Expert Forum

Melanoma Summit New Zealand 2015

Making Education Easy

November 2015

In this review:

Welcome to this review of the fourth national Melanoma Summit, which was a two-day multidisciplinary meeting held in Auckland during 6–7 November 2015. This review features summaries of selected presentations and workshop outcomes that covered topics ranging from epidemiology and service provision through to the current and future prevention, diagnosis, and treatment of melanoma. The meeting featured local and international speakers and was attended by melanoma researchers, trial co-ordinators, and study nurses in addition to oncologists, surgical oncologists, pathologists, and cancer nurse specialists.

DAY 1: SESSION 1

Dr Chris Boberg, Chair

Challenge to participants from a patient perspective

Kathryn Williams

In August 2008, I was diagnosed with incurable stage IV metastatic melanoma. I learnt about melanoma the hard way. I was not a sun bunny. I did not use coconut oil or baby oil. And I did not suffer the significant sunburn event in my formative years often denoted as a precursor for melanoma.

I have had both of my ovaries removed, my right adrenal gland removed, compassionate access to a dendritic cell vaccine from Malaghan Institute of Medical Research, part of my right collar bone removed, retroperitoneal lymph node dissection involving a para-aortic node and five weeks of daily radiation therapy to two resected sites. Unfortunately, in the final analysis, this probably will not be enough.

New Zealanders affected by metastatic melanoma are desperately seeking opportunities to secure an effective first-line treatment. I attended the inaugural Melanoma Summit in 2008 and believe much has been achieved since then by those working to reduce the incidence and impact of melanoma in NZ. I believe New Zealanders do have a better understanding of the serious impact of melanoma and the simplistic ideologies of melanoma often being referred to by New Zealanders as a 'bad mole' are the illiteracies of a naive nation of the past.

The cautionary tales from many New Zealanders who have since lost their lives to melanoma – coupled with the well documented research regarding sunbed use and the significant sunburn event have been particularly effective tools in the drive to raise awareness. And these must continue.

However, these are prevention campaigns and patients living with metastatic melanoma are focused on treatment campaigns.

To date, there has been nothing formidable enough in the medical arsenal to retaliate effectively. Melanoma stands out from other cancers in its defiance to respond to traditional cancer treatment options of chemotherapy and radiotherapy. These are palliative tools for melanoma, not curative tools.

Recently I familiarised myself with the 2015 Systemic Treatment Options for Metastatic Melanoma in NZ – translated – the options currently on offer to a patient with metastatic melanoma in NZ.

If a metastatic melanoma patient is unable to access targeted and/or immunotherapy treatment and is ineligible for participation in a clinical trial, the outcome in 2015 for a New Zealander diagnosed with stage III and IV melanoma remains as dismal as it did for me in 2008.

Every clinician working alongside metastatic melanoma patients knows this to be true. The predicament of the metastatic melanoma patient is a tormented existence exacerbated by the burden of a diagnosis offering insignificant treatment options and a bleak prognosis.

It is time to take responsibility for this disease as a nation and formulate an effective clinical response to melanoma treatment and propel it to the next level. For the first time, scientific evidence shows the rules of engagement with melanoma are changing. Targeted and immunotherapy treatment options are now a reality and exist in the NZ pharmaceutical market.

I implore each and every one of you here today to be bold, and to be brave, and do what is necessary to advance treatment options for New Zealanders affected by melanoma.

I implore those of you in a position with the capability to effect change, to do so. As a stage IV incurable metastatic melanoma patient, I remain acutely aware my tomorrows remain uncertain amidst the burden of this disease. I cannot change that. But we can transform the landscape of melanoma in NZ. And most importantly make a difference in the lives of all New Zealanders.

Trends in melanoma incidence and mortality in New Zealand

Dr Mary Jane Sneyd

The current status of the epidemiology of melanoma in NZ is informed by data for 2012, the most recent published statistics from the New Zealand Cancer Registry. They show the following:

- Melanoma is the fourth most common cancer in NZ (2324 new cases registered in 2012).
- Age-standardised incidence rates of melanoma were 43.3 and 36.5 per 100,000 in non-Maori men and women, respectively, versus 5.4 and 8.5 per 100,000 in Maori men and women.
- There were 354 deaths from melanoma in 2012, of which three were in Maori.
- Age-standardised mortality rates were 7.2 and 3.8 per 100,000 in non-Maori men and women, respectively.

In short, these data show that melanoma incidence and mortality are consistently higher in non-Maori men than in women and are much lower in Maori than in non-Maori. Since 1997, the incidence of melanoma has increased in both men and women but with a greater rate of increase in men. Mortality has also been increasing for men since 1997 but has been static in women.

Important differences in incidence trends exist among certain age groups. The incidence of melanoma has increased greatly (by >50%) in both men and women aged ≥65 years, with the incidence being much higher in men than women. However, there has been no linear change over time in men and women aged 35–44 years and in adults aged 15–34 years there has been an approximate 50% decrease in incidence in men and 30% in women.

Melanoma prevention and early-diagnosis campaigns have been run for about 30 years in NZ, which is a sufficient period of time to reveal some effect on incidence and mortality rates. If the prevention messages were having an effect via reducing sun exposure and precursors in children then we would expect to see a lower incidence in younger adults, which appears to be the case.

There is a caveat, however, in the implications of this trend in incidence. The data pertain to all melanomas but there will only be a significant impact on mortality rates if the incidence of thick melanomas with poor prognosis is decreasing as well as that of thin melanomas and if the incidence decrease is maintained as these younger people age.

If early diagnosis messages are having an impact, a reduction in thick melanomas over time would be expected. Thin melanomas have increased by 15% in men with no linear increase in women and intermediate thickness melanomas have increased by approximately 20% in both sexes. Thick melanomas have increased 27% in men but with no linear increase in women. In New Zealanders aged <50 years, incidence of thin melanomas is decreasing. There is a suggestion of a recent decrease in thick melanomas in younger people but this needs to be confirmed in the next few years.

Standards of service provision for melanoma patients in New Zealand

Mr Richard Martin

National tumour standards are building blocks for quality of care. They ensure that patients receive care along the cancer pathway that is timely and of good quality and describe the level of service that should be accessible to patients. The aim of the standards is to improve outcomes, reduce inequalities, and improve communication.

The Ministry of Health, which funds development of the standards to promote nationally coordinated and consistent standards of service provision across NZ, has divided the standards into eight different cancer groups and melanoma is one of those streams. The basis of the standards are the Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand, in addition to other core locally and internationally developed resources.

A total of 33 standards were developed by the melanoma standards working group, which was multidisciplinary and included patient advocacy representatives. The draft of the standards, Standards of Service Provision for Melanoma Patients in New Zealand – Provisional, was published in 2013. The standards have been divided into 10 clusters covering the management of melanoma from prevention through to research:

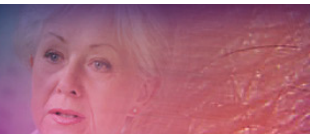
1. Prevention and early identification.
2. Timely access to services.
3. Referral and communication.
4. Investigation, diagnosis and staging.
5. Multidisciplinary care.
6. Supportive care.
7. Care co-ordination.
8. Treatment.
9. Follow-up and surveillance.
10. Clinical performance monitoring and research.

The provisional standards were well received. Not surprisingly, however, sentinel node biopsy (SNB) definition proved controversial and work on a consensus definition continues. The melanoma standards are scheduled to be audited in 2016/2017 by the Midland Cancer Network.

Following publication of the provisional standards in 2013, the melanoma standards working group reconvened to examine high suspicion of melanoma definition and data collection. The outcome was the development of a template for referrals for high suspicion of cancer (**Table 1**), which is intended not only for referrers but also for graders of melanoma in hospitals.

