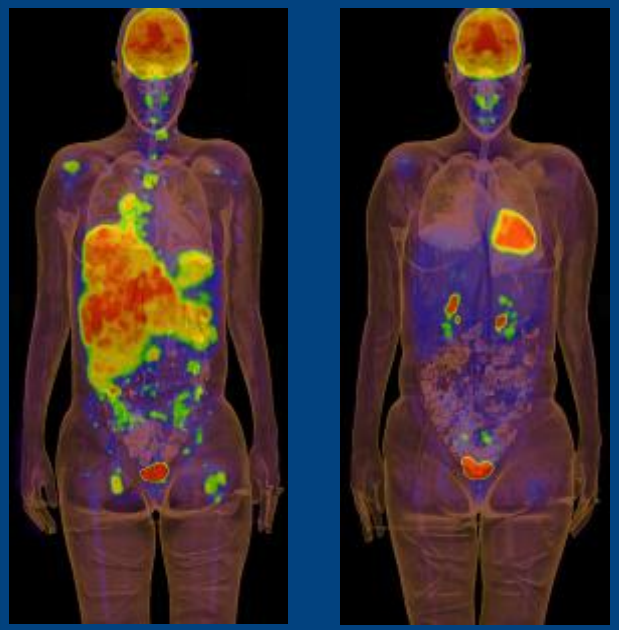

How can we reduce the mortality from melanoma in Australia?

Professor Grant McArthur MB BS PhD
Peter MacCallum Cancer Centre Melbourne, Australia
University of Melbourne, Parkville, Australia

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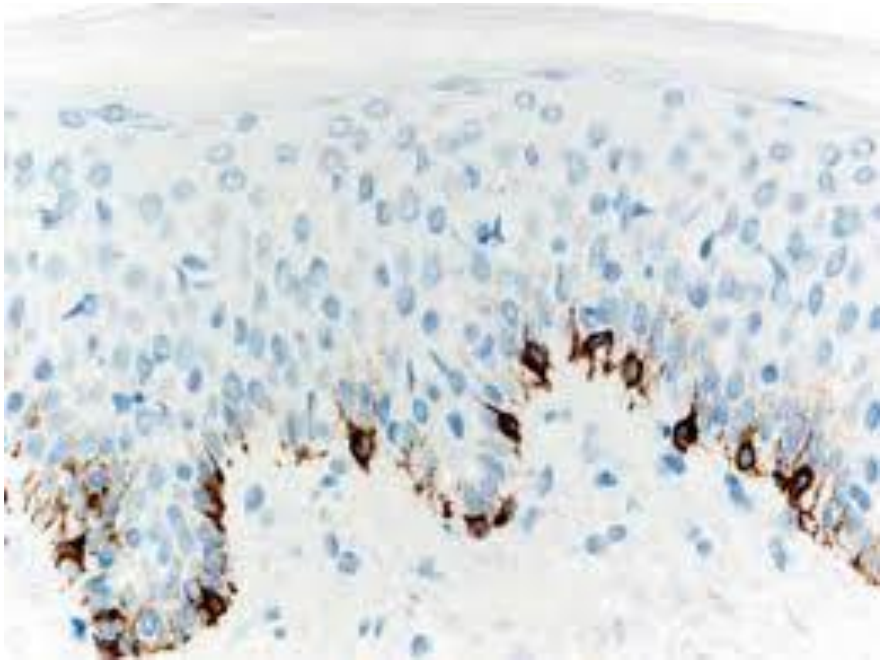
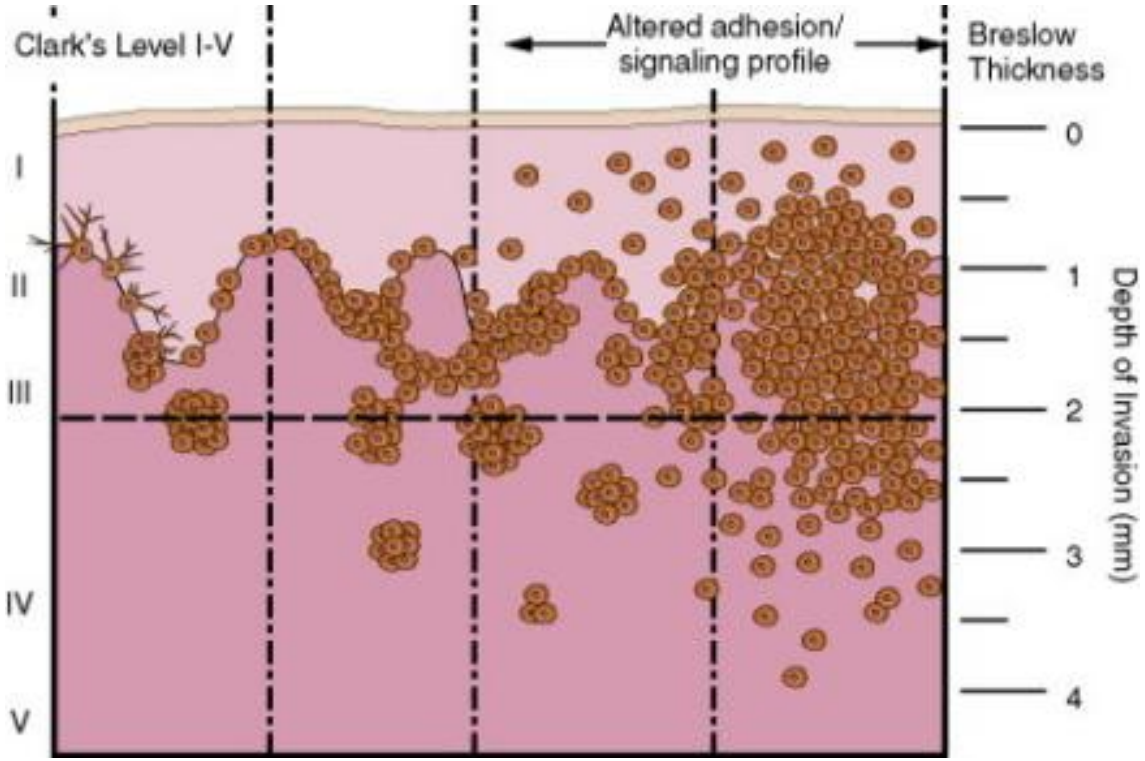
What is melanoma?

