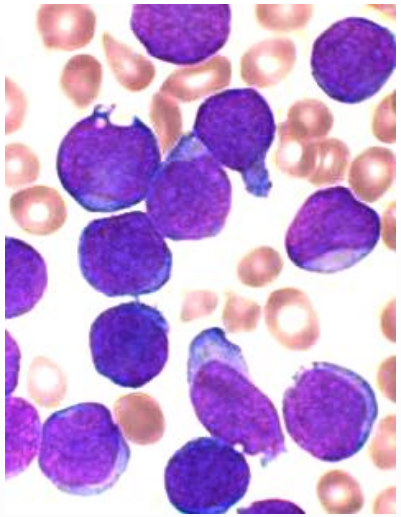
Haematological malignancy



Despite the improved survival of of all haematological malignancies many remain highly treatable but incurable:
Myeloma, CLL, MDS, Myelofibrosis, Follicular lymphoma, Marginal zone lymphoma, Mantle cell Lymphoma.

Several common haematological malignancies are increasingly associated with high cure rates (AML, DLBCL, Hodgkin Lymphoma, B-ALL).

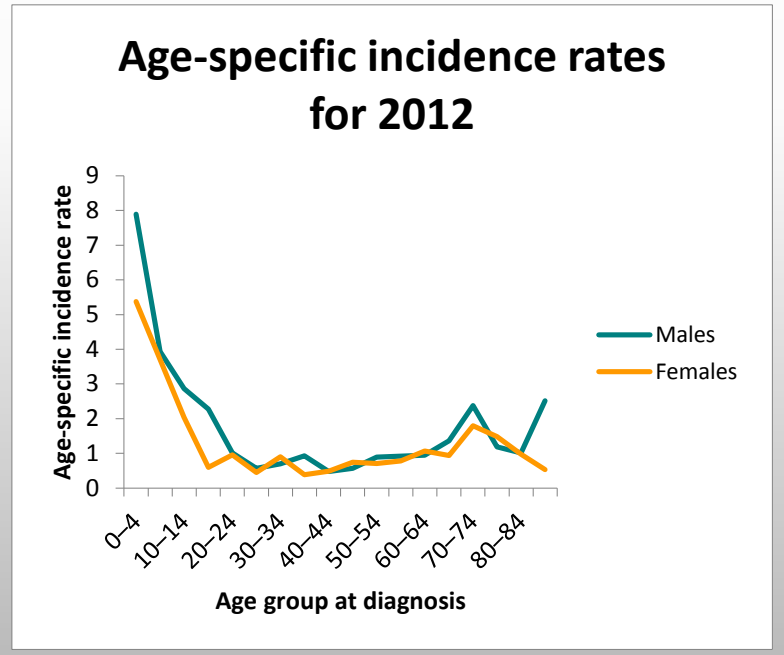
Smith A et al, British J Cancer 2001;105:1684-1692.

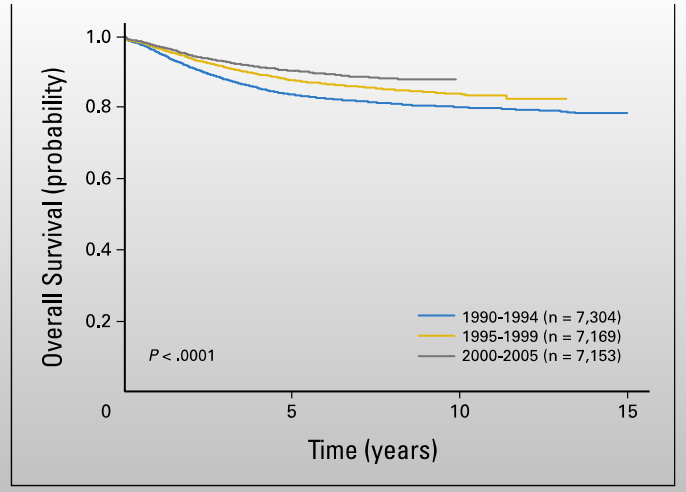


Acute Lymphoblastic Leukaemia

Intensive multi-agent chemotherapy

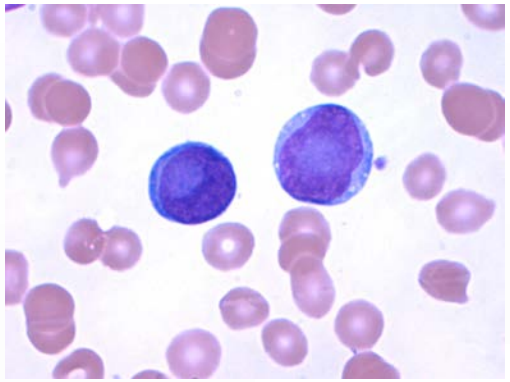
given over 6 mths (prolonged high dose steroids +/- cranial radiotherapy)



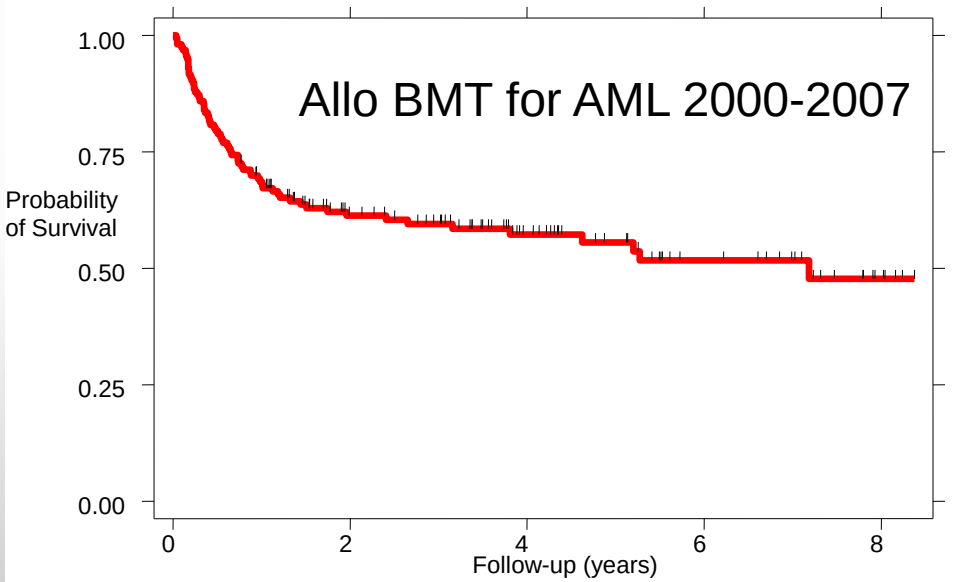


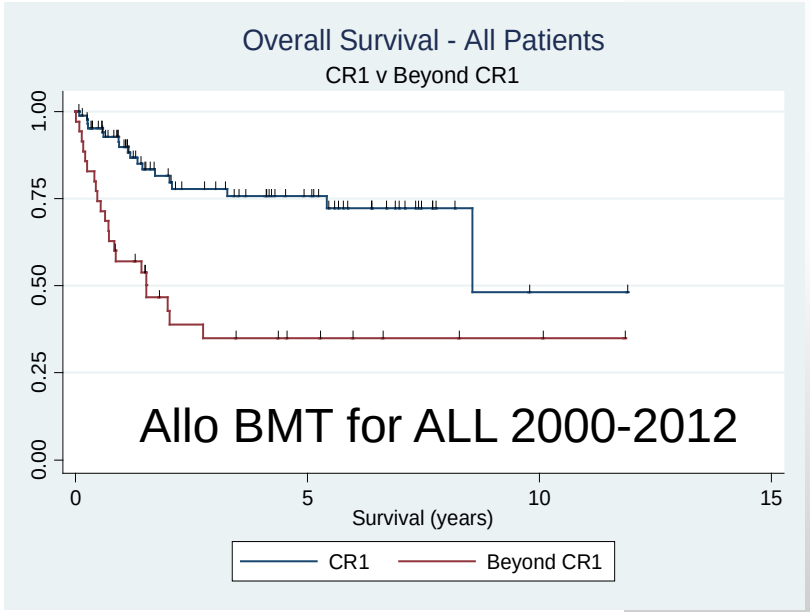
Hunger SP et al JCO 2012; 30:1663-69

Australian Institute of Health and Welfare (AIHW) 2016. Australian Cancer Incidence and Mortality (ACIM) books: Acute Lymphoblastic Leukaemia. Canberra: AIHW. <http://www.aihw.gov.au/acim-books>.