MALIGNANT MELANOMA OF SKIN	
Red flags	
EITHER:	
Skin lesion AND three or more of the following features:	
A. Asymmetry of shape, structure or colour	Y/N
B. Border irregularity	Y/N
C. Colour variation/multiple colours	Y/N
D. Different from other lesions ('ugly duckling')	Y/N
E. Evolving, changing	Y/N
Risk factors	
Personal history of melanoma	Y/N
Family history of 2+ first - degree relatives <40 yrs diagnosed with melanoma	Y/N
OR:	
Dermoscopy of skin lesion is suspicious for melanoma	Y/N
IN ADDITION:	
All referrals must include the following supporting results:	
Required: Size of lesion	(space to write size)
Required: Body location	(attachment or description) (space to write location)
Required: Digital macroscopic image of lesion	(attachment)
If available: Dermoscopic image of lesion	(attachment)

Table 1. Definition of high suspicion of melanoma for triage purposes (referral template).



In terms of data that will enable clinicians and service managers to measure the quality of services provided and patient outcomes, the working group has identified 233 melanoma data points that should be captured, ranging from the start of the referral process through to tailored patient-focussed follow-up programmes.

The melanoma standards will be reviewed by the working group in February 2016 prior to full publication of the standards in February 2017.

Melanoma early detection and diagnosis

No one should die of melanoma

Assoc. Prof. Cliff Rosendahl

No one should die of melanoma. That is the challenge from the late Bernie Ackerman,[1] one of the founding fathers in the field of dermatopathology. In terms of causation, the problem is not the sun. The problem is a mass migration from the region of the lowest ultraviolet light (UV) index on the planet to the region of the highest UV index on the planet by people who were not prepared by nature to live in that particular place. Early detection is critical in increasing the likelihood of survival in melanoma patients.

Dermatoscopy is a non-invasive diagnostic technique for skin lesions. A dermatoscope is a low-powered microscope that uses either contact fluid immersion or polarising filters to reduce surface reflection of light and look into the structure of the skin. Dermatoscopes allow better visualisation of patterns formed by pigment and blood vessels. These patterns are the basis of diagnosis using dermatoscopy. In addition, dermatoscopy provides information in both the horizontal and vertical planes to produce a 3-dimensional view, which is a valuable attribute as melanin appears as different colours at different skin depths.

A dermatoscope is a useful tool in the diagnosis of all skin lesions and can be essential for accurate assessment of pigmented lesions, such as when differentiating a solar lentigo from a melanoma. Research into the dermatoscopy of facial melanomas has shown that grey colour is 95.8% sensitive for melanoma but it is only 30.6% specific.[2] However, pigmented circles (sensitivity of 70.83%) are 76.39% specific for melanoma. Therefore, the presence of grey colour is a clue to malignancy regardless of pattern while pigmented circles are a very specific clue to melanoma on the face and should not be ignored.

Dermatoscopy has been the standard of care for the routine assessment of pigmented skin lesions since 2008, as recommended in the Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand. Dermatoscopy is also important in the mapping of excision margins. In a study that ascertained whether dermatoscopy can detect more accurately the lateral borders in BCCs than clinical examination alone, the use of 2mm dermatoscopically-determined excision margins achieved clearance in all but three of 200 consecutive cases and in 69 cases (34.5%) the excision margins determined without dermatoscopy were insufficient to clear the tumour.[3]

In terms of education for earlier melanoma detection, the Chaos & Clues (For Pigmented Skin Lesions) algorithm was developed as a tool to help clinicians to be able to detect any type of pigmented skin malignancy. Its trained use in clinics in Australia and overseas has been shown to increase melanoma detection rates. There is also no substitute for experience. General practitioners (GPs) who sub-specialise in skin cancer use dermatoscopy more often and diagnose melanoma with greater accuracy than GPs who did not sub-specialise.[4]

One method of diagnosing lesions earlier is dermatoscopic monitoring, and automated multi-camera-array total body photography has proved valuable in the diagnosis of clue-poor minute melanoma. However, the future of early detection may be every clinic having one or more dedicated melanographers, i.e. a person specifically trained to diagnose melanomas and employed solely to perform that task.

The only way to confidently prevent a death from melanoma in every case is to diagnose and remove the melanoma before it metastasises and that is achieved only while it is still *in situ*. To achieve this aim, there is a need to become better at detecting them at an early stage whether that is done using technology and/or by training personnel specifically for the task.

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Teledermatoscopy in New Zealand: An update

Assoc. Prof. Amanda Oakley

Teledermatoscopy is the transmission of dermatoscopy images for expert opinion over telecommunication networks not only via e-mail or a web application but also smartphones. The importance of a obtaining an expert opinion is necessary to diagnose melanoma early (i.e. *in situ*) and because the ABCDE rule clinical criteria are somewhat misleading with many benign lesions possessing these criteria.

The primary reasons for using dermatoscopy include expert-assessed dermatoscopy being better than clinical diagnosis, particularly with regard to identifying benign lesions, small-diameter lesions, and melanomas without ABCD rule characteristics, and for detection of change over time. Thus, dermatoscopy also leads to a lower benign:malignant lesion ratio and a higher *in situ*:invasive lesion ratio.

Teledermatoscopy improves early diagnosis of melanoma and other skin cancers and reduces the number of unnecessary surgeries and unnecessary outpatient clinic appointments and reduces surgical clinic wait times.

Digital dermatoscopy is the use of photography for the clinical record. It permits observation of a lesion over time and clinico-pathological correlation and facilitates education and access to expert opinion. Digital dermatoscopy used for surveillance is for patients with multiple atypical moles or many lesions, and patients with high risk of melanoma. A trained nurse can take a patient's medical history, perform total body imaging, and also select lesions for macroscopic and dermatoscopy imaging. The images can then be reviewed by an expert and the patients regularly followed up.

The rise of smartphones has played an important role in digital dermatoscopy, i.e. mobile dermatoscopy. These devices are readily available, have in-built high-quality cameras, and make it easy to share images (via messaging and e-mail). Mobile dermatoscopy makes direct GP-to-specialist consultation easier. In addition, melanoma standards now encourage teledermatoscopy referral and the use of images for clinical and histopathological correlation.

Digital dermatoscopy has become widespread in primary care and district health boards (DHBs) and primary health organisations are investing in teledermatoscopy. Also new in 2015 is the consumer marketing of dermatoscopes, which patients will use and send images to clinics for expert review.

In summary, the aims of teledermatoscopy are to:

- Increase rates of early diagnosis of melanoma.
- Reduce unnecessary surgeries for benign lesions.
- Improve clinical-pathological correlation.
- Provide timely clinical advice and education to non-specialists.

Cutaneous melanoma: Staging, surgical management, and adjuvant treatment

Prof. Charles M. Balch

There is no single- or combination-treatment regimen that fits all patients. Physicians need to understand the heterogeneity of disease in each individual patient and tailor treatment to the biology of the disease.

Prognosis and staging

In the context of clinical management, there are three important features in the pathology of melanoma that serve as crude surrogates for something occurring at a deeper biological level but which is still to be elucidated at a molecular and genetic level:

- Thickness: indicates the duration of tumour growth.
- Mitotic rate: indicates how fast the melanoma is growing.
- Ulceration: indicates a poorly differentiated or locally advanced melanoma and may also serve as a biomarker for selecting patients for adjuvant interferon therapy.

Ulceration is a particularly important prognostic feature that prompts upstaging of patients compared with non-ulcerative melanoma for stage I, II, and even stage III melanoma. Mitotic rate is also an important prognostic and staging factor. Mitotic rate, like thickness, is a continuous variable and as the rate of proliferation (i.e. number of mitoses) increases the patient survival rate decreases in a highly significant way.[1]

Patients who progress to stage III disease are a very heterogeneous group and some do not need to be exposed to the toxicity of chemotherapy. The calibration of risk among stage III patients is based on three factors:

1. Macroscopic tumour burden (i.e. clinically detectable).
2. Microscopic tumour burden (i.e. detected by SNB).
3. Number of metastatic nodes.