- Cancer of melanocytes

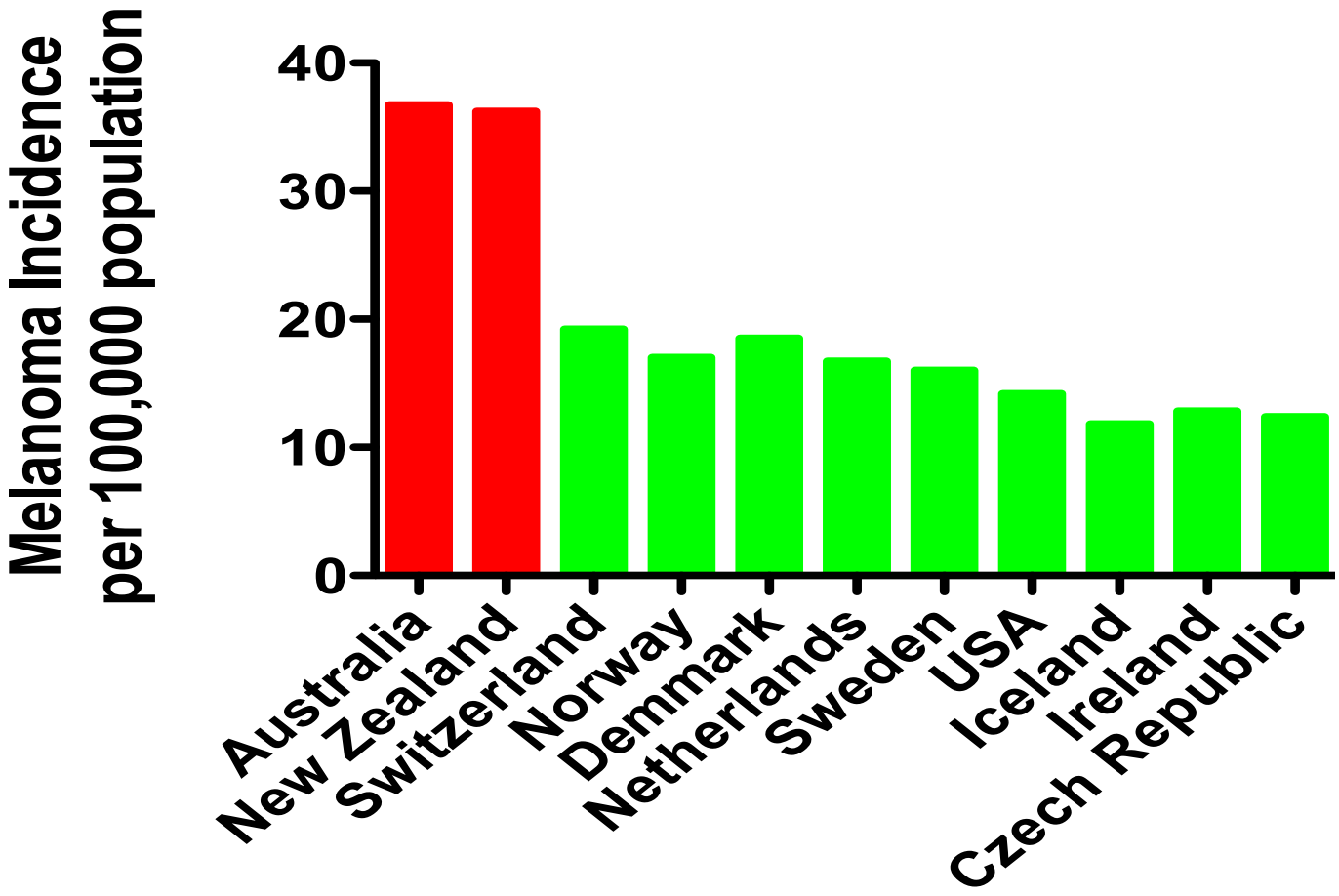


The progression of melanoma - how it spreads



Mendelsohn. *The Molecular Basis of Cancer.* Saunders 2001.

Melanoma age adjusted incidence



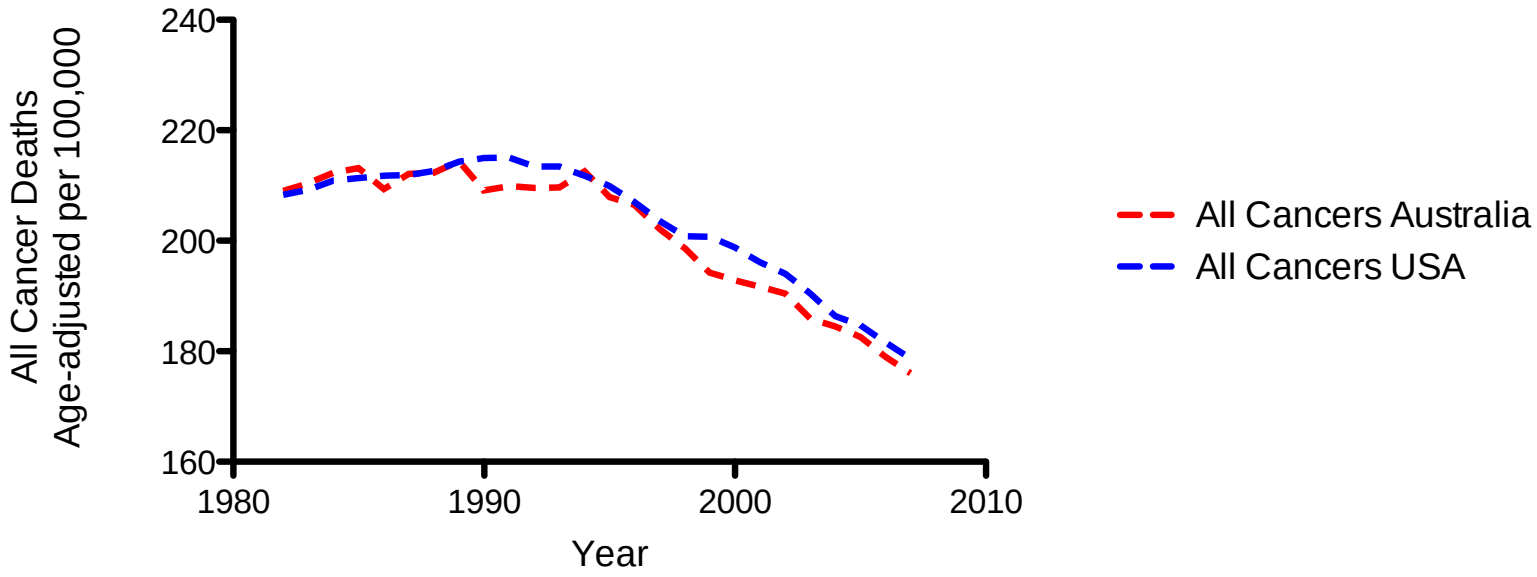
Melanoma in Australia

- 1 in 18 lifetime risk (breast cancer 1 in 16)
- 1 in 14 (males); 1 in 24 (females)

Good news – over 90% of patients with melanoma are cured by surgery if the melanoma is detected early