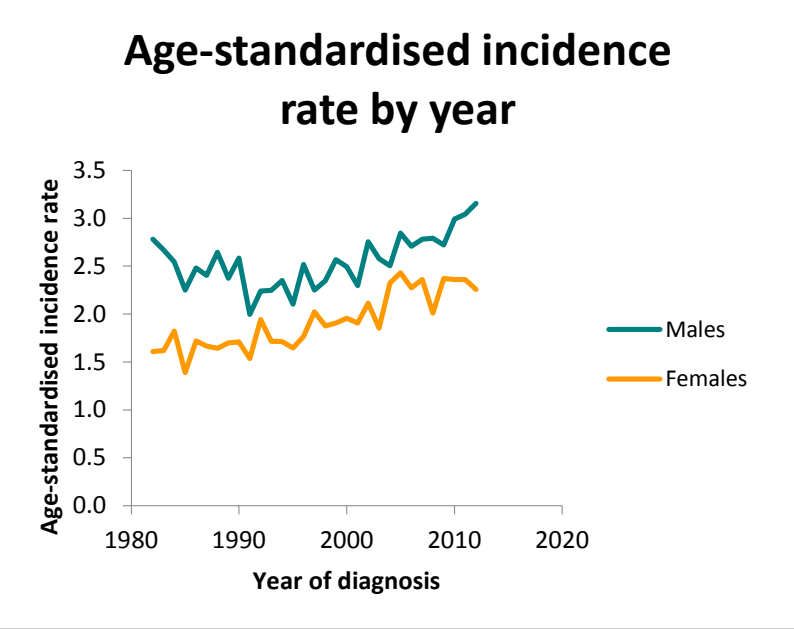


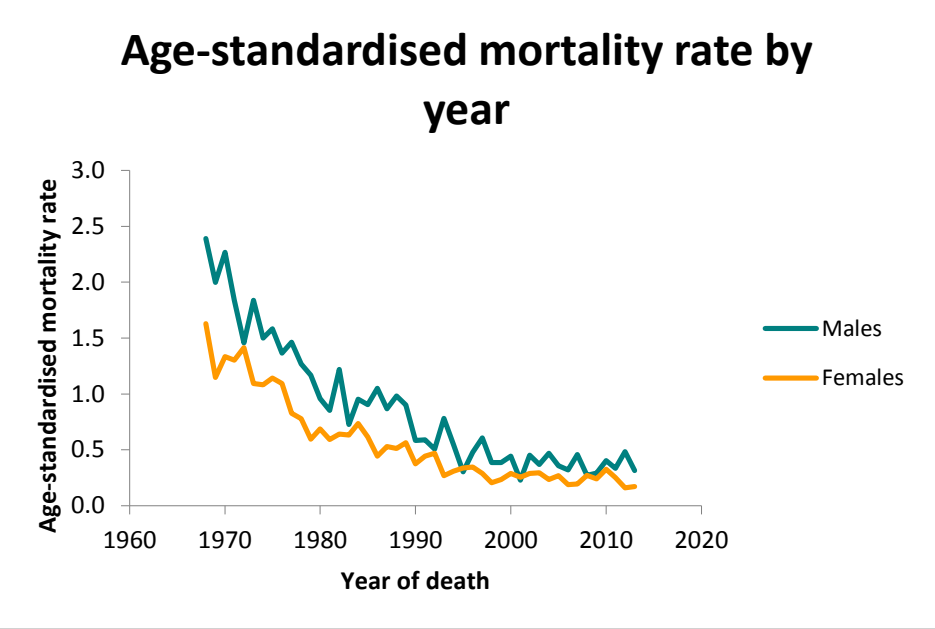
Adult AML and ALL in QLD





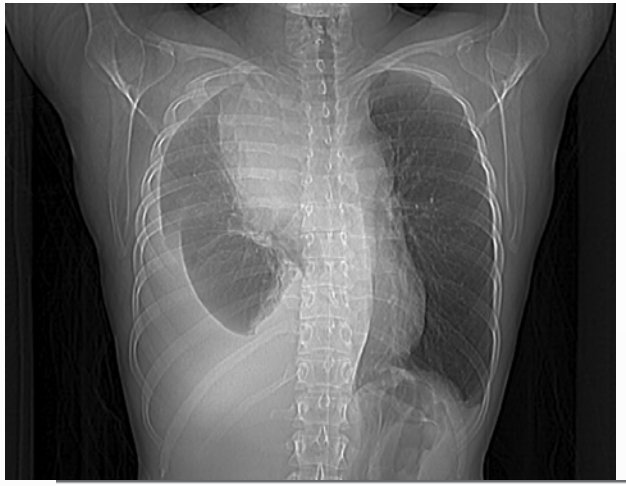
Hodgkin Lymphoma

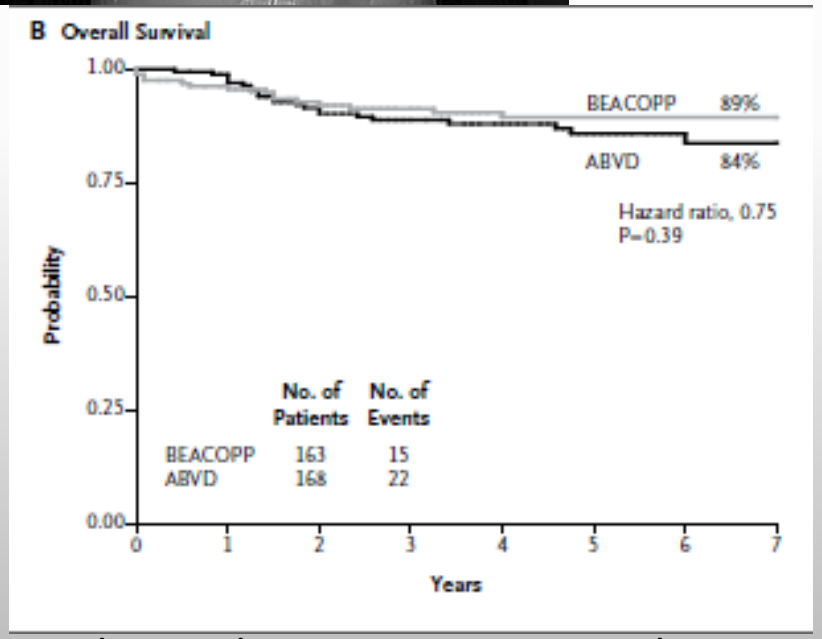




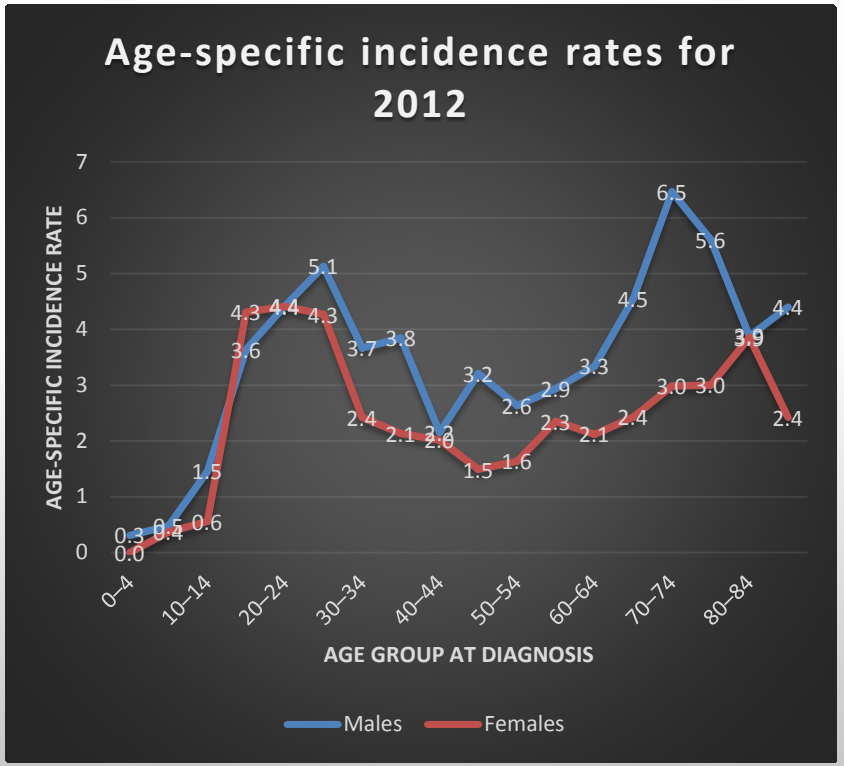
Australian Institute of Health and Welfare (AIHW) 2016. Australian Cancer Incidence and Mortality (ACIM) books: Hodgkin lymphoma. Canberra: AIHW. <http://www.aihw.gov.au/acim-books>.