Research has shown that survival rate is more than doubled by identifying disease at an earlier stage in its course, i.e. by using microscopic versus palpable nodal metastases detection methods, and that survival decreases as the number of lymph nodes with metastases increases.[2] These prognostic factors should be used when deciding on how to treat patients both in terms of how radical should the surgery be and whether adjuvant radiation or adjuvant systemic therapy in the form of targeted therapy, immunotherapy, or chemotherapy should be used.

There is remarkable heterogeneity of prognosis among patients with stage III melanoma. For example, 5-year survival rates can range from 81.5% in patients with non-ulcerative melanoma with a single nodal micrometastasis, i.e. low-risk group, through to 29% in patients with ulcerative and multiple nodal macrometastases arising from an ulcerative melanoma, i.e. high-risk group (**Table 2**).[3]

Ulceration	No. of nodal micrometastases (+/- SE)			No. of nodal macrometastases (+/- SE)		
	1	2-3	4+	1	2-3	4+
Absent	81.5±1.9	73.2±3.7	38.0±8.5	51.6±7.2	46.6±7.9	45.4±9.1
	(777)	(246)	(46)	(75)	(67)	(50)
Present	56.6±2.9	53.9±4.2	34.0±8.3	49.4±6.2	37.7±6.2	29.2±6.7
	(531)	(223)	(49)	(88)	(93)	(68)

Table 2. Survival rates in 3434 patients with stage III melanoma, by tumour burden, number of nodes, and primary tumour ulceration.[3]

Surgical management of the primary melanoma

For a locally advanced melanoma with microsatellites, a radical wide excision taking the underlying fascia should be used, not to just treat the primary tumour but also to treat the first metastases in the lymphatics surrounding the primary melanoma.

Patients with a local recurrence of their melanoma have a high risk of death. The most important point is not to under-treat these patients as doing so may leave behind with intra-lymphatic metastases, which may ultimately cause the death of the patient.

The ability to diagnose melanoma at an earlier stage has allowed for smaller surgical excision margins for treatment of primary cutaneous melanoma. Current randomised trial data suggest that a 2cm resection margin is sufficient and safe for patients with a cutaneous melanoma thicker than 2mm and a 1cm margin is sufficient for a melanoma thickness of <1mm. However, the excision margin should be tailored to an individual patient's tumour biology, anatomic site, and risk for surgery. For example, given that ulceration doubles the risk of recurrence, an ulcerated primary melanoma would at require a wider margin than a non-ulcerated melanoma.

Stage III melanoma: Multidisciplinary management of metastatic melanoma

Achievement of a survival benefit is not the only justification for surgery. The goals of treating regional lymph nodes with surgery and/or radiation therapy are:

- Staging: when the information will guide subsequent therapy and counsel patients about prognosis.
- Regional disease control: to prevent symptomatic growth of metastases before a patient dies of distant metastases.
- Increase survival rates: intercepts the metastatic process and prevents regional metastases from spreading further.

Any of these goals can be justified when the benefits outweigh the risks.

In most places of the world, SNB is standard of care. As a staging technique, it is the most accurate, reproducible and cost-effective test available today for regional node micrometastases. The SNB technique will become an increasingly important staging procedure in all clinical practices for patient selection of complete node dissection and of adjuvant interferon therapy.

There is compelling clinical trial evidence favouring the staging value of SNB. In terms of nodal disease control, it virtually eliminates the risk of future nodal recurrence, reduces tumour burden at the time of complete lymphadenectomy, and virtually

eliminates the need for adjuvant radiation therapy as indicated for multiple bulky metastases.

Surgery for stage IV melanoma

Melanoma can metastasize even after 5-20 years. In patients with stage IV melanoma, surgical excision is the preferred treatment for limited distant metastases in one organ site, especially with a >1 year disease-free interval. The primary goals of surgery for stage IV melanoma are symptom relief (accept a higher risk:benefit ratio) and preventing symptoms (accept a lower risk:benefit ratio). There are patients with limited disease for which surgery can produce a complete response at lower expense than with any other type of intervention. Therefore, surgery still has a role in selected patients with stage IV disease either alone or increasingly as neo-adjuvant therapy whereby an effective systemic agent is given and then the lesion is removed for analysis of how much is inflammation and how much is viable tumour.

Role of adjuvant interferon therapy and checkpoint inhibitors in stage III melanoma

High-dose Interferon, as interferon alfa-2b, has been available since 1996 and is an approved adjuvant regimen for resected high-risk melanoma. Clinical trials assessing its use as an adjuvant therapy have mainly been performed in patients with macroscopic node-positive disease and have shown that the benefit, if anything, is marginal.

However, a randomised trial of low-dose pegylated interferon, which is a slow-release interferon, maintained over 5 years in patients with resected stage III melanoma produced an overall survival benefit with the benefit primarily being evident in patients with microscopic node-positive disease.[4] Overall survival in patients with microscopic node-positive disease arising from ulcerative melanoma was >9 years with pegylated interferon versus 3.7 years in the control group. Subsequent research suggests that ulcerative melanoma might be predictive of an overall survival benefit with pegylated interferon treatment.

More recently, the checkpoint inhibitor ipilimumab as adjuvant therapy for patients with completely resected stage III melanoma at high risk of recurrence significantly improved recurrence-free survival in a phase III trial.[5] However five (1%) patients in the ipilimumab died because of drug-related adverse events.

Multidisciplinary treatment options for melanoma

Table 3 presents suggested starting points for managing melanoma at different stages, but which may change depending an individual patient's conditions and circumstances.

In short, awareness and understanding of the prognostic factors that predict the risk of local recurrence, regional metastases, and distant metastases is essential to apply the best treatment in each melanoma patient.

Stage I and III	• **IA:** 1cm radial margin, no sentinel lymph node (except high-risk patients) • **IB, IIA, IIB, IIC:** 1-2cm margin, sentinel lymph node in most patients
Stage III	• Complete lymphadenectomy • Clinical trials with adjuvant biological therapy • Interferon (pegylated or high-dose), especially for ulcer-positive primary • External radiation treatment for >4 macroscopic nodes, recurrent node-positive
Stage IV	• Surgical excision of limited disease • Immunotherapy with a checkpoint inhibitor • Targeted systemic therapy with BRAF blocker

Table 3. Summary of multidisciplinary treatment options for melanoma.

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Oncological management of melanoma

Prof. Antoni Ribas

Advances in systemic therapy for metastatic melanoma are based on increased understanding of cancer biology (**Figure 1**). The improvements have been in two areas: targeting the cancer directly and tuning the immune system to attack the cancer. Research into the clinical biology of melanoma has led to a new understanding of the disease. Genomic analyses have identified the targetable oncogene, the protein kinase BRAF, and biological studies have identified the immunologic targets, the programmed death 1 (PD1) and cytotoxic T-cell lymphocyte-associated antigen 4 (CTLA4) inhibitory molecules expressed on T lymphocytes.