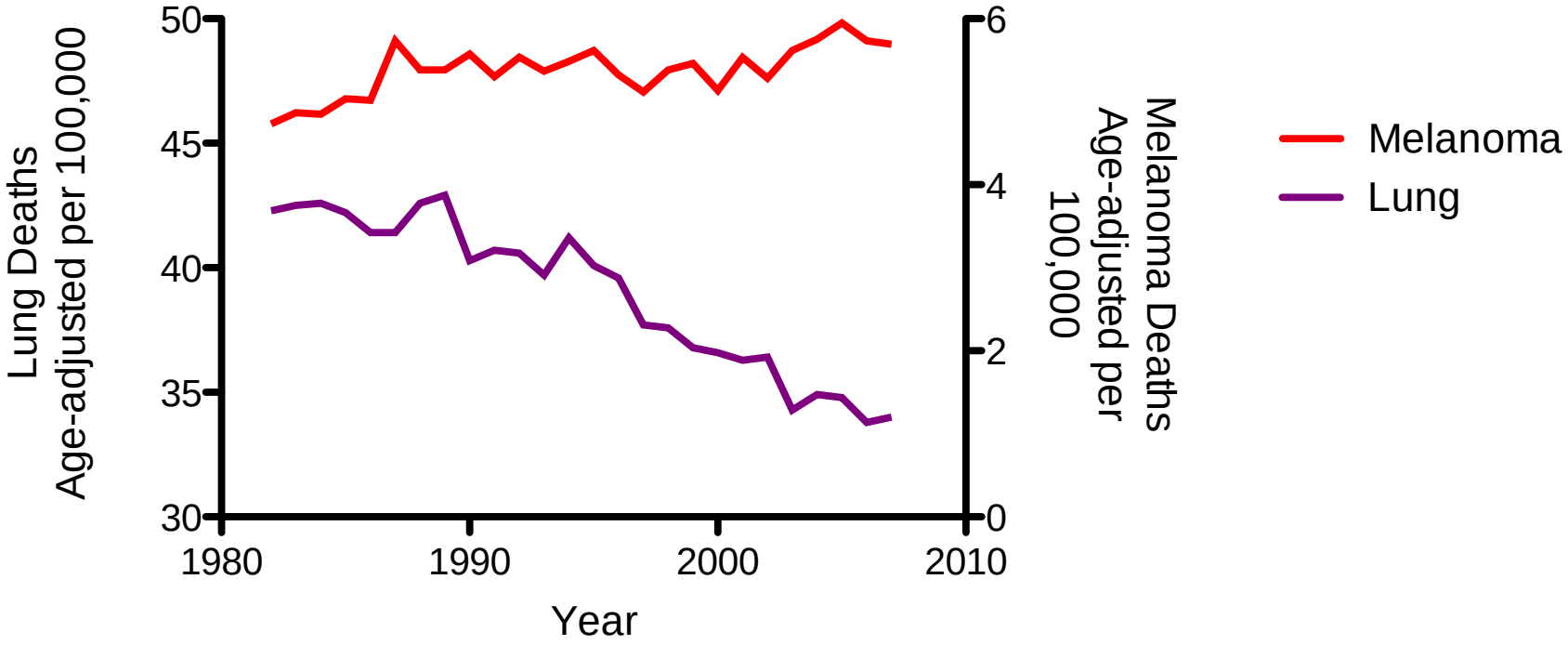
- Death rates increasing by 0.5% pa (males, especially those aged over 60).

Recent reductions in cancer mortality



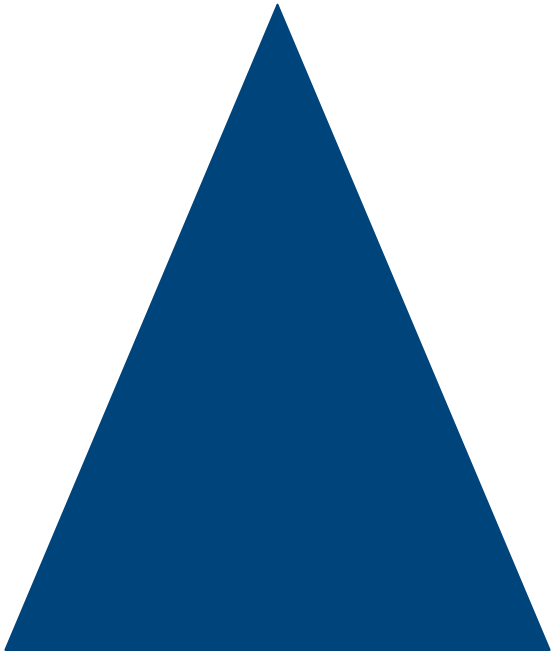
Source of data Australian Institute of Health and Welfare (AIHW) 2011. ACIM (Australian Cancer Incidence and Mortality) Books. AIHW: Canberra and SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations), National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2009_pops09/

Recent reductions in cancer mortality - not in all cancers



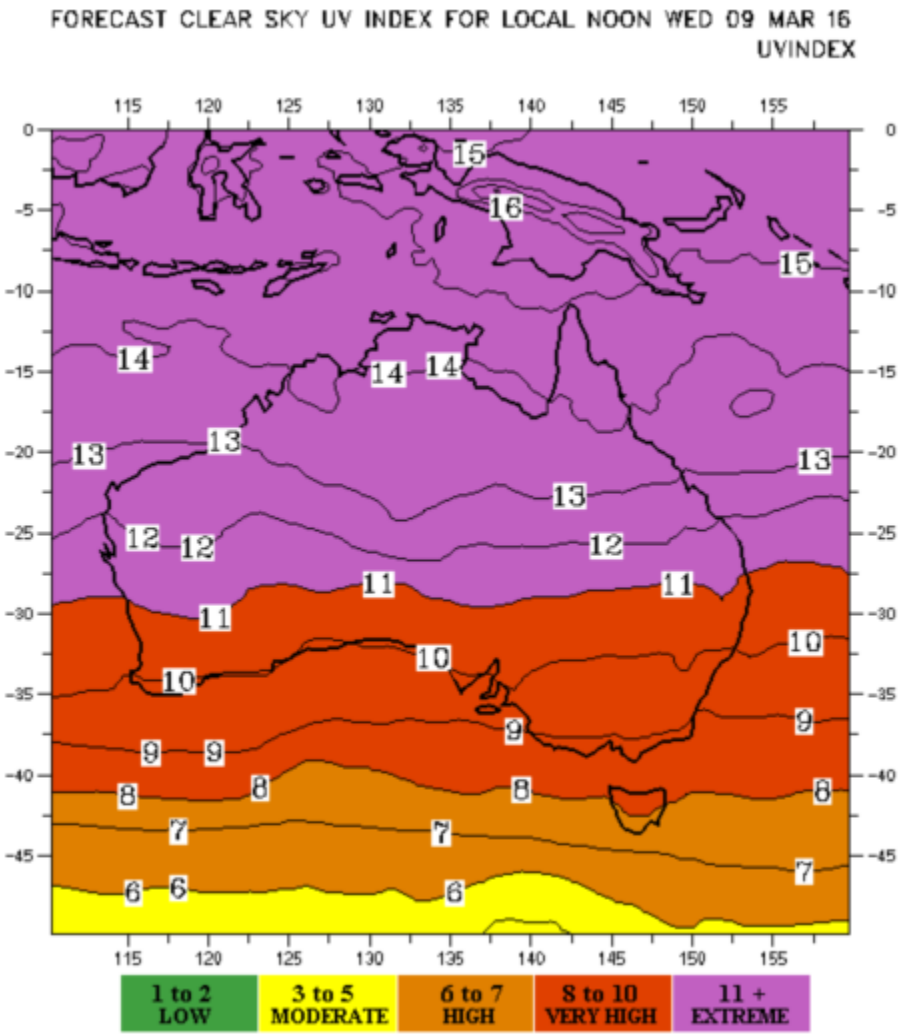
Source of data Australian Institute of Health and Welfare (AIHW) 2011. ACIM (Australian Cancer Incidence and Mortality) books. AIHW

Melanoma - how to reduce mortality?