Hodgkin Lymphoma





Advanced stage – Viviani S et al 2011



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Hodgkin Lymphoma

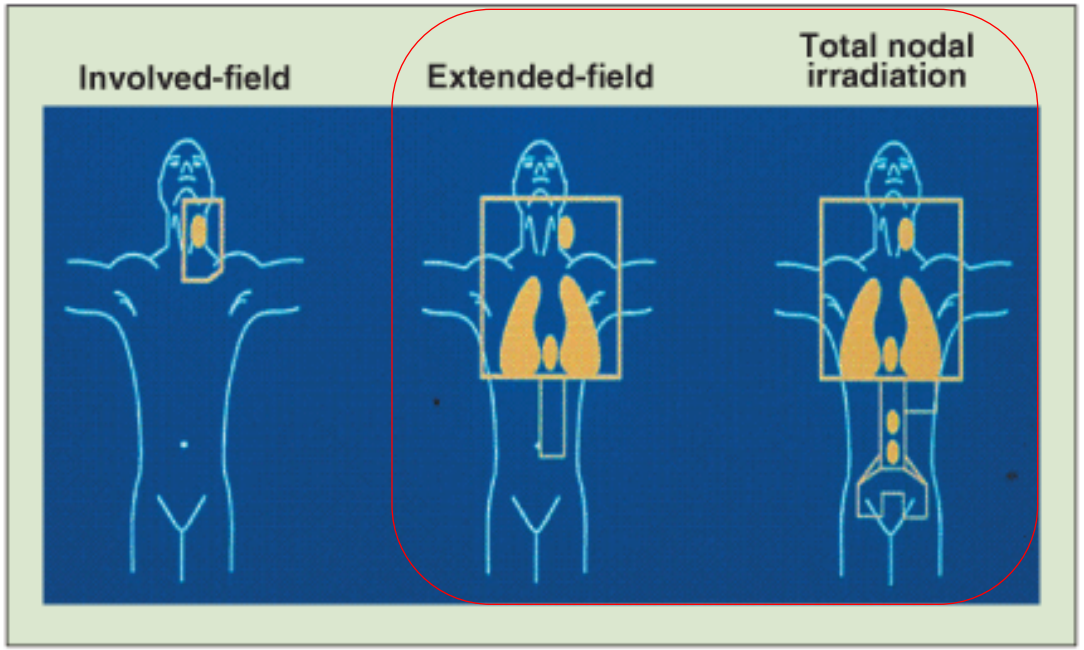


Figure 1: Radiotherapy Techniques and Fields—Involved-field, extended-field, and total nodal irradiation in a patient with left cervical involvement of Hodgkin's lymphoma (clinical stage I).

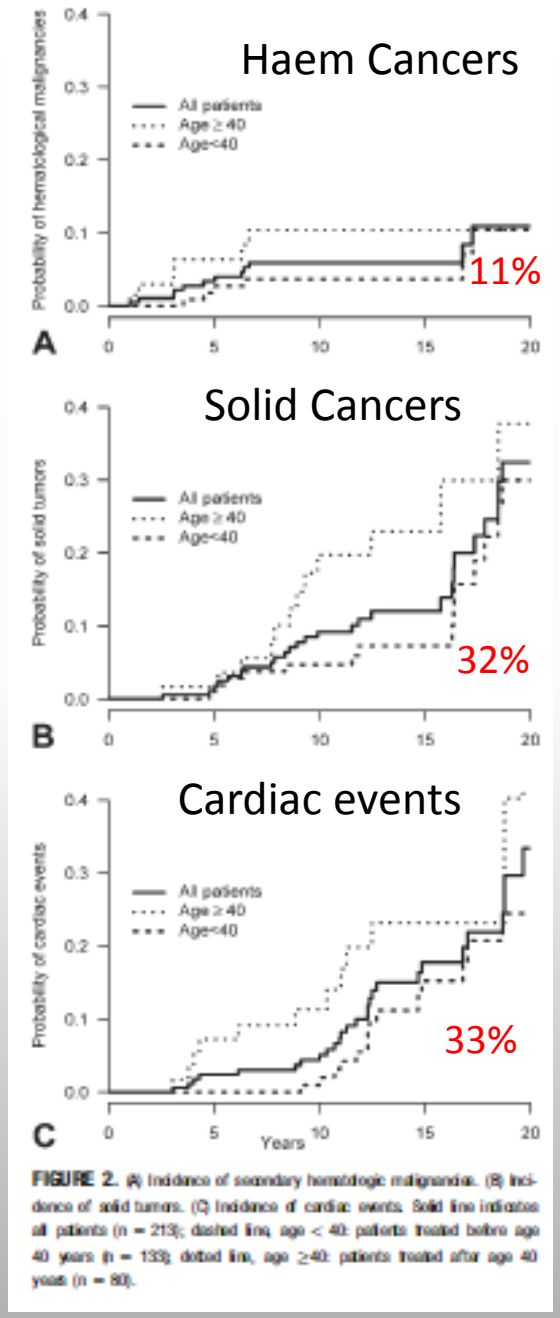
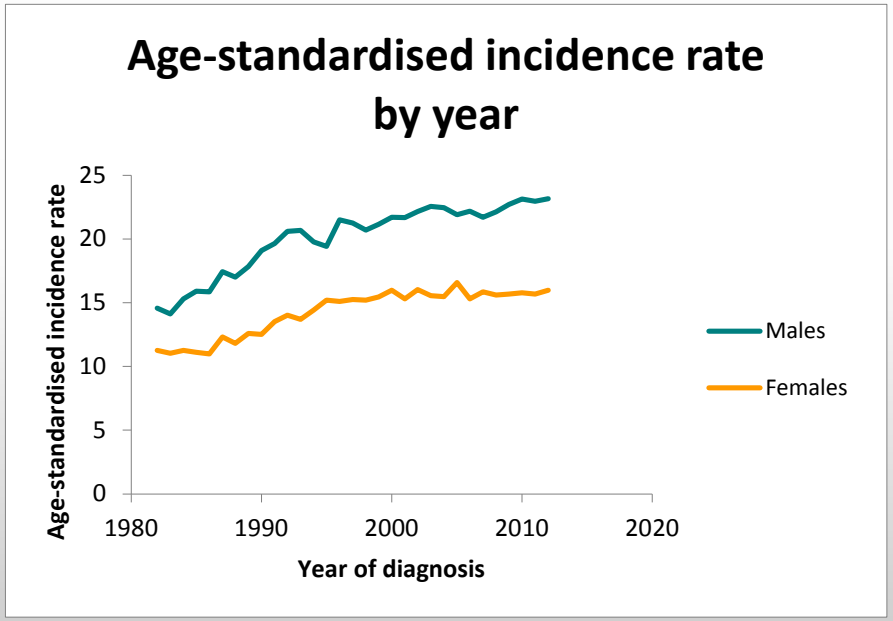
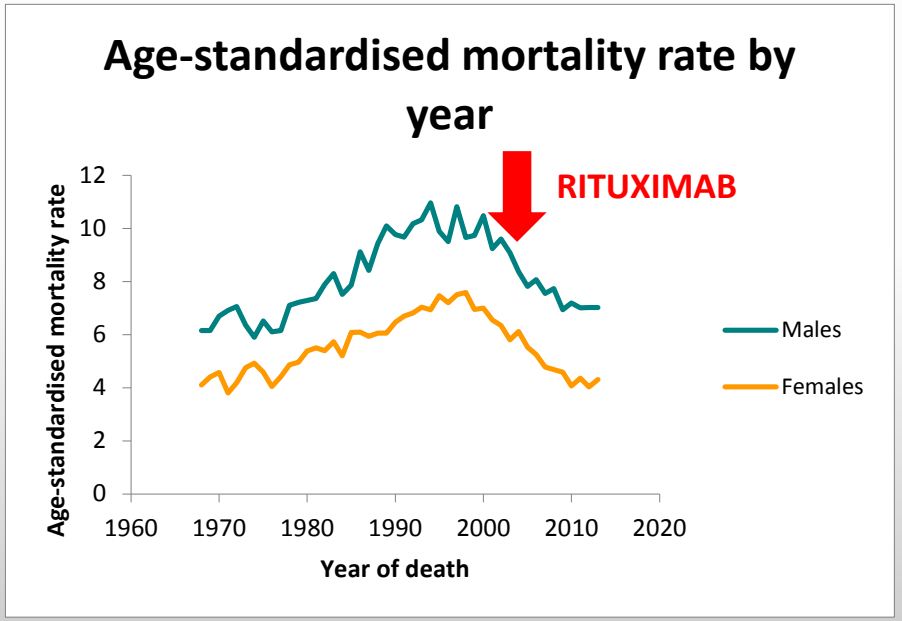


FIGURE 2. (A) Incidence of secondary hematologic malignancies. (B) Incidence of solid tumors. (C) Incidence of cardiac events. Solid line indicates all patients (n = 213); dashed line, age < 40: patients treated before age 40 years (n = 133); dotted line, age ≥40: patients treated after age 40 years (n = 80).