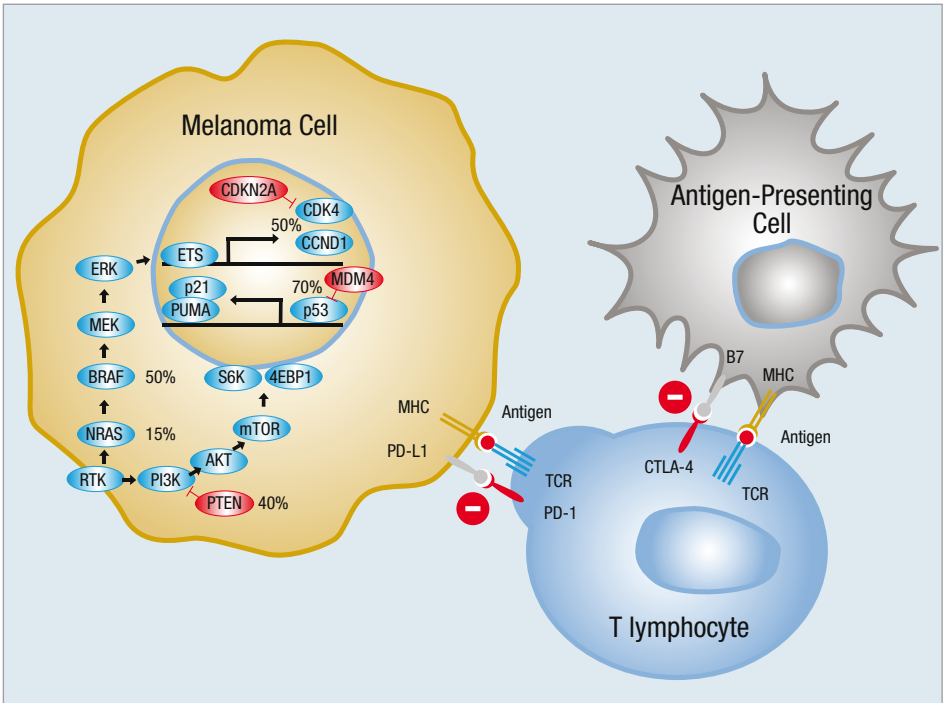

Figure 1. A deeper understanding of the biology of melanoma has led to the development of targeted therapy via BRAF and MEK inhibition and immunotherapy via CTLA4 and PD1 antigen inhibition.

Standard of care

Current medical management for advanced melanoma in the US is still based on whether or not a patient has a BRAF gene mutation, since the BRAF mutation is the driver oncogene in ≥50% of patients with melanoma. Following the introduction of the targeted therapies, BRAF and MEK inhibitors, and the immunotherapy agents, anti-CTLA4 and anti-PD1, chemotherapy is now rarely used. A BRAF inhibitor plus MEK inhibitor in combination or anti-PD1 alone are both front-line treatments for BRAF-positive melanoma. Anti-CTLA4 plus anti-PD1 in combination or anti-PD1 alone are front-line treatments for BRAF-negative melanoma (**Figure 2**).

Targeted therapy

The mutated BRAF gene produces an altered BRAF protein that signals the melanoma cells to proliferate. BRAF inhibitors prevent production of the BRAF protein leading to tumour shrinkage and extended survival. However, the majority of BRAF-positive tumours eventually become resistant to BRAF inhibitor therapies. To counter the development to resistance, the BRAF pathway can be re-activated by inhibiting the MEK gene, which is in the same signalling pathway inside cells as the BRAF gene. This observation led to the development of MEK inhibitors. Research showed that vertical blocking of these driver oncogenes leads to secondary responses, albeit shorter than the initial responses.

Different metastases can have different mechanisms of resistance, which emphasises the heterogeneity of melanoma tumours. Indeed, branched evolution underlies acquired BRAF inhibitor resistance. Therefore, treatment should not 'chase resistance'. Treatment should prevent resistance by using combinations of targeted therapies. Randomised clinical trials have demonstrated the superiority of combined therapy with BRAF and MEK inhibitors versus monotherapy in patients with BRAF-mutated melanoma, including better initial responses, more durable responses (via blocking some of the mechanisms of resistance), and improved overall survival.[1-3] Combination therapy also resulted in reduced toxicities from paradoxical mitogen-activated protein kinase (MAPK) activation, i.e. RAS-induced hyper-proliferative skin lesions, including cutaneous squamous carcinoma and actinic keratosis.

Concerns regarding BRAF inhibitor resistance and clinical relapse fostered by melanoma adaptation to drug exposure are being addressed in phase I/II clinical studies. The effects of intermittent dosing of BRAF inhibitors as a strategy to delay the development of drug resistance and the addition of an AKT inhibitor to single or combination therapy with BRAF and MEK inhibitors are two strategies being investigated.

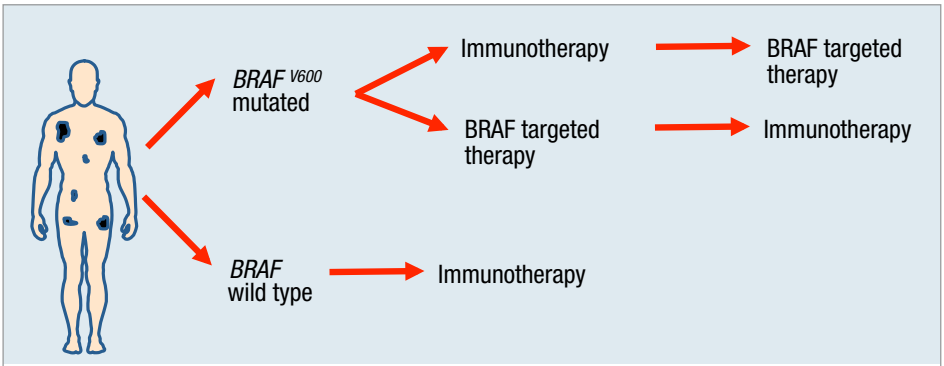

Figure 2. Treatment options for a patient with metastatic melanoma.

Immunotherapy

The biological basis of immunotherapy is the release of brakes on the immune system so that it can attack the cancer. In a subset of melanoma patients, there are immune cells (i.e. T cells) that are ready to strike the cancer but are prevented from doing so by the checkpoint (or brake) mechanisms of the immune system, which includes the ability to turn off T cells against self-antigens to prevent 'collateral' damage. One of the checkpoint mechanisms is via the CTLA4 inhibitory molecule expressed on T cells. Inhibition of CTLA4 by anti-CTLA4 agents, allows T cells to proliferate and attack melanoma cells leading to durable responses and improved survival in patients with advanced disease.

However, tumour cells can protect themselves from T cell attack via the PD1/PDL1 mechanism that results in the PD1 checkpoint being turned on, which in turn turns off turns off the T cell. Therefore an antibody that blocks PD1 or PDL1 will allow T cells to proliferate and to invade and kill the tumour. Indeed, preliminary clinical trial evidence indicates that anti-PD1 and anti-PDL1 agents improve survival in melanoma patients with advanced disease.

The key is to identify which patients have an interaction between the immune system and tumour that is ready to be released by this break. This can be done via biopsy: patients who have high numbers of immune system cells in the margin of the tumour that are primed to attack the tumour but the tumour is protected via PD1/PDL1 are likely to be the patients who will respond to immunotherapy. The understanding of this mechanism has advanced combination immunotherapy in which both CTLA4 and PD1 checkpoint breaks are released. Combination anti-CTLA4 and anti-PD1 therapy has produced improved progression-free survival versus mono-component therapy in clinical trials.[4,5]

Conclusions

- Combination therapy with BRAF and MEK inhibitors improves antitumor activity and reduces toxicities from paradoxical MAPK activation in patients with BRAF-mutated melanoma.
- PD1 blockade induces responses by inhibiting adaptive immune resistance.
- When T cells blocked by PD1 are not present in tumours:
  - Combine with other immunotherapies.
  - Combine with targeted therapies (BRAF plus MEK inhibitors).