Preventing melanoma

Preventing melanoma



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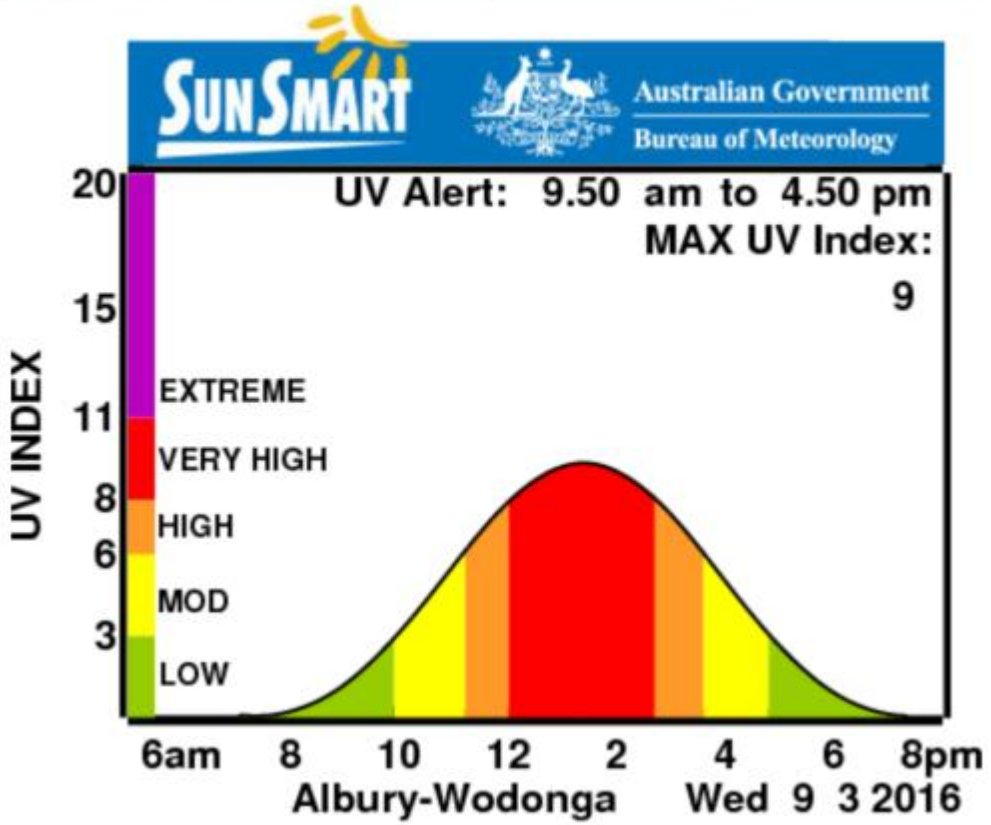
Preventing melanoma

Sun Protection Recommended	Maximum UV Index (Clear Sky)
9.50 am to 4.50 pm	9



Ultravoilet (UV) Index		
Index	Colour	Definition
11+	Violet	Extreme
8,9 & 10	Red	Very High
6 & 7	Orange	High
3, 4 & 5	Yellow	Moderate
1 & 2	Green	Low*

* When UV Index is low, sun protection is generally not needed unless outside for extended periods.

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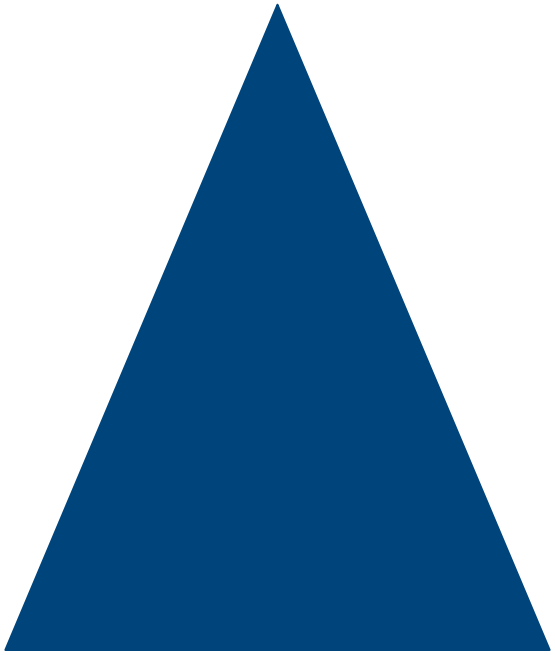
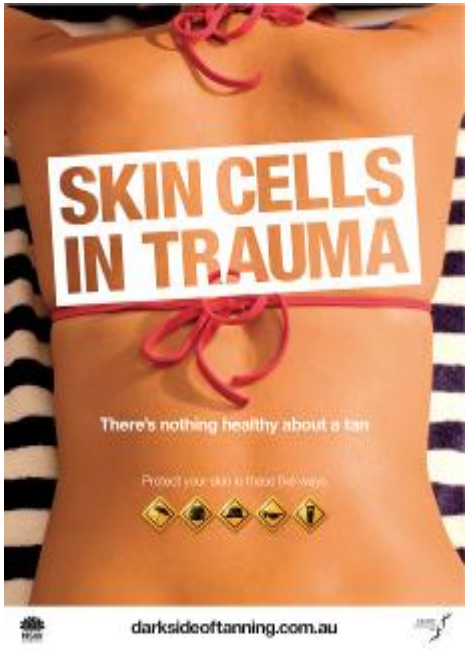
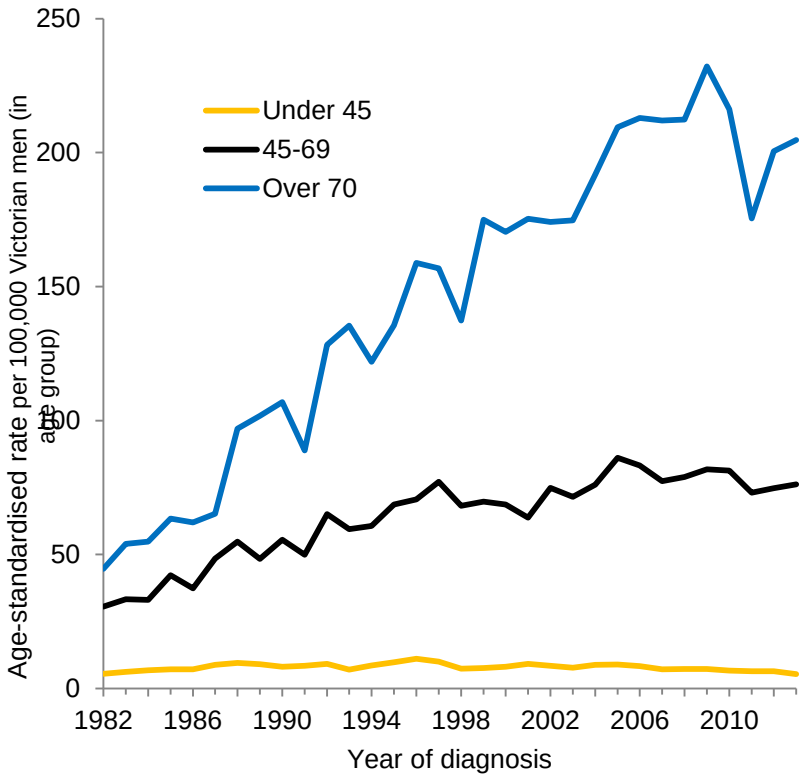
Melanoma - how do we reduce mortality?