Senecal D et al, Cancer 2008;112(4):846-855.

Non-Hodgkin Lymphoma





Australian Institute of Health and Welfare (AIHW) 2016. Australian Cancer Incidence and Mortality (ACIM) books: Non-Hodgkin lymphoma. Canberra: AIHW. <http://www.aihw.gov.au/acim-books>.

R-CHOP for DLBCL

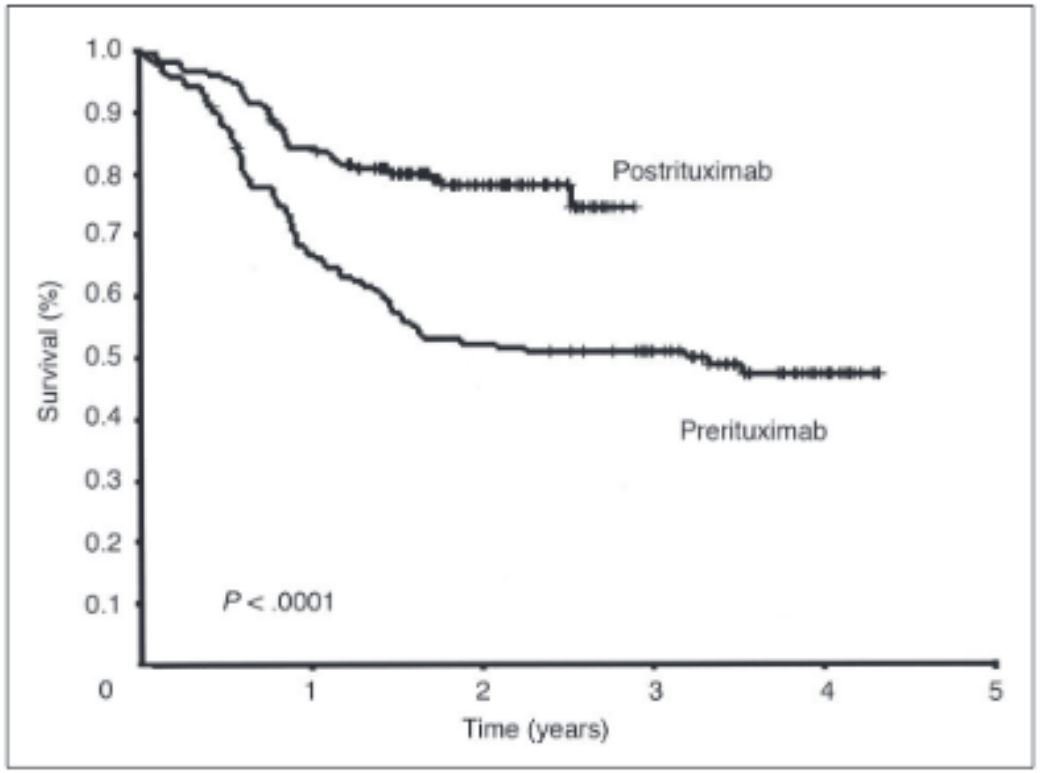


Fig 2. Overall survival by treatment era. All patients, N = 292.

Sehn L et al J Clin Oncol 2005; 23(22):5027-33.

Definitions

Long term complications =

Defined as side effects present during therapy that persist following completion of therapy

Late effects =

Side effects of therapy that develop first after therapy is completed, often many years later

Long term complications

1. Fatigue
2. Cognitive impairment
3. Insomnia
4. Psychological issues – anxiety/depression
5. Peripheral neuropathy (Vincristine)
6. Chronic kidney disease (Cisplatin)
7. Immune deficiency
8. Graft versus host disease
9. Sexual dysfunction
10. Pulmonary toxicity (Bleomycin)

Fatigue

Whilst some studies have suggested 80% of patients are affected, true longitudinal studies suggest an incidence of 15-20%, compared with <10% in the general population.

Pain and psychological stressors of living with cancer and as consequence of therapy are important however do not explain all cases.

NCCN guidelines Survivorship 2016

Fatigue

Interventions:

1. Psychostimulants – 7 placebo RCT's evaluating methylphenidate and modafinil in the treatment of CRF. Only 1 of the 7 showed objective improvements in fatigue.
2. Dietary supplements –
   - L-carnitine = no benefit in RCT
   - Ginseng = clinically meaningful and significant improvement at 8 weeks in placebo controlled RCT. No clear toxicity.
3. Exercise – key intervention with level I evidence supporting mild to moderate level exercise
4. Cognitive behaviour therapy – small randomised trial demonstrating benefit

NCCN guidelines Survivorship 2016

Cognitive impairment

Mild short term memory impairment is commonly reported during and shortly after completion of most forms of chemotherapy.

Often referred to by patients as “chemo brain” – objective testing is usually normal, and a combination of non-chemotherapy related factors may contribute.

Objective permanent cognitive impairment (dementia) is a rare late effect, with most cases occuring in patients treated for primary CNS lymphoma with high dose methotrexate protocols and or cranial radiotherapy, particularly in patients over the age of 60yrs at the time of therapy.

Long term survivors of childhood ALL whom received 24Gy or greater doses of cranial radiotherapy demonstrate permanent memory impairment on objective testing.

NCCN guidelines Survivorship 2016

Peripheral neuropathy

Either associated with numbness alone, paraesthesia or sensory ataxia, peripheral neuropathy is common with specific chemotherapies.

Vincristine is a vinca alkyloid used primarily in the treatment of non-hodgkin lymphoma, acute lymphoblastic leukaemia and rare cases of Hodgkin lymphoma. (ie CHOP, CVP, hyper CVAD, Hoeltzer style therapy, BEACOPP)

Vinblastine is an alternate vinca alkyloid associated with less neuropathy than vincristine, and is used as a key part of standard hodgkin lymphoma therapy (ie ABVD)

May require – podiatry, lyrica/gabapentin, physiotherapy programs if severe.

Chronic kidney disease

Key treatments associated with renal dysfunction (either temporary or permanent) include:

1. Cisplatin (salvage therapy for lymphoma)
2. Ifosfamide (salvage therapy for lymphoma)
3. Gemcitabine (salvage for lymphoma)
4. Cyclosporin/Tacrolimus (post transplant)
5. Radiation (either involved field, extended field or total body irradiation TBI as transplant)
6. Post BMT thrombotic microangiopathy (red cell fragmentation, low platelets and microvascular thrombosis)

Requires similar care to all forms of CKD – BP control, monitor for proteinuria, lipid control, pre-dialysis planning if stage 4.

Immune Deficiency

The type and degree of immune deficiency present post completion of therapy of haematological malignancy is highly variable and depends on intensity of chemotherapy, whether T cell suppressive therapies such as fludarabine, B cell depleting monoclonal antibodies such as Rituximab have been used and most importantly whether a bone marrow transplant has been performed.

Patients post BMT have the most severe and long lasting immune deficiency and should be approached quite differently (will discussed independently).

Immune Deficiency

Most forms of chemotherapy lead to a temporary lymphopenia of T cells, NK cells and B cells during treatment with functional recovery within 3 months.

Rituximab containing regimens are associated with B cell lymphopenia lasting 9-12 months however hypogammaglobulinaemia develops in approximately 40-50% of patients only. Consider IVIG if recurrent severe infection.