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Improving services and outcomes for patients in New Zealand. A patient-centred focus on co-ordination of care

Natalie James

Effective care co-ordination is a person-centred, assessment-based, interdisciplinary approach to the integration of the full range of health and support services that a patient with cancer may need. With care co-ordination, an individual's needs and preferences are assessed, a comprehensive care plan is developed, and outcomes are measured.[1]

Cancer nurse co-ordinators were established as a new Ministry of Health initiative that has funded 40 additional senior nurses to act as specific nurse co-ordinators across the country. They serve as the primary contact for patients and are required to have an expert knowledge and understanding of the comprehensive diagnostic and treatment pathway that patients travel. They are also required to lead systems improvements and develop prioritisation tools and triage tools to help to identify the patients who will benefit most.

Approximately 17% the cancer nurse co-ordinator case load is currently allocated to skin cancer and the nurses are slowly developing tumour stream expertise. Future effort will be focussed on improving liaison with primary care, helping patients to self-manage, and identifying who is missing out on co-ordinated care.

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Dr Andrew MacGill

With the rapid advancements in the treatment options for advanced melanoma disease, co-ordination of care will become increasingly challenging. Providing co-ordinated care is further complicated by the wide array of specialties that remove melanomas and/or are involved in melanoma patients. To ensure all doctors that remove melanomas are up to date with the current treatment options, each synoptic report should include current management guidelines.

When a patient's histology requires a multidisciplinary team to review the case, a cancer nurse specialist should attend this meeting and thereafter serve as the key co-ordinator for that patient. The nurse specialist should be the first point of contact for the patient's GP.

Mr John Kenealy

In addition to effective treatment, good patient care and quality patient service are required for optimal outcomes in the management of melanoma patients and central to achieving this is the clinical nurse specialist.

At Middlemore hospital, a melanoma pathway based on a 'see and treat' model has been implemented to address the 2000 skin cancer patients seen every year (1700 done under local anaesthesia) and address total wait times that can be ≤7 months from referral. 'See and treat' has reduced total waiting time by 50% through enabling same-day excision biopsy of suspicious pigmented lesions and same-day excision of some melanomas. Ongoing improvement efforts will focus on minimising under- and over-investigation as well as under- and over-treatment.

Kathryn Williams

Being resident in a main centre contributes substantially to a melanoma patient's ability to access all aspects of the care needed to ensure an optimal outcome. Consistency of care that comes from having the same treatment team from the day of diagnosis is also beneficial, not least in eliminating the need to continually reiterate the patient's story and treatment history to clinical staff not familiar with the case. Robust co-ordination of care and open communication benefits the patient and medical team, which operates across private practice and the public health system.

From a melanoma patient's perspective, the following are important existing initiatives contributing to the quality of patient care:

- Melanoma New Zealand provides access to good and credible patient support and information.
- MelNet facilitates communication and collaboration among healthcare professionals and promotes education best practice.
- Standards of Service Provision for melanoma patients have improved the consistency and co-ordination of service provision.

Looking forward, melanoma patients would like to see the following:

- Increased access to effective first-line treatments
- Development of co-ordination of care best-practice templates nationwide to ensure an equitable and consistent pathway for the melanoma patient.
- Development of co-ordination of care best-practice templates for clinicians not located in main centres and not able to physically participate in the multidisciplinary team setting.
- Identification of the challenges and barriers encountered by patients in relation to accessing good care co-ordination
- Roll out of a consistent care co-ordination template for public hospital oncology.
- Establishment of a clinical centre of excellence.

Mr Jeremy Simcock

One of the major frustrations for melanoma patients who do not develop metastatic disease is the interface between primary and secondary care. Efforts to improve the co-ordination of melanoma care across the Canterbury DHB started about five years ago. At the heart of these efforts is HealthPathways Melanoma (Cutaneous), which is a process of local co-ordination centred on patients. Its aim is to bridge the transition from primary to secondary care and provide consistency of care for the melanoma patient.

HealthPathways was developed through joint collaboration of primary and secondary care clinicians. A pragmatic approach was used to identify gaps in service and set expectations within hospitals and primary care practices. It is mirrored in HealthInfo, which is the patient version of HealthPathways, so that expectations around treatment and treatment times are in plain view for everyone to see. Healthpathways also serves as a reference point for medical, nursing, and administrative staff. It also facilitates change implementation (e.g. changes around SNB, introduction of teledermatotogy), which is easily done because the pathway is specialty independent.

GP liaison is another important component of the pathway as it helps to maintain standards, particularly with regard to GP referrals. In terms of follow-up, the pathway is working to become consistent with the Ministry of Health direction around stage I/II melanoma patients being discharged back to their GPs for follow-up. Finally, to ensure a quality service is provided, expectations need to be set, consistent communication is required, and the process needs to be audited to ensure that outcomes are safe and sensible.

DAY 2: BREAKFAST PANEL: THE FUTURE OF MELANOMA TREATMENT IN NEW ZEALAND

Dr Catherine Barrow, Chair

Overview of rapid changes to the landscape of melanoma treatment, the availability of new treatments in New Zealand and implications for funding

Prof. Antoni Ribas

The current standard of care in NZ for treatment of advanced melanoma is 'watch and wait' or dacarbazine. Ten international randomised clinical trials involving several thousand patients have demonstrated that targeted therapy and immunotherapy are superior to dacarbazine in the treatment of advanced melanoma. Furthermore, clinical trials are now differentiating single agent and combination agent regimens among the available targeted therapy and immunotherapy agents. Patients and government agencies responsible for healthcare budgets need to be made aware that the science says that these drugs work.

Prof. Rod Dunbar

Clearly there is a revolution occurring in cancer care at the moment, particularly around immunotherapy and aiding T cells, and NZ drug researchers would very much like to be able to take part in this revolution.

A striking clinical feature of immune therapy remains the durable remissions that are achieved with these agents, first demonstrated with anti-CTLA4 but now, and potentially even more impressively, with anti-PD1 or combinations of the two. The remarkable thing is these drugs target T cells in the immune environment not the tumour cells that have been targeted to date with chemotherapy, which still largely seems to fail to give durable remissions.

Combinatorial therapy for cancers, including melanoma, offers huge opportunity not only in terms of combinations of immunotherapies but also smarter ways of using chemotherapy and radiotherapy to aid the immune system to control the tumour. Combinatorial therapy also comes with considerable complexity in determining which combinations work best for which patients.

NZ has a proud history of bringing new cancer drugs into the clinic. Experimental immune therapies currently being developed in NZ include small molecule drugs, vaccines, and cell therapy. In particular, vaccines have the potential to be an affordable means of continually stimulating the immune system against a cancer.

It is puzzling that access to immunotherapy agents cannot be offered to NZ cancer patients when they are standard of care in many other parts of the world. Patients need to be placed at the heart of this debate. There is also a need for investment so that clinical trials using these agents can be conducted in NZ.

Dr Rosalie Fisher

There are seven drugs that are registered and available in NZ for the treatment of advanced melanoma, including targeted agents and immunotherapy agents. Of these treatments, only the chemotherapy agent dacarbazine is funded and dacarbazine has never been demonstrated to improve survival compared with supportive care.

In NZ, Standards of Service Provision for melanoma patients recommend the availability of BRAF and immune checkpoint inhibitors for advanced disease. In reality, medical oncologists are prescribing dacarbazine and providing supportive care — essentially becoming observers of the natural history of metastatic melanoma — which is distressing for both patients and healthcare providers.

In 2015, New Zealanders' access to effective therapies for advanced melanoma is limited to private funding, clinical trial participation, compassionate/expanded access programmes, and seeking treatment overseas. For patients, and their families, these options mean economic hardship, pressure to enter clinical trials, emotional distress, and geographical relocation — all of which ultimately equate to inequity.

Some suggestions as to what can be done to improve access to systemic treatments for advanced melanoma in NZ include:

- Patient advocacy, undertaken by patients.
- Open discussion on reimbursement process reform.
  - Look to comparable healthcare systems overseas, where reimbursement agencies have been part of the solution and recognised the unmet need for melanoma patients.
  - Consider early access/managed entry schemes.
- Improve clinical trial access on a national level.
  - This in turn may facilitate expanded access.