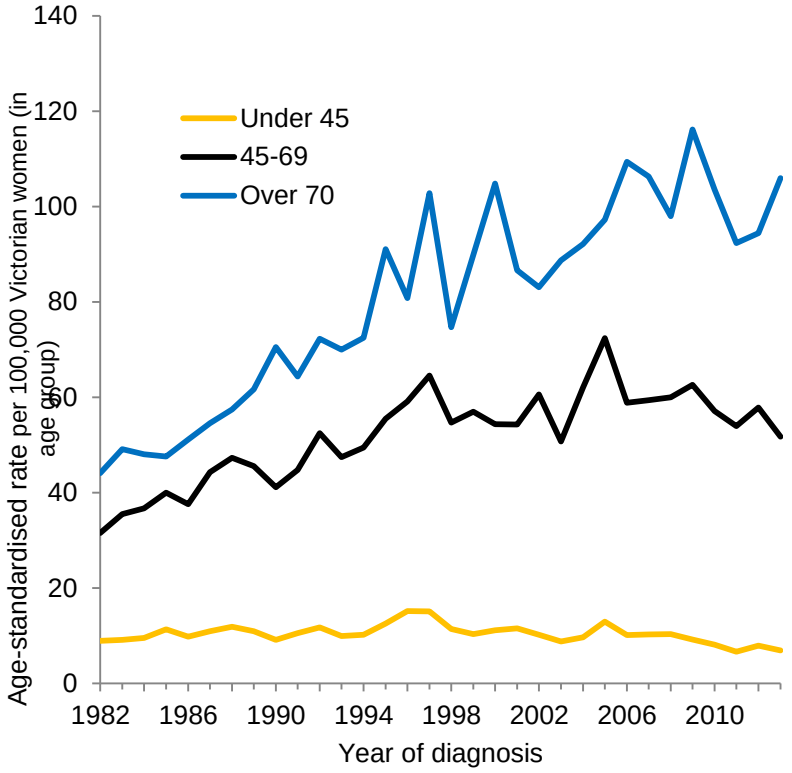


Detecting melanoma – early awareness



Victorian melanoma incidence trends by age group between 1982-2013





Incidence – Male

Incidence – Female

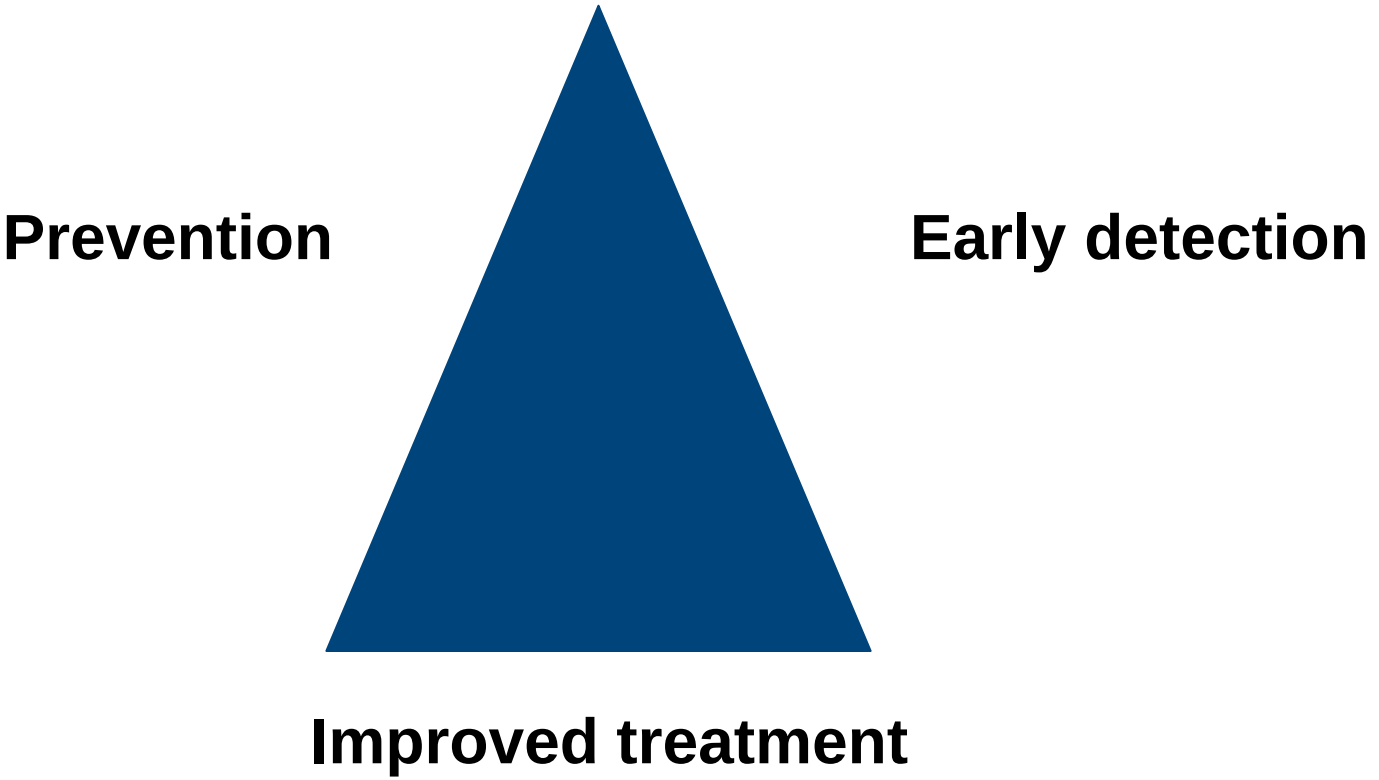
1. Thursfield V, et.al. Cancer in Victoria: Statistics & Trends 2013. Cancer Council Victoria: Melbourne, Australia 2014.

This is a warning for men

- **Men spend more time outside:**
  78% of men 45 and over spent more than 15 minutes outside during peak UV times on the weekend.[2]
- **Men use sun protection less than women:**
  Clothing, sunglasses, seeking shade and applying sunscreen before going outside
- **Men are less likely to go their doctor:**
  A cancer diagnosis at a later stage mean's it more difficult to treat

2. Volkov A, Dobbinson SJ. 2013–14 National Sun Protection Survey: Report 2. Sun protective behaviours and sunburn incidence on summer weekends among Australians in summer 2013–14. Centre for Behavioural Research in Cancer, Cancer Council Victoria: Melbourne, Australia, November 2014.

Melanoma - how to reduce mortality?