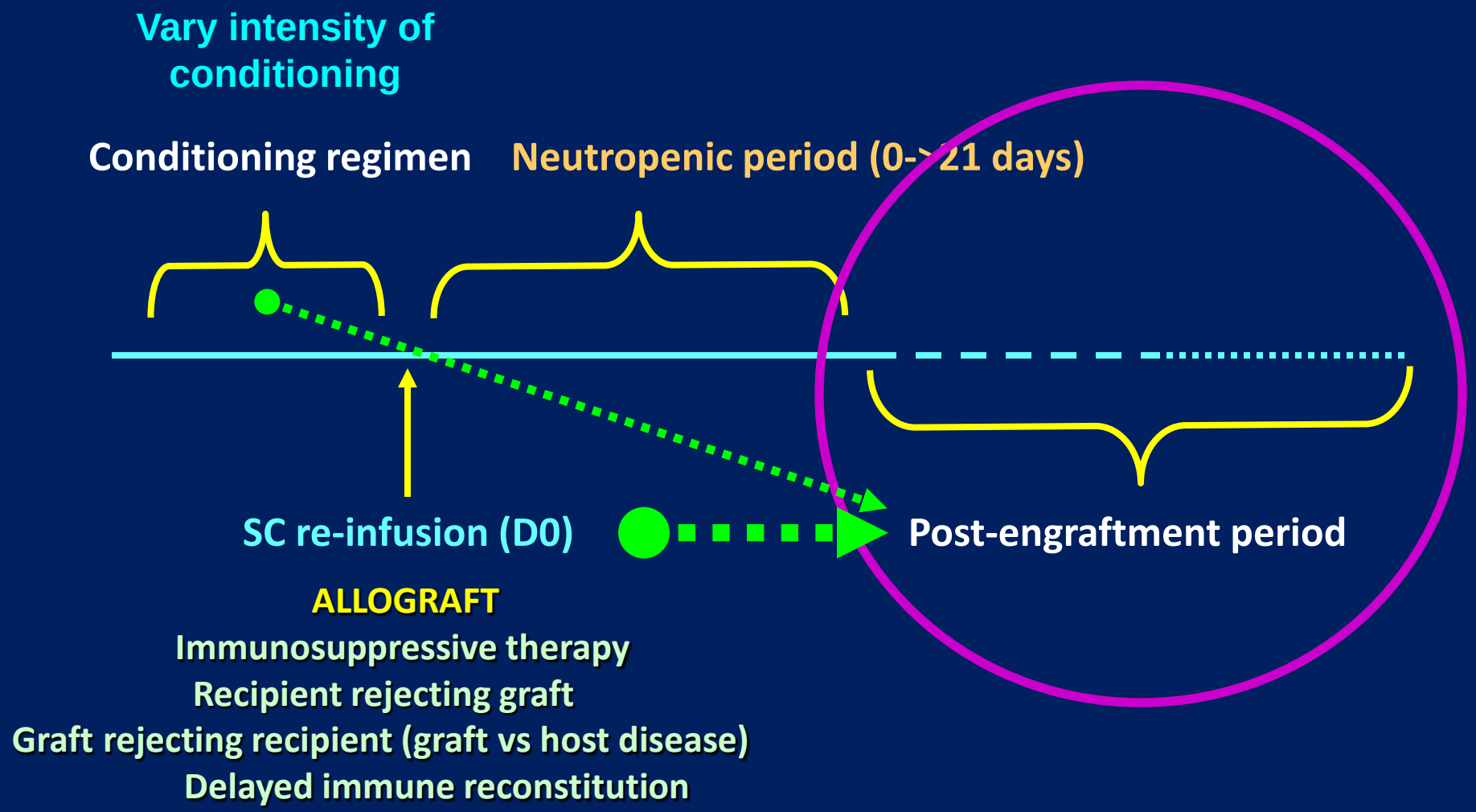
Fludarabine containing regimens lead to selective CD4 lymphopenia which may persist for 6 months rendering patients more susceptible to opportunistic infections like PCP during this period.

Vaccinations: non BMT patients

Vaccine	6mths (post therapy)	7mths
dTpa	yes	-
MMR (live)	Yes**	-
IPV	Yes	-
HepB	Yes	-
Prevenar 13	Yes	-
Pneumovax 23	-	Yes
Varicella (live)	Yes**	-
Fluvax	Yes (annually)	

**Caution with live vaccines, pts must NOT be receiving any immunosuppression including steroids and have not received a BMT (either auto or allogeneic)

Allogeneic SCT



BMT vaccinations

The key differences are:

1. Need to repeat total schedule
2. Need to cover meningococcus, HiB
3. Need 3 doses Prevenar13 pre Pneumovax23
4. Leaving live vaccines till at least 2 years (must be off all immunosupression with no GVHD)

Australian Immunisation handbook 10th edition

Table 11.3 Re-vaccination schedule post Haematopoietic stem cell transplant (HSCT) in adults (irrespective of prior vaccination history) [76]

VACCINE	Months after HSCT				
	6	8	12	24	Comments
Streptococcus pneumoniae					
13-valent pneumococcal Conjugate vaccine (13vPCV)[Prevenar13]	yes	yes	yes	not needed	
23-valent pneumococcal polysaccharide vaccine (23vPPV)[Pneumovax23]	no	no	no	yes (after 13vPCV)	
Haemophilus influenza type b					
Hib [Hiberix]	yes	yes	yes	not needed	
Diphtheria, tetanus, pertussis					
dTpa containing vaccine [Boostrix]	yes*	no	no	not needed	#1st dose dTpa followed by 2 doses of dT [ADT booster]
dT vaccine	no	yes#	yes#	not needed	
Poliomyelitis					
IPV	yes*	yes	yes	not needed	*1st dose can be given as dTpa-IPV [Boostrix-IPV]
Hepatitis B^					
Hep B vaccine	yes*	yes*	yes*	not needed	*Given by GP
Influenza^					
Two doses of inactivated influenza vaccine^ at least 4 weeks apart are recommended for all HSCT recipients with first dose at 6 months after HSCT, then single dose annually thereafter					
Neisseria meningitides					
Quadrivalent meningococcal conjugate vaccine (4vMenCV) [Menveo]	yes	yes	not needed		Consider 4CMenB [Bexsero], 2 doses 1-2 months apart avoiding co-administration with other vaccinations
Human papillomavirus					
HPV vaccine [Gardasil]	no	no	consider a 3 dose course of 4vHPV in appropriate clinical circumstances (see comment)		ie, limited sexual exposure
Measles, mumps and rubella					
MMR vaccine (live attenuated)	no	no	no	consider in non-immunosuppressed patients	ie, no active GVHD or immunosuppression with normal cell mediated immunity
Varicella					
Varicella vaccine (live attenuated VV) [Varilrix or Varivax Refrigerated]	no	no	no	Consider only in non-immunosuppressed patients whom are seronegative	ie, no active GVHD or immunosuppression with normal cell mediated immunity NB. Zoster vaccines [Zostavax] are not recommended.

Chronic Graft-v-host disease

Most common post allo SCT complication

Incidence 20-80%

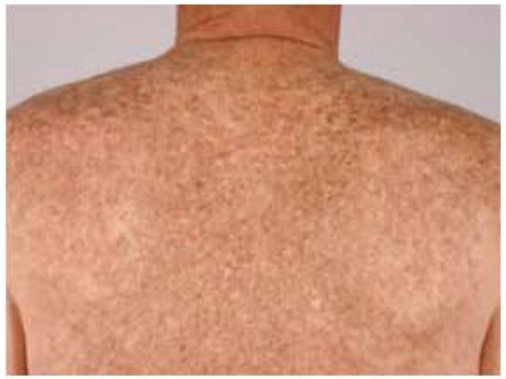
Associated with:

1. Increased non-relapse mortality
2. Increased risk 2nd-malignancies
3. Reduced QOL
4. Graft versus malignancy (GVM) effect – less chance of relapse

Pleiotropic syndrome characterized by oral and ocular sicca in association with fibrotic and / or autoimmune manifestations and immunodeficiency

Can occur in any organ –

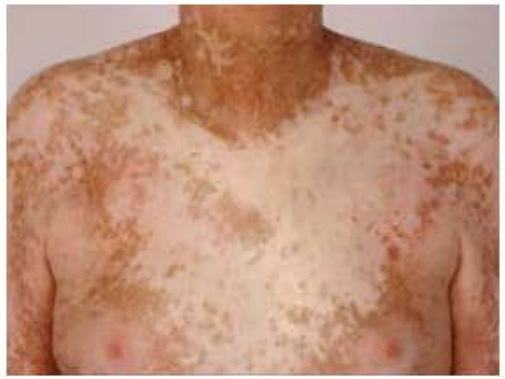
liver, skin, eyes, mouth, lungs, pancreas, pleura, pericardium.