Dr George Laking

Part of the reason for the high price of new medicines is that we, as a society, have opted for a particular model of drug development that is expensive, with most development being undertaken in the private sector. Consequently, there is a skewed relationship between the cost of drug development and the price that is asked for medicines. The price that can be asked for medicines will be the price that the market can hold and it would seem that the market can hold a high price when it comes to dreaded diseases, such as melanoma.

There are, however, other models of drug development that are more streamlined with potentially less expensive pathways to getting new medicines into clinics, which might mitigate their prices. An example is the Medicines Adaptive Pathways to Patients (MAPP) project that was evaluated in Europe.

In support of NZ's system of socialised medicine, there are some medicines available here for which access is restricted in other Western countries. NZ's system of socialised medicine, of which PHARMAC is a part, compares the priority of funding one treatment versus another within a fixed budget. This is fair in terms of making medicines available across all diseases. In terms of opportunity cost, the funding of one drug potentially means no funding of another drug. Bypassing PHARMAC via use of political mandate has health consequences. Making desperately needed medicines available by mandate limits the ability to negotiate on price. The price difference is a cost that is transferred to other areas of the healthcare system resulting in other treatments not being made available.

Dr Andrew Simpson

Although there was an emphasis on drug therapy in this session, there are many other components in the melanoma pathway. These include prevention, early diagnosis, effective surgery and other treatment, and effective follow-up. These are supported by the health target and the faster cancer treatment programme, including the tumour standards. In NZ, 20% of government expenditure is on health and this proportion is one of the highest in the OECD. We need to be aware of the resources we have available and how we use them. The many ongoing efforts to improve delivery of care are based on how services are provided, the needs of the patient and what is important to the patient. The system needs to be designed from the perspective of the patient and the improvements that can be made are not only about access to drugs.

Our changing understanding of melanoma aetiology: Implications for prevention and control

Prof. David Whiteman

Melanoma is the third most common cancer in NZ. The magnitude of the problem is further exemplified by steady year-on-year increases in the incidence of melanoma. Although there are signs of a turn-around — some recent data points suggest that NZ may be on the cusp of a decline in melanoma incidence — there remains the problem of undiagnosed melanoma and melanoma mortality.

The future melanoma problem

Melanoma rates among older adults are going to continue to rise very steeply, particularly in those aged >60 years, which will contribute substantially to a projected 50% increase in the number of people diagnosed with melanoma in NZ over the next 20 years. Moreover, although melanoma mortality has remained static in women, it continues to rise year-on-year in men. Melanoma mortality remaining stubbornly high is troubling given investments in its prevention.

Prevention of melanoma in the first instance requires an understanding of the causal factors that underlie the development of melanoma, and the time course over which it develops, in order to identify the most effective points for intervention. This understanding has accumulated through several eras of melanoma research.

Descriptive epidemiological era (1950 onwards)

The descriptive epidemiological era established that melanoma incidence is strongly associated with the ambient levels of UV radiation received by the resident population, early life exposure to UV radiation appears to establish long-life risk, and melanoma incidence is highest on sun-exposed sites. The descriptive era also demonstrated that there is an age-specific effect in that the most common site of melanoma at younger ages is the trunk whereas in at older ages the most common site is the head and neck. This observation raised the question of whether the assumption that all melanomas arise through the same causal pathway was too simplistic.

Analytical epidemiological era (1965 onwards)

The analytical epidemiological era commenced with, four case-control studies of similar design, but conducted in different parts of the world, and which all identified a range of phenotypic risk factors that predicted a higher risk of melanoma.[1-4] These risk factors were: high nevus count, freckling, fair-skin type, lighter hair and eye colour, and a family history of melanoma. The strongest risk factor was number of nevi and meta-analyses have confirmed a linear relationship between nevi count and melanoma risk.[5,6] Additionally, monozygotic/dizygotic twin research suggested that genetic factors were a strong genetic driver of nevus count.

These observations produced the nevus hypothesis, which proposes that individuals with a high propensity to develop nevi have an inherent instability of their melanocytes and require less sunlight exposure to develop melanoma than those with a resistance to developing nevi who require recurrent cumulative exposure to sunlight to develop melanoma.

In testing this hypothesis, research has revealed patterns in how risk factors vary by site of melanoma. Melanomas on the head and neck are more associated with cumulative sun exposure and outdoor occupations whereas melanomas on the trunk are more associated with sunburns and childhood sun exposure. Additionally, head and neck melanomas are more closely linked with actinic skin damage and dermal elastosis while trunk melanomas are more closely linked with nevus number and neval remnants.

The analytical epidemiological era of melanoma research produced a body of knowledge showing the role of sunlight in the development of melanoma as well as the role of certain phenotypic factors. Towards the end of the analytic era, interest in the role of genes preceded an explosion of research into the genetic underpinnings of melanoma.

Genetic epidemiological era (1990 onwards)

Genetic risk is determined by the DNA that is inherited at conception, which determines overall phenotype. In contrast, somatic genetic mutations are acquired in the target cells during childhood and adulthood. In the case of melanoma, the target cells are the melanocytes of the skin.

In terms of constitutional (inherited) genes and melanoma, early pedigree analyses that traced the inheritance of melanoma in melanoma-dense families ultimately led to the identification of high-risk familial melanoma genes, i.e. genes very strongly associated with melanoma. Subsequently, genome-wide association studies using high-throughput DNA sequencing technology identified genes and their chromosomal locations that are highly associated with risk of developing melanoma.[7] These genes are divided into two classes: i) high-risk constitutional genotypes, which occur in a small proportion of people with a dense family history of melanoma; and ii) low-risk constitutional genotypes, which occur commonly in the population, such as genes that lead to red hair and freckling. Today, the focus is on identifying moderate risk and moderate frequency constitutional genes.

In the context of somatic mutations, melanoma has the highest mutation rate of all of the cancers and because it arises on the skin, which is exposed to environmental insults, predominantly UV radiation, melanomas acquire many mutations. The challenge is to differentiate the mutations that are causing the melanoma, i.e. the driver mutations, from the passenger mutations that are acquired as the cancer evolves. The most studied somatic gene mutations that cause melanocytes to become malignant are: i) oncogenes, which are genes that gain a function from being mutated, e.g. BRAF; and ii) tumour suppressor genes (the 'policeman' genes in the genome), which lose their function when mutated, e.g. TP53, CDKN2A, PTEN. Melanomas that have lost function of TP53 tend to be associated with a particular set of characteristics, i.e. in people of older age, with low nevus counts, and with accumulated sun exposure, as well as in head and neck melanomas. In contrast, melanomas resulting from mutations of the BRAF gene tend to arise in people of younger age, people with high nevus counts, people with early-life sun exposure, and in trunk melanomas.

Melanoma causality

Pulling all of this epidemiological knowledge together produces a current overview of melanoma causality (**Figure 3**), in which melanoma is initiated and then followed by a phase of promotion and progression. The first insults to melanocytes occur early in life, predominantly UV radiation exposure in childhood, which is facilitated by host factors. Some host factors will make the mutation more or less likely to occur while others will code for pigmentation and UV protection ability, but it is the combination of the constitutional genome and sun exposure that drives this process.

For some people, the pathway is predominantly driven by continual sun exposure and when melanomas do develop they are likely to have TP53 mutations and a constellation of associated features. There is another group of people, probably the majority, who have early-life UV exposure and go on to develop melanoma because they are prone to developing nevi and have unstable melanocytes. They are likely to have features such as BRAF mutations and melanomas on trunk sites. This presents a challenge in terms of prevention because it leaves a narrow window of opportunity for targeting prevention activities.