Multi-disciplinary care – the cornerstone of modern management of melanoma

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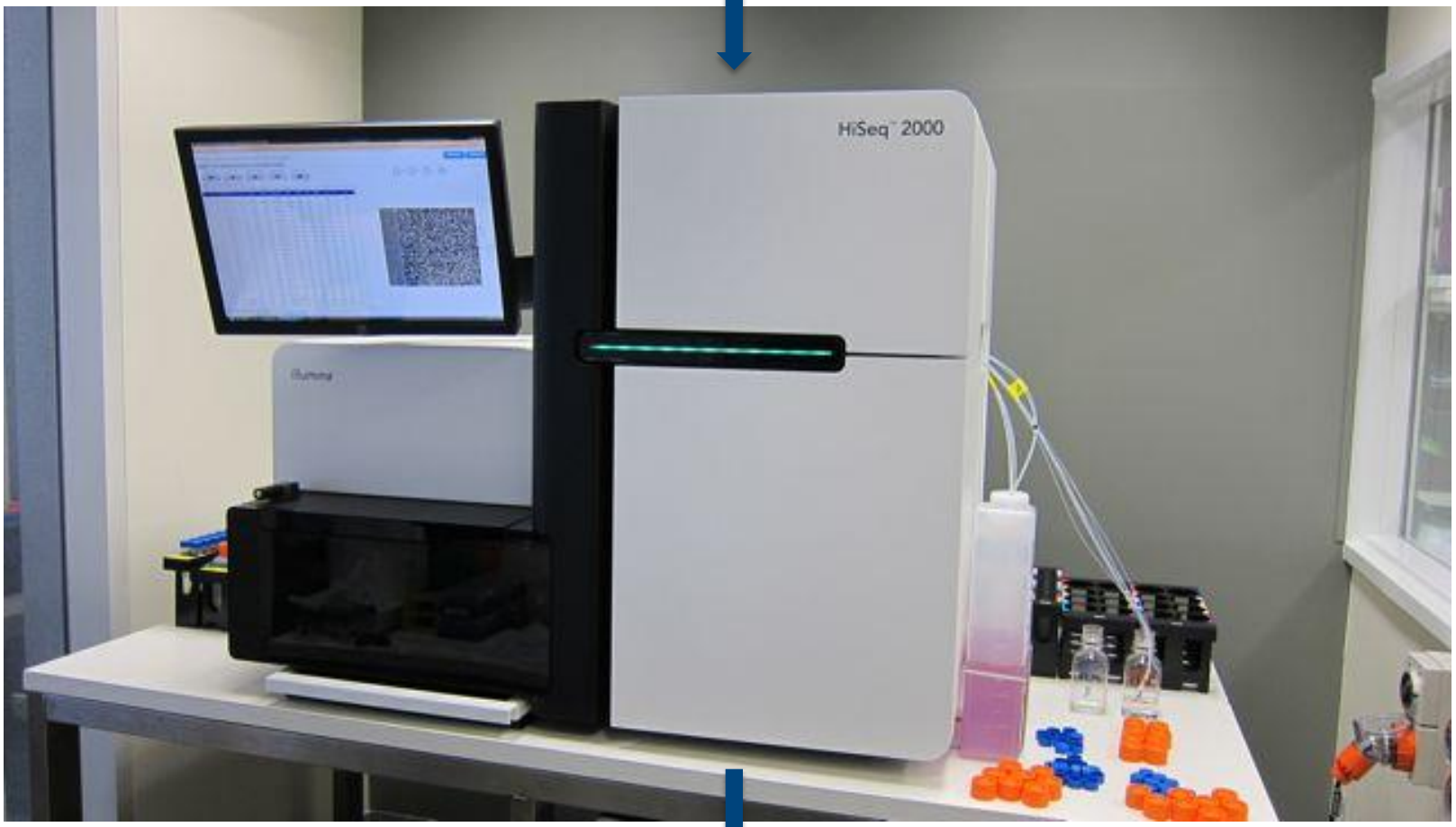
DNA



Lots (and lots) of data

Very frequent gene mutations in melanoma

Table 1 | Somatic mutation prevalence by cancer type.

Cancer type	Mutations per Mb of DNA	Number of samples	Number of mutations
ALL	0.57	8	2
Breast	2.70 (†0.19)	16	56
Colorectal	1.21		
Gastric	2.10		
Glioma	22.37 (‡0.32)		
Lung carcinoma	4.21		
Lung carcinoid	0.00		
Ovarian	1.85		
Renal	0.74		
Testis	0.12		
MMR-deficient	32.29		
Melanoma*	18.54		
Other cell lines*	5.64		
All tissues	3.93		