7. Hyperpigmentation

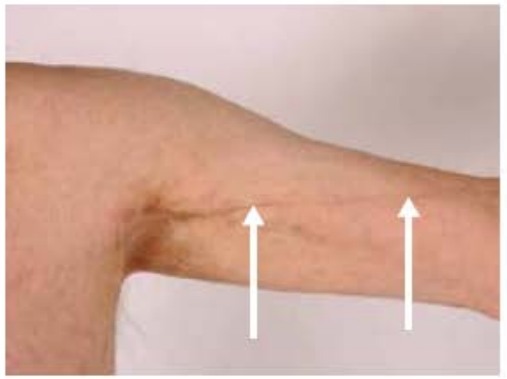
Excess pigmentation in the skin; may manifest in a widespread reticulated pattern.

See Chart page 4



8. Hypopigmentation, hyperpigmentation, sclerosis

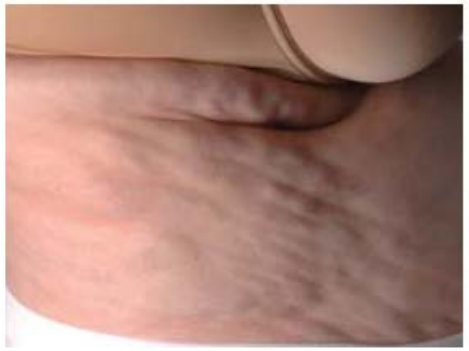
Diminished (hypo-) or excess (hyper-) pigmentation in the skin. Sclerotic tissue is hard and fibrous, with a decreased ability to pinch. Superficial sclerosis is moveable upon palpation, while deep sclerosis is hidebound



9. Sclerosis, fasciitis

Subcutaneous sclerosis/fasciitis can be detected by a "groove sign" seen here.

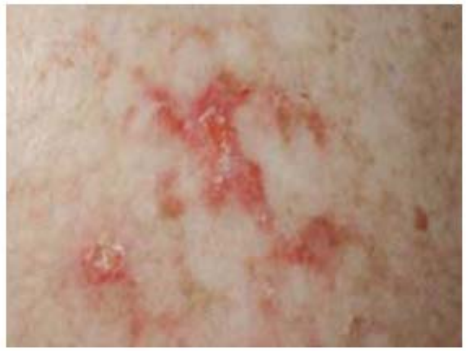
See Chart page 3



10. Sclerosis

Subcutaneous sclerosis can be manifested by rippling, dimpling of the skin and a resultant cellulite-like appearance.

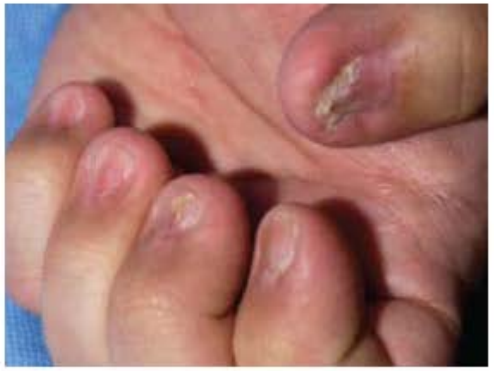
See Chart page 3



11. Erosion

Localized tissue destruction characterized by complete or partial loss of only the epidermis.

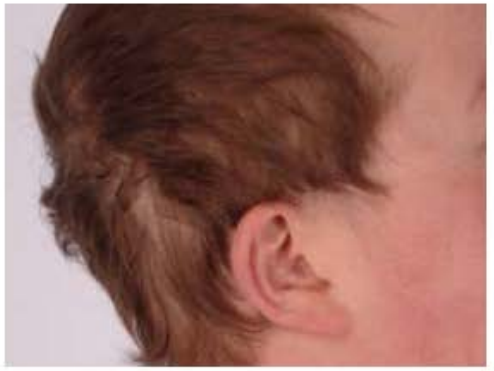
See Chart page 4



13. Nail dystrophy

Longitudinal ridging, splitting, or brittle features of nails. Note periungual erythema.

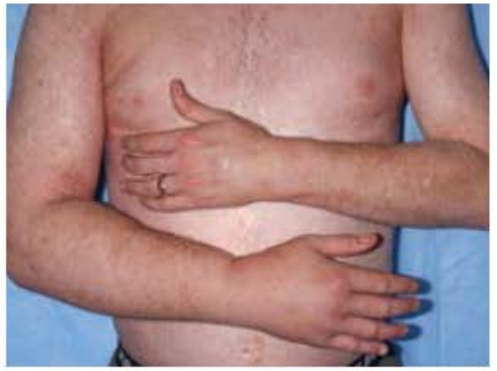
See Chart page 5



14. Alopecia

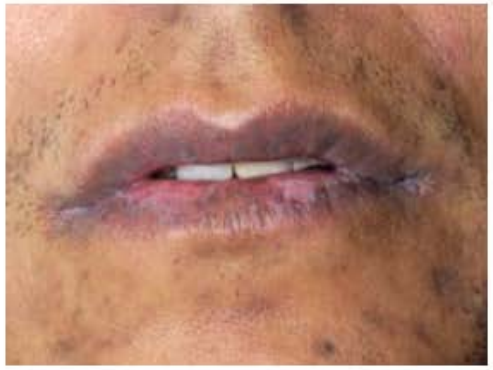
Patchy alopecia is shown. May also include loss of body hair (after initial recovery of hair growth following chemotherapy or radiotherapy).

See Chart page 5



15. Edema

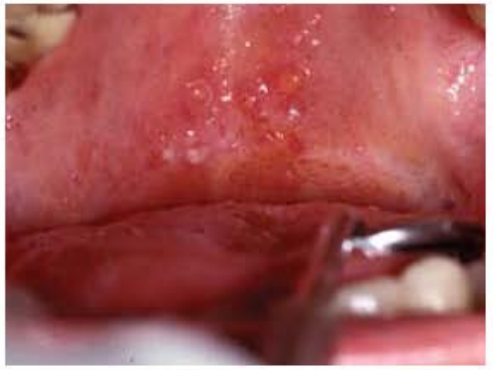
Edema in the extremities can be bilateral or unilateral (shown). May be present with erythema and peau d'orange skin. Edema may be associated as prodromal symptom to subcutaneous sclerosis and fasciitis.



16. Lichen planus

Lichenoid changes extending from the labial mucosa to the lip. Cheilosis (surface scaling and fissures in the corners of the mouth) is also present.

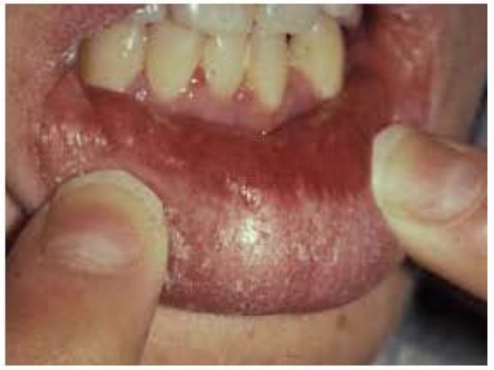
See Chart page 7



17. Mucoceles

Numerous vesicle-like mucoceles are seen along the center of the soft palate. Patchy white lichenoid hyperkeratosis and interspersed moderate erythematous changes are also evident across soft palate.

See Chart page 7



18. Erythema

Chapping and erythema of the vermillion lip. Erythema of labial mucosa.

See Chart page 7

22. Keratoconjunctivitis sicca

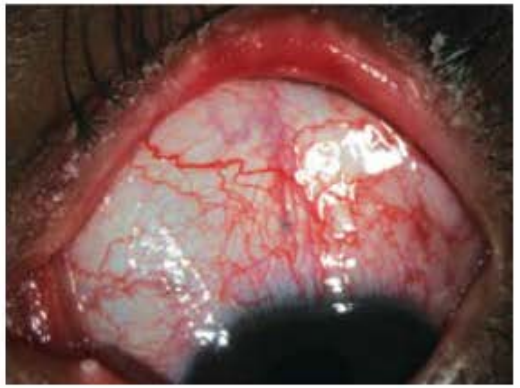
Inadequate tear production (measured by Schirmer test) and conjunctival erythema. Also note scleral injection and chemosis (conjuctival edema).