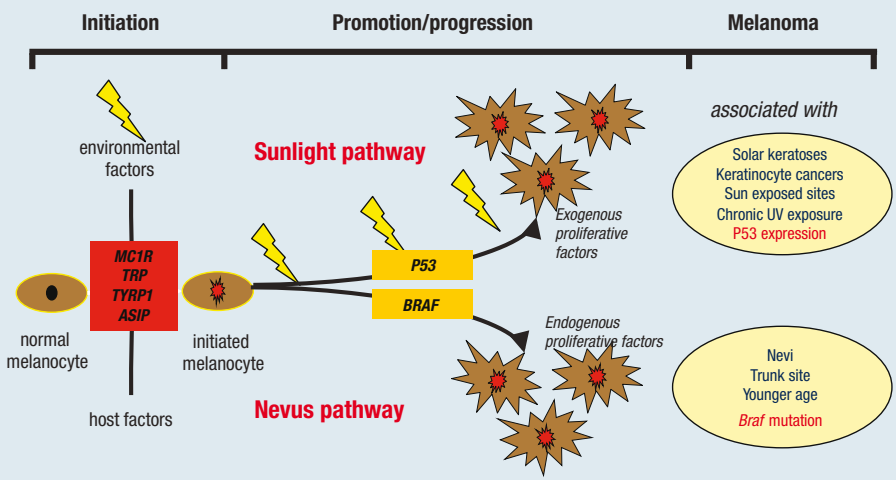

Figure 3. A contemporary simplification of melanoma causality.

Strategies for melanoma control

Given epidemiological evidence of a massive number of as yet undiagnosed melanomas, primary prevention will be critical in controlling melanoma, in addition to early detection and treatment (**Figure 4**). In the context of primary prevention, the main targets are childhood sun exposure, high-risk individuals (i.e. those carrying a set of phenotypic factors and who have genetic risk), and the use of sunscreen. In terms of secondary prevention, the main component is early detection. Part of early detection is predicting which people are at high risk of melanoma and then following them up with counselling and surveillance.

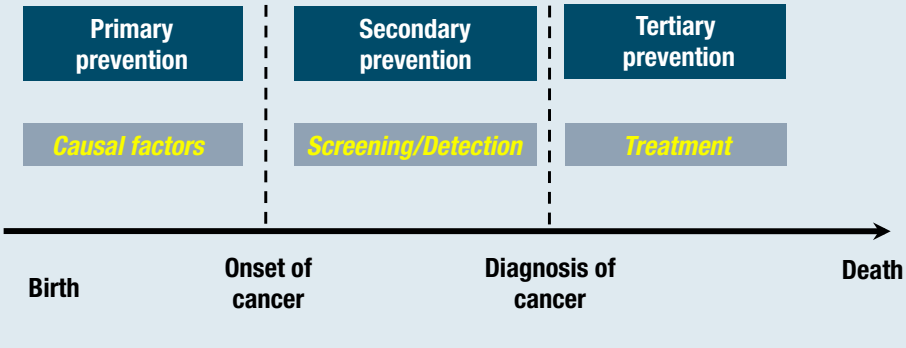

Figure 4. Strategies for melanoma control.

The future

The future of melanoma control will be based, in large part, on the integration of somatic and constitutional genome data, together with phenotypic and environmental data, to identify the changes that drive melanoma progression and to identify new targets for therapy.

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Action to address melanoma risk

Interventions for the primary prevention of skin cancer: CDC 'Guide to Community Preventive Services' systematic review of evidence of effectiveness

Assoc. Prof. Anthony Reeder

In 2000, the CDC's Task Force on Community Preventive Services conducted a systematic review of the effectiveness, applicability, other harms or benefits, and barriers to the use of selected interventions to prevent skin cancer by reducing exposure to UV radiation.[1]

The focus of this update of original CDC systemic review was on interventions that changed behaviours and the subsequent consequences of these behavioural changes (**Figure 5**). The updated review followed the Community Guide interval update process.[2,3]

The primary research questions asked how effective primary interventions are in:

1. Changing quantifiable individual UV radiation protective behaviours?
2. Reducing erythema, nevi formation and actinic keratoses?
3. Reducing skin cancer incidence?

The updated review followed the original process of evaluating interventions using five settings-based strategies, including child care, schools, outdoor recreational and tourism settings, and outdoor occupations. Three intervention strategies that cut across settings were also evaluated, including mass media campaigns, community-wide interventions, and programmes for caregivers.

To summarise outcomes, the updated CDC review of evidence supports primary prevention interventions in the following settings:

- Child care centres.
- Primary and intermediate schools.
- Outdoor workplaces.
- Visitors to tourist and recreational settings.
- Use of multicomponent community-wide strategies.

There was also complementary and reinforcing evidence for:

- Counselling in primary care settings for 10- to 24-year-olds with fair skin.
- A mass media campaign in Australia.

However, additional well-designed and well-described studies with longer follow-up are required and at the present time it is difficult to identify the most effective components within these programmes.

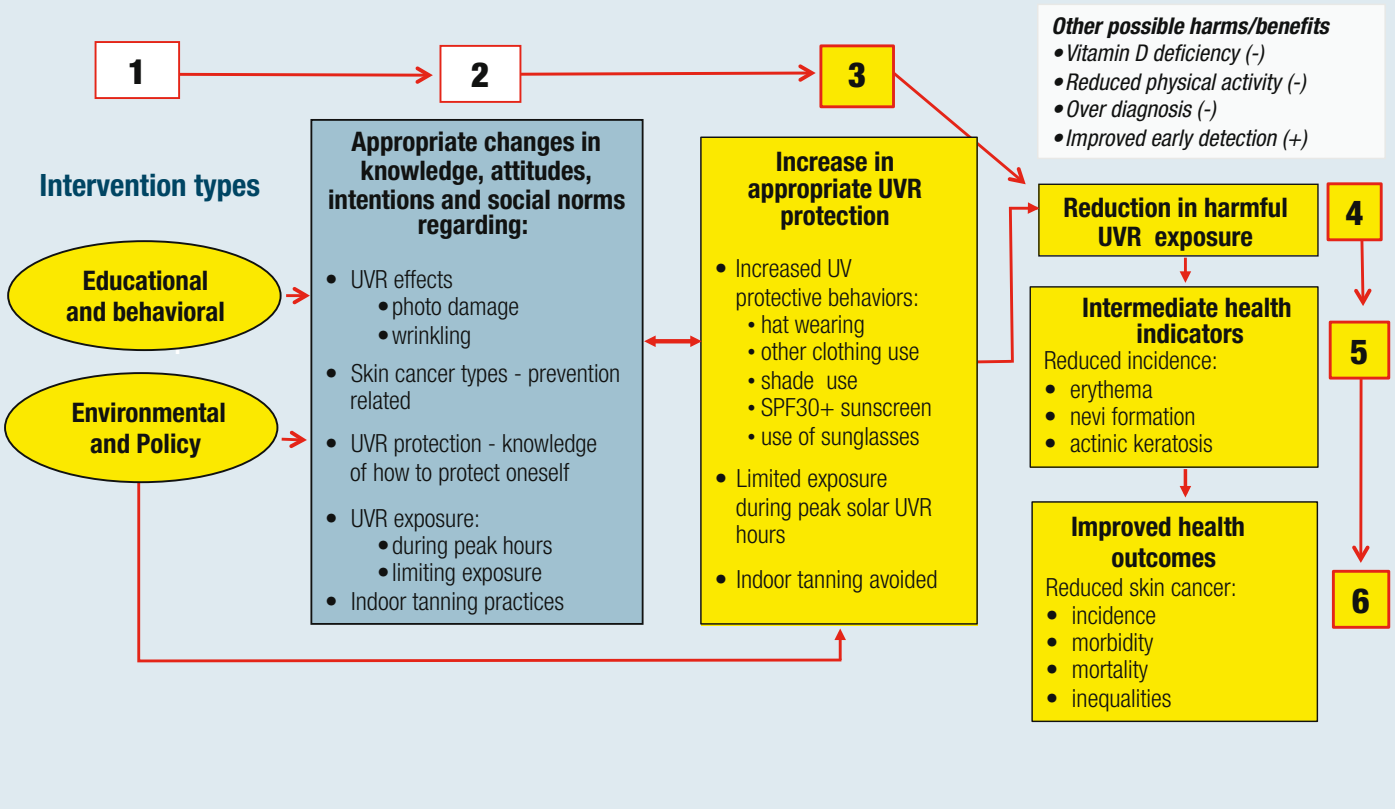

Figure 5. Extended framework adapted from Community Guide team revision of CDC systematic review of primary preventions for skin cancer.