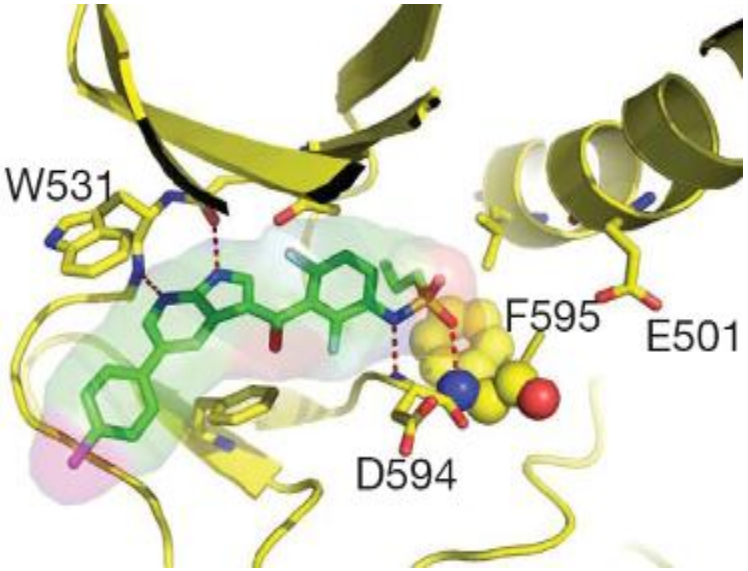
4x rate of mutations

10x rate of mutations compared to ovarian cancer

5x rate of mutations compared to all other cancers

Greenman….Stratton, Nature, 2007

Targeting melanoma – BRAF



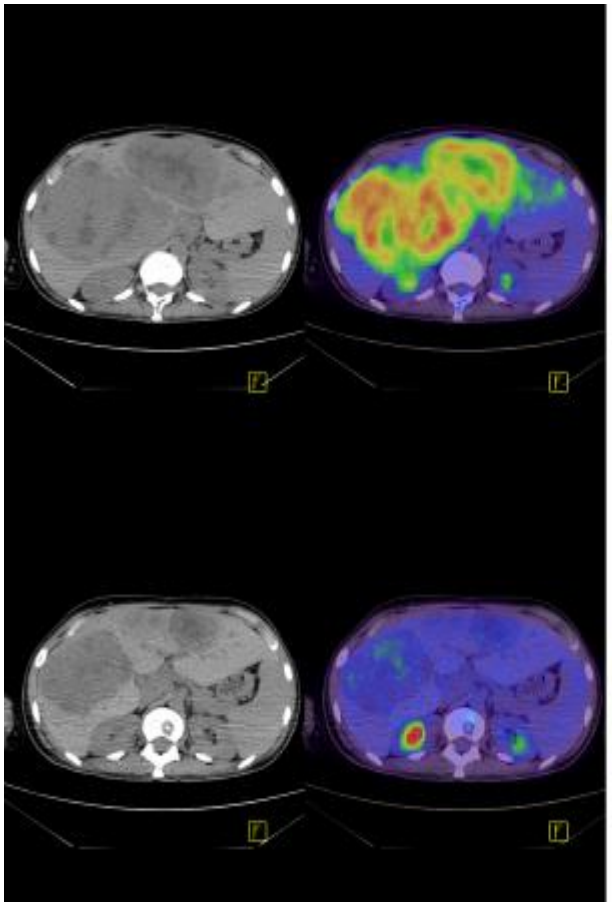
Control

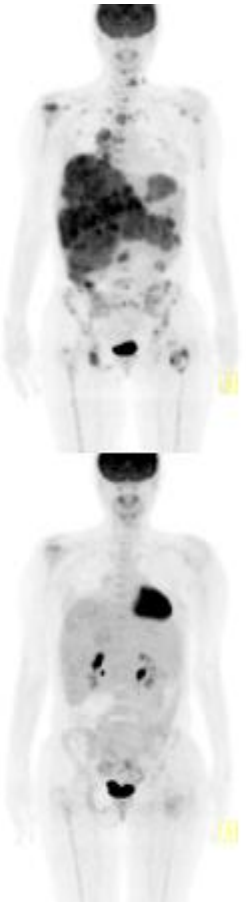
Targeted therapy

Turning off the genes driving melanoma – BRAF

Baseline

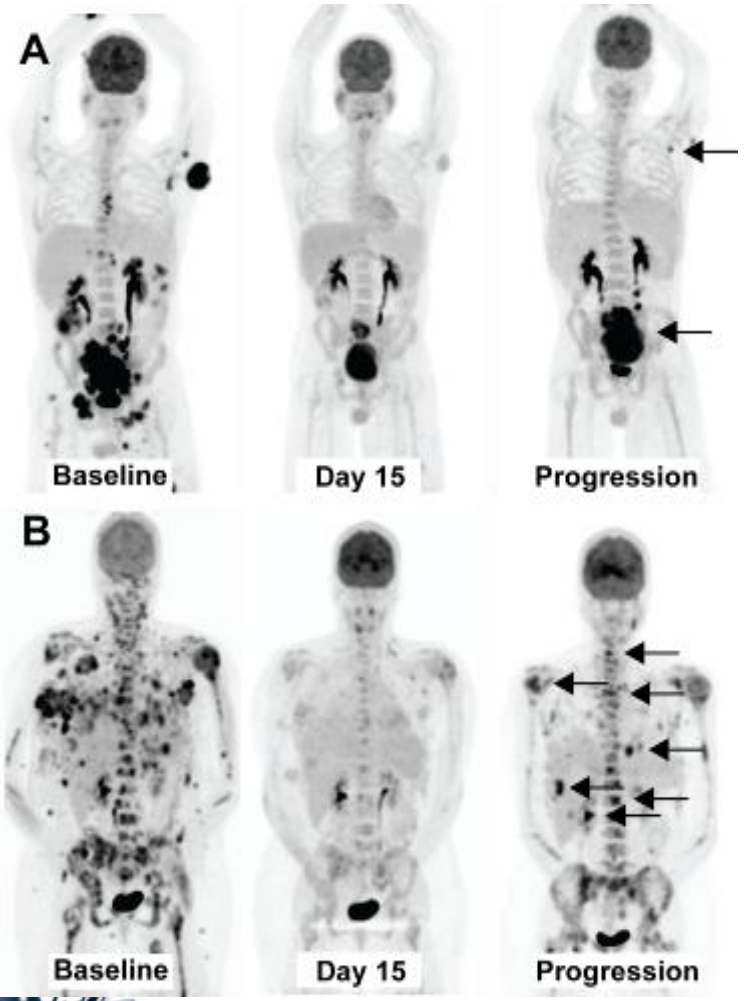
Two weeks of targeted therapy with BRAF inhibitor

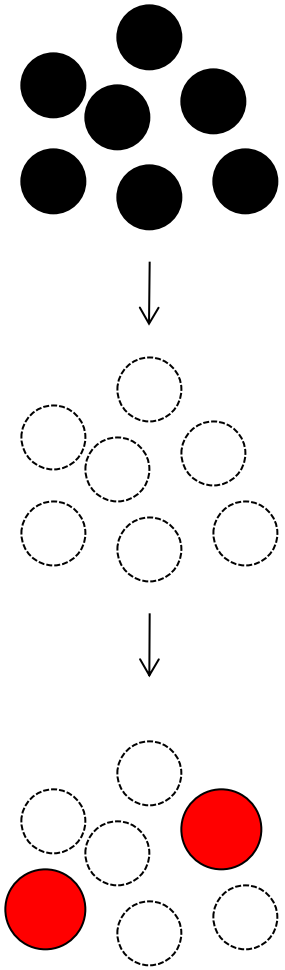




McArthur et al, Journal of Clinical Oncology

Research and more clinical trials are vital





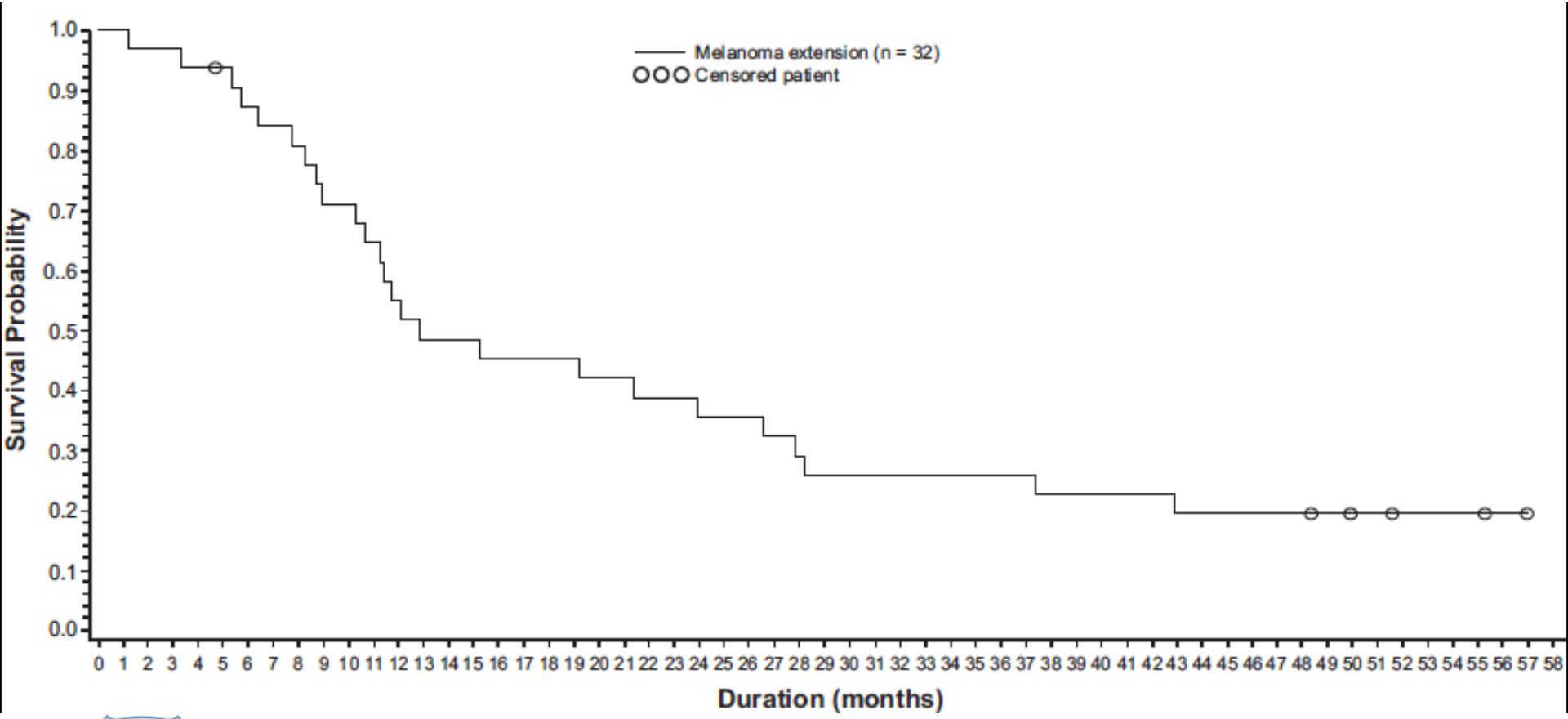
Baseline

Response

NRAS mutation

Progression

Long Term Responses in Advanced Melanoma after BRAF inhibition



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Puzanov et al, *Eur J Cancer*, in press, 2015