See Chart page 6

23. Keratoconjunctivitis sicca

Note scleral injection and conjunctival erythema.

See Chart page 6



24. Blepharitis

Thickened, edematous and erythematous eyelid margins. Also note plugging of meibomian gland orifices (along the eyelid margin) and significant conjunctival hyperemia/injection.

See Chart page 6

Chronic GVHD

Immunosuppressive therapies required to control cGVHD lead to a host secondary complications that require management –

hyperlipidaemia, infection, osteoporosis, diabetes, renal dysfunction, catarracts, infectious morbidity and mortality, increased risk of skin and head and neck malignancy.

Late effects of curative therapy

1. Secondary malignancy
2. Pre-mature coronary artery disease (RT)
3. Cardiomyopathy
4. Pulmonary disease
5. Infertility/ premature menopause
6. Cognitive impairment and psychological issues
7. Endocrine dysfunction
8. Bone health
9. Catarracts and dental health
10. Financial impacts

Secondary Malignancy

Risk depends on the therapy and age of therapy.

HODGKIN LYMPHOMA:

1. Chemotherapy alone = RR 2.0
2. Combined modality therapy (CMT) = RR 3.9

Peaks at 5-9 yrs post therapy, still raised at 25 years.

ABVD alone associated with no increase in rates of solid malignancy, but increased rates of NHL (RR 2.0).

The risk of secondary breast cancer is strongly related to a younger age at the time of delivery of combined modality treatment (CMT). RR 18.2 if <20yrs when CMT given, compared to RR 2.3 if age 20-34yrs, versus 1.2 if age >34yrs at time of treatment.

Swerdlow AJ et al JCO 2011;29:4096-4104

Secondary Malignancy - Hodgkin

But…

Should remember that the risk of malignancy increases with age independent of chemotherapy so whilst the RR decreases with increasing age at time of initial therapy, the absolute 20yr incidence of secondary malignancy post therapy (CMT) is 13% for those patients less than 25yrs of age at time treatment compared to 43% in those treated first at age greater than 55yrs.

Swerdlow AJ et al JCO 2011;29:4096-4104

Secondary Malignancy- allo HSCT

Second malignancy is linked to prior chemotherapy, radiation but also the immunosuppressed state required to perform allo HSCT. This is do to poorer immune surveillance and increased infective drivers (HPV, EBV) and inflammatory drivers (cGVHD) of malignancy.

The RR increases with time post transplant: ranging from 2-6 times the base age matched population.

Risk factors in this group include:

1. Age <18yrs at BMT
2. cGVHD (particularly oral GVHD - HNC)
3. TBI (total body irradiation) based conditioning
4. Age >50yrs + smoking history (RR 11 for lung cancer)

Ajhail NS et al Br J Haematol 2011; 154:301-310

Swerdlow AJ et al JCO 2011;29:4096-4104

Screening secondary malignancy

Table III. Guidelines for screening for secondary solid cancers in allogeneic HCT recipients.

Site	Screening recommendations
Breast	Mammogram annually starting at age 40 years*; begin at age 25 years or 8 years after radiation, whichever occurs later, in women who have received ≥20 Gy to the chest region
Cervix	Papanicolaou (PAP) smear every year (for regular PAP test) or every 2 years (for liquid based PAP test); after age 30 years, if patient has had 3 consecutive normal tests, may screen every 2–3 years*
Colorectal	Beginning at age 50, faecal occult blood annually and/or flexible sigmoidoscopy every 5 years, or double contrast barium enema every 5 years, or colonoscopy every 10 years; certain high risk groups (e.g. patients with inflammatory bowel disease) may need earlier initiation and more frequent screening*
Lung	Yearly pulmonary examination with imaging as appropriate
Oral	Yearly oral cavity examination
Thyroid	Yearly thyroid examination
Skin	Skin examination as a part of annual periodic health examination*

Ajhail NS et al Br J Haematol 2011; 154:301-310

Premature Coronary artery disease

Mediastinal radiotherapy represents the most significant risks for survivors of haematological malignancy. Long term allo HSCT survivors also have an increased risk of CAD

The RR of fatal CAD is 2.2-7.2 and risk seems to progressively increase over time.

The are limited evidenced based screening guidelines for CAD post mediastinal RT, however recommendations range from CT coronary angiography or EST every 5 years from 10yrs post RT to cardiovascular RF management alone and investigation of symptoms.

Cardiomyopathy

Severe systolic dysfunction is a rare but a well recognised complication of anthracycline chemotherapy and cardiac radiotherapy (<5% to 30%).

Common anthracyclines, …doxorubicin, idarubicin, epirubicin, daunorubicin, mitozantrone.

Major risk factors = childhood exposure (particularly <5yrs), concurrent chest RT (>15Gy), total cumulative dose, bolus rather than infusion, concurrent CV RF (DM, HTN), age >65yrs, extremes of body weight and female gender.

Screening: ECHO at 2 yrs, 5yrs then 10yrs in high risk groups

Armenian SH et al,Lancet Oncol 2015;16:e123-36

Pulmonary disease

Late lung effects of treatment include:

1. Chemotherapy related pulmonary fibrosis
   a. Bleomycin (avoidance of high flow oxygen)
   b. Carmustine
   c. Busulphan
2. Radiation induced interstitial progressive fibrosis
3. Bronchiolitis Obliterans – obstructive picture post allogeneic BMT

High risk populations have lung function done during and/ or for 1 years post therapy. Symptom based assessment thereafter. Annually thereafter when established diagnosis.

Infertility

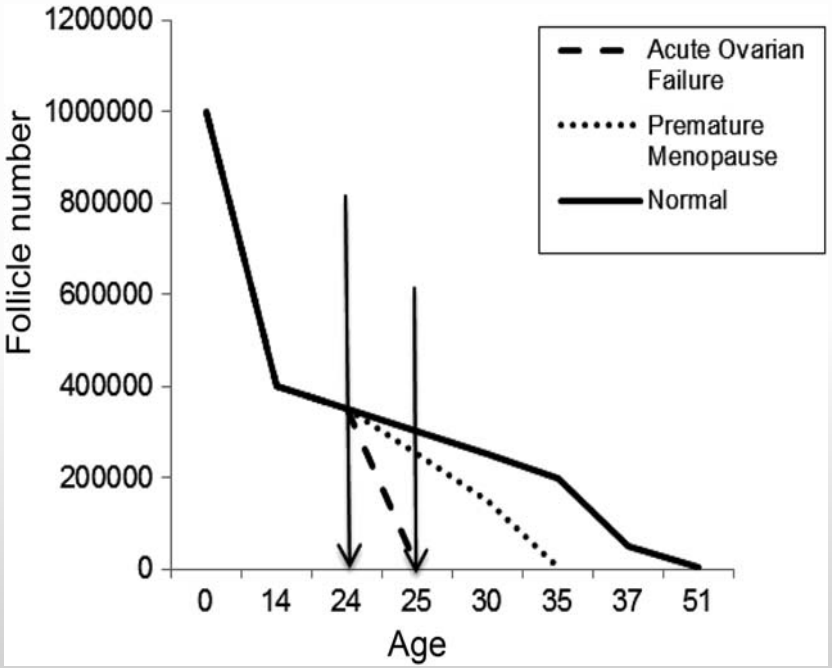


Figure 1. Depletion of Ovarian Reserve.

Represents a significant late effect/ complication of curative therapy for haematological malignancy.

Dependent on many factors:

1. Chemotherapy type – most common with alkylators (cyclophosphamide, procarbazine)
2. Radiation field and intensity (12Gy TBI – allo BMT)
3. Age at time of therapy (>30yrs)
4. Ability for fertility preservation procedures prior to therapy at diagnosis (sperm cryo vs egg harvest)

Levine JM et al, Cancer 2015;121:1532-9

Lee SJ et al JCO 2006;24:2917-31.