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Implementation of a risk-predictor tool for melanoma in New Zealand

Dr Mary Jane Sneyd

Despite nearly 30 years of health promotion, prevention, and early detection campaigns, melanoma rates continue to increase. Moreover, population screening has proved too expensive and been shown not to work well. It is time to try additional approaches to control melanoma, such as targeting people at higher risk for increased prevention activities, early diagnosis and surveillance, and use of individualised strategies dependent on absolute risk. To target people at higher risk of melanoma first requires the means to be able to identify them. Currently, however, there is no reasonably accurate way of identifying high-risk individuals.

Rather than using relative risk (RR), which is a comparative measure used for studies of disease causation, identification of high-risk individuals requires use of absolute risk, which is the probability of a person developing disease in a defined period of time taking into account all of the person's risk factors and their interactions. Calculation of absolute risk requires the use of risk predictor models, and often an online tool for ease of use.

We have developed a personal risk assessment model that estimates the probability of an individual developing their first melanoma within the next 5 years.[1] The NZ prediction model has been accepted for listing on the National Cancer Institute, USA, risk predictor website.

The risk predictor calculator estimates the probability that an individual will develop melanoma by using inputs provided by a GP. Risk prediction for women includes the following variables: skin colour, number of large moles on right arm, family history of abnormal/dysplastic moles, and history of non-melanoma skin cancer (NMSC). Risk prediction variables for men include: age, indoor/outdoor occupation when age <18 years, place of birth (inside vs outside NZ), number of large moles on right arm, and history of NMSC.

After calculating an individual's probability of developing melanoma in the next 5 years, the tool provides GPs with recommendations for management, based on most recent Australasian standards and guidelines for melanoma.

Currently, the pilot risk prediction model is being implemented as a web-based tool integrated as a module in 'bestpractice' Decision Support services provided by Best Practice Advocacy Centre (BPAC). GPs are invited to volunteer to help test the tool. In addition, a new melanoma case-control study has been completed and data from the study will be used to validate and update the pilot risk prediction model.

The updated model and tool will be implemented via BPAC and a finalised version of the risk predictor tool will be accessible to primary care practices in NZ via BPAC in 2016. Finally, a risk prediction tool is also being developed for thick melanoma alone to determine whether it is possible to better predict the melanomas with poor prognosis.

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DAY 2: SESSION 2
Mr Gary Duncan, Chair

Workshop reports and proposed resolutions

Workshop 1. Are primary prevention campaigns worth the effort?

Claire Austin

The following were identified as key commitments in running a primary prevention campaign:

- What is it that needs to be achieved?
- What are the barriers that need to be overcome?
- How will it be achieved?
- Who will take responsibility?

To be influential, there is a requirement for collaboration and not working in isolation, and knowing what data should be captured and how best to share that data. There is also a need for inter-agency collaboration, in particular with the Ministry of Education to integrate melanoma prevention into the secondary school curriculum.

In terms of raising public awareness, the target audience and the different means of reaching that audience must be identified. For example, social media campaigns have proved effective (e.g. the Cancer Society's Junk Free June website). Software apps may also be useful.

Workshop 2. National approach to melanoma translational research in New Zealand

Prof. Mike Eccles

The need for a translation research network was identified, with the objects of research to be clearly articulated.

A collaborative group of volunteers will drive this initiative forward and devise a national plan. Melnet will work with the collaborative group to facilitate the development of the network. An initial project idea is to create a database of research initiatives (who, where, and what) possibly hosted on the Melnet website. Another suggestion was to set up a melanoma research blog site.

Workshop 3. Dermatoscopy/histopathology correlation: The challenge of diagnosing melanoma

Dr Ben Tallon

From a pathology point of view, the more information submitted on a request form the more likely it is that a good result will be received in terms of an accurate answer. The inclusion of photographs of lesions with submissions and annotation of areas of interest on the lesion are helpful.

In terms of physician-pathologist relationships and interaction, pathologists are happy to be contacted directly to review cases on the basis of clinical findings.

Workshop 4. Lymphoedema and other treatment complications

Trish Leathem

Every DHB provides access to lymphoedema physiotherapy but not access to garments, with each DHB having different criteria for supplying garments. If patients are to purchase their own garments, they need to know where they can be purchased. Hence, there is a need for a list of suppliers.

Workshop 5. Sentinel node biopsy: A review of the evidence

Mr Richard Martin

Despite there being polarising views on the value of SNB, some common ground was established with both surgeons and dermatologists being prepared to compromise.

The future of melanoma prevention, diagnosis, treatment, care and research

Prof. Charles Balch

Conducting more clinical trials in NZ should be encouraged, particularly given the country's very high incidence of melanoma and that melanoma treatment is experiencing an era of revolutionary change. Clinical trials not only benefit patients by allowing access to new treatments but also allow the knowledge and expertise of NZ researchers and clinicians to be shared with those who treat melanoma elsewhere in the world. As such, the barriers to conducting clinical trials need to be reviewed and dismantled.

Assoc. Prof. Cliff Rosendahl

Trained dermatoscopy is an important message for the future. Without formal training, dermatoscope use worsens performance in detecting melanoma. The absence of a training programme for dermatopathologists in NZ or Australia is a problem. The Royal College of Pathologists of Australasia needs to organise an accreditation process for dermatopathologists. Melanographers can become experts in the diagnosis of melanoma and have the advantage of being a cost-effective resource. The future of melanoma diagnosis is also lies in automated total body photography for high-risk patients, which can be driven very competently by melanographers.

Prof. David Whiteman

NZ has both a melanoma problem and a non-melanoma skin cancer problem, both of which are caused by UV radiation exposure affecting a predominantly Caucasian population. It is a problem that is only going to get worse and will place a huge drain on NZ's healthcare system. As a country, early detection to diagnose these lesions as soon as possible is critical. Primary prevention must maintain a major role in melanoma control efforts. The emphasis needs to be on changing culture and attitudes around sun exposure and skin damage as well as targeting certain groups, especially secondary school students and the adolescent population in general. These groups are the adults of tomorrow. This will take leadership, commitment, and resources.

Prof. Antoni Ribas

NZ has the potential to be a global leader in melanoma prevention and treatment. All of the critical components are here: the patients, the clinicians, the surgeons, and the research teams. An area requiring active advocacy is to have more clinical trials in advanced melanoma conducted in NZ. Clinical trial participation advances the treatment of patients and elevates the level of the clinics involved and the science in general. Another area for advocacy is the training of staff, especially of young investigators, e.g. programmes for visits to overseas clinics and centres of excellence. The NZ government and Ministry of Health need to act to facilitate clinical trial investment in NZ. In terms of access to effective drugs, there is no health economic argument that can justify dacarbazine being the standard of care for treatment of advanced melanoma.

MSD

This publication has been created with an educational grant from MSD New Zealand. Please consult the full data sheets for any medications mentioned in this article at www.medsafe.govt.nz before prescribing. Treatment decisions based on these data are the full responsibility of the prescribing physician.