Table 2. Risks of Permanent Amenorrhea in Women Treated With Modern Chemotherapy and Radiotherapy

Degree of Risk	Cancer Treatment
High risk (> 80%)	Hematopoietic stem cell transplantation with cyclophosphamide/total body irradiation or cyclophosphamide/busulfan
	External beam radiation to a field that includes the ovaries
	CMF, CEF, CAF × 6 cycles in women age 40 and older (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin)
Intermediate risk	CMF, CEF, CAF × 6 cycles in women age 30-39 (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin)
	AC × 4 in women age 40 and older (adjuvant breast cancer therapy with doxorubicin/cyclophosphamide)
Lower risk (< 20%)	ABVD (doxorubicin/bleomycin/vinblastin/dacarbazine)
	CHOP × 4-6 cycles (cyclophosphamide/doxorubicin/vincristine/prednisone)
	CVP (cyclophosphamide/vincristine/prednisone)
	AML therapy (anthracycline/cytarabine)
	ALL therapy (multi-agent)
	CMF, CEF, CAF × 6 cycles in women less than 30 (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin)
	AC × 4 in women less than 40 (adjuvant breast cancer therapy with doxorubicin/cyclophosphamide)
Very low or no risk	Vincristine
	Methotrexate
	Fluorouracil
Unknown risk (examples)	Taxanes

Ovarian failure

Age, intensity of therapy and acuity of illness are the key factors.

Whilst the risks of Ovarian failure with standard chemotherapy for ALL and AML are <10-20%, many patients require an allo BMT in first remission and fertility preservation is not feasible.

Premature menopause (<40yrs):

1.4% with ABVD

75% with BEAM auto BMT

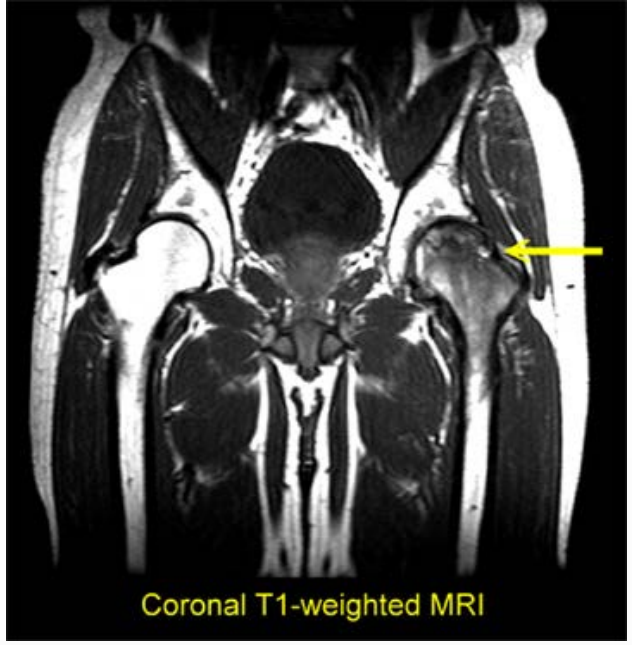
49% with 6 cycles of alkylators

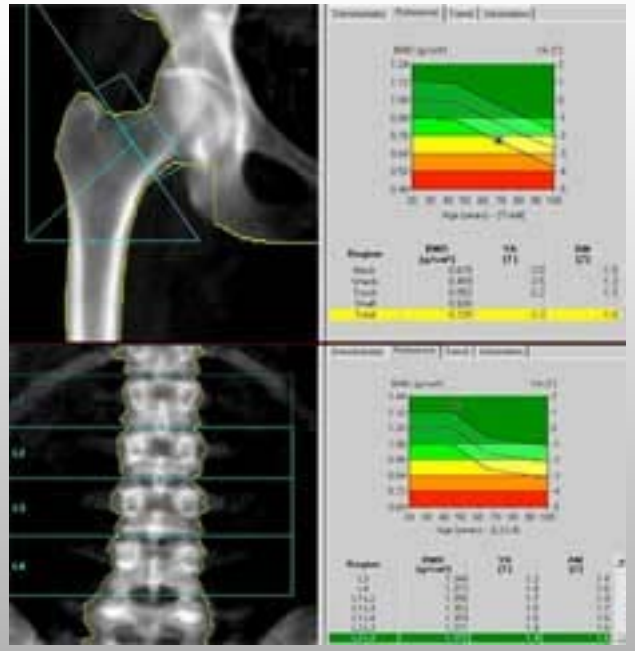
Lee SJ et al JCO 2006;24:2917-31.

Gonadal Failure

Hormone replacement therapy is recommended post allo BMT and auto BMT for women less than 45-50yrs of age to preserve bone health, prevent peri-menopausal symptoms and reduce atherosclerosis associated mortality. Any HRT should cease at age of usual age of expected menopause 50-51yrs.

Male infertility occurs in between 20% and 99% of patients depending on the intensity of therapy and baseline fertility status. Hypotestosteronaemia is frequent post BMT and testosterone replacement frequently required for bone health and in maintenance of sexual health.





Bone Health

Avascular necrosis is a defined late complication of high dose steroids with an increased in children and young adults and patients post TBI allogeneic BMT. Incidence is 7% in childhood ALL populations. No clear evidence for preventative or therapeutic benefit of bisphosphonates for AVN.

Osteopenia/Osteoporosis is found in up to 50% and 25% of long term survivors of allo BMT, depending on steroid requirements.

Screening BMD at 1 yr then annually if established diagnosis requiring therapy if ongoing RF (steroids).

Rizzo JD et al BBMT 2006;12: 138-51.

Other late effects – Financial stressors

Financial stress:

Many cancer diagnoses have a significant impact on financial circumstances of patients and families due to inability to work, carer needs, and costs of ongoing health care. This is most noticable post allo BMT where the recovery is often delayed.

A recent survey of post allograft survivors showed 54% of pts had not returned to work by 2 years, 80% of pts/carers reported the BMT having moderate to great impact on household income.

Denzen EM et al BMT 2016; doi:10.1038/bmt.2016.103

Complication/late effect	History/RF	Follow up /intervention
Fatigue/Insomnia	Nil	CBT, exercise
Neuropathy	Vincristine Vinblastine	Podiatry Pregabalin
CKD	Cisplatin Ifosfamide Cyclosporin Allo BMT	Annual Cr Urinary Prot/Cr ratio
Cardiomyopathy	Anthracycline -Doxorubicin >300mg/m2 Mediastinal RT	ECHO 2yr, 5yr and 5yrly thereafter
Premature CAD	Mediastinal RT Allo BMT	Manage CV RF Inv symptoms

Complication/late effect	History/RF	Follow up /intervention
Pulmonary disease	Radiation Allo BMT Bleomycin/BCNU	PFT's annually (for 2-5 years)
Immune Deficiency	Chemotherapy Allo/Auto BMT Rituximab Recurrent bacterial inf	Vaccination at 6mths Vaccination at 6,8,12,24 mths IgG levels - IVIG
Endocrine dysfunction	TBI or RT to neck	Annual TFT

Complication/late effects	History / RF	Follow up /Intervention
Secondary malignancy - Skin - Bowel - Cervical - Breast - Head and Neck - Thyroid - Prostate - MDS/AML	Allo BMT cGVHD Immune suppression F.Hx	Screening - Annual skin check - 5yr scopes/FOB - Annual PAP - Annual Mammogram - Annual oral exam - Annual neck exam - Biannual PSA?? - Annual FBC
Bone health	Steroids Age TBI	Annual BMD Monitor for symptoms of AVN

Complication/late effects	History/RF	Follow up /intervention
Infertility	Cyclophosphamide >5g/m2 Age >30yrs TBI Auto BMT	Assess FSH,LH, estradiol, menses, anti mullerian hormone (AMH) HRT/COCP
Hypotestosteronaemia	TBI, alkylator, Auto, Allo	Annual LH, free testosterone
Anxiety, Depression		Support gp Psychology Psychiatry

Summary

1. Survivorship is an increasingly important and previously poorly recognised aspect of the management of haematological malignancy.
2. Curative therapy for many patients affected by AML, ALL, Hodgkin lymphoma and Non-Hodgkin lymphoma is associated many long term consequences and late effects which impact survival and future well being.
3. Risk of subsequent late effects vary from patient to patient, and is determined by factors including: age at initial therapy, intensity and type of chemotherapy, radiotherapy dose and site and whether allogeneic stem cell transplantation was required.
4. Screening of at risk patients for significant and potentially modifiable complications and late effects is essential in providing optimal care for cancer survivors.

Thank you