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Oncology

And then there were five

CHICAGO

Doctors are trying—with some success—to recruit the immune system to help with the war on cancer

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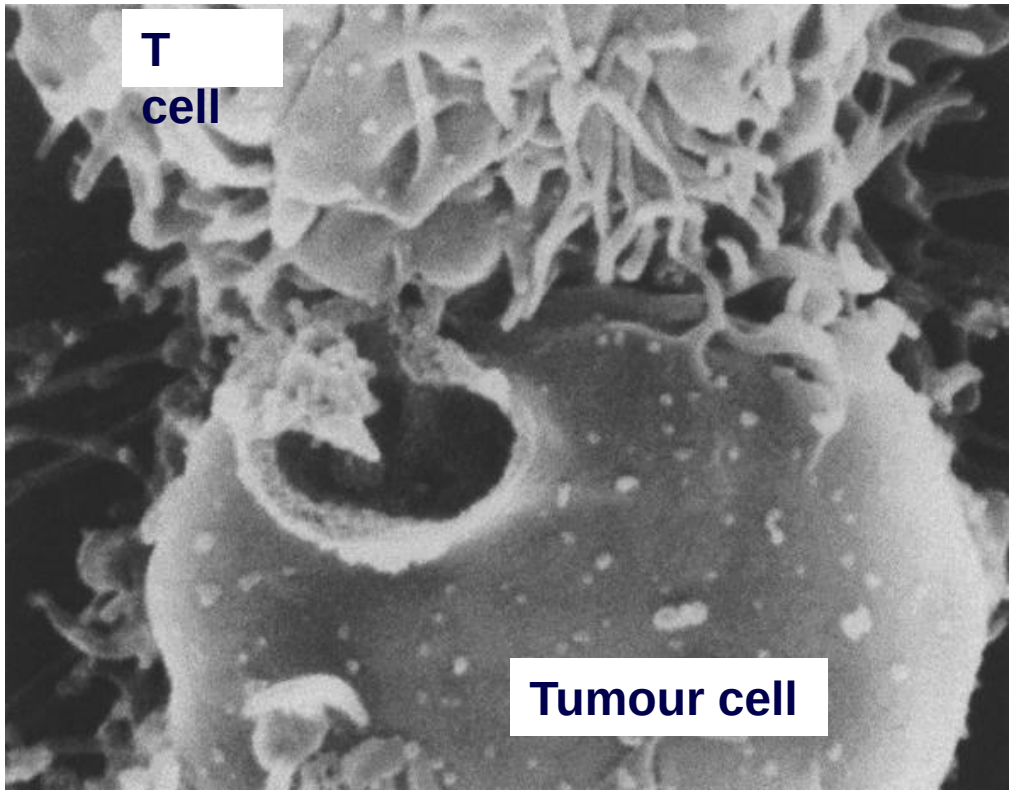
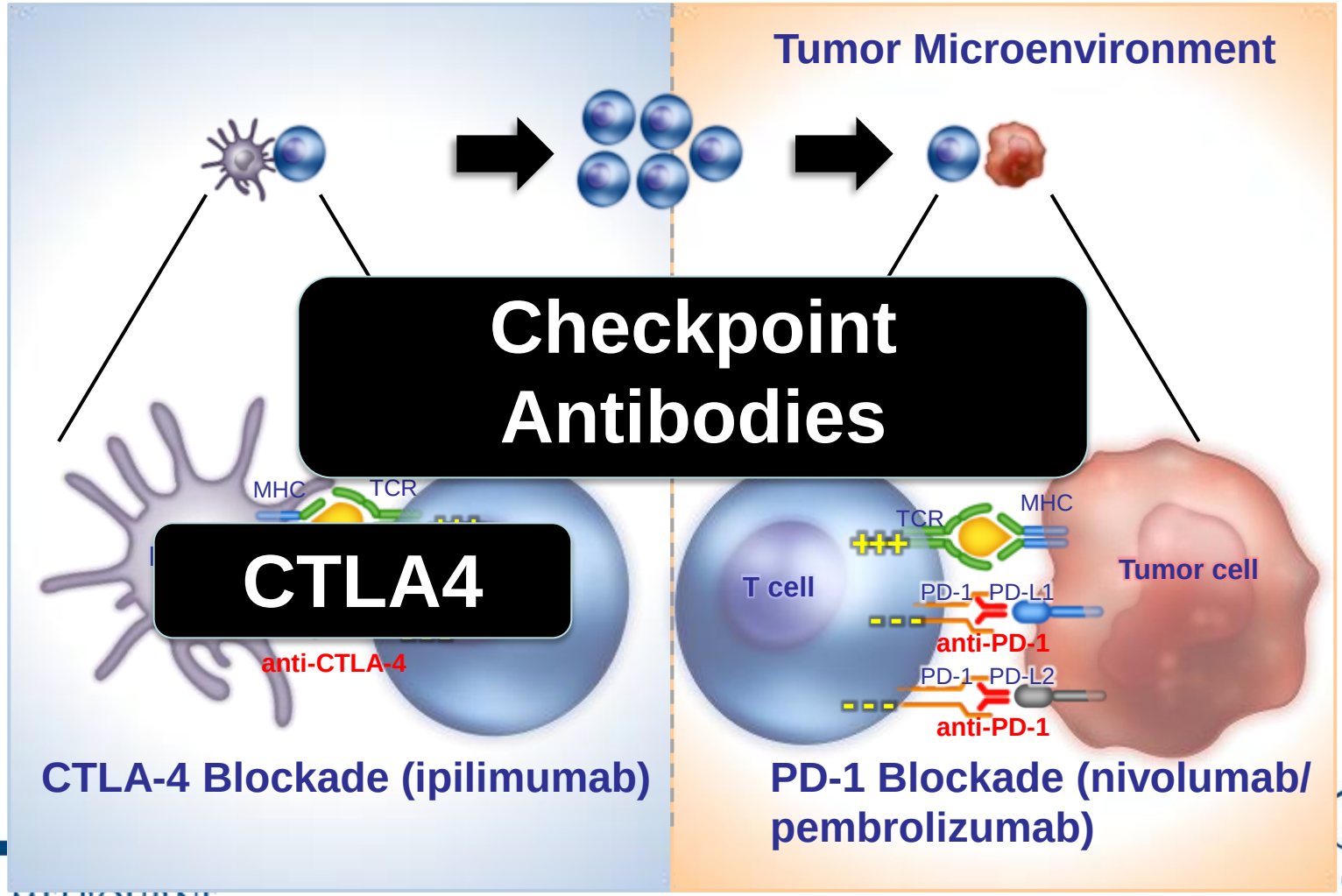
POSTERA CRESCAM LAUDE
Peter Mac

Unlocking the immune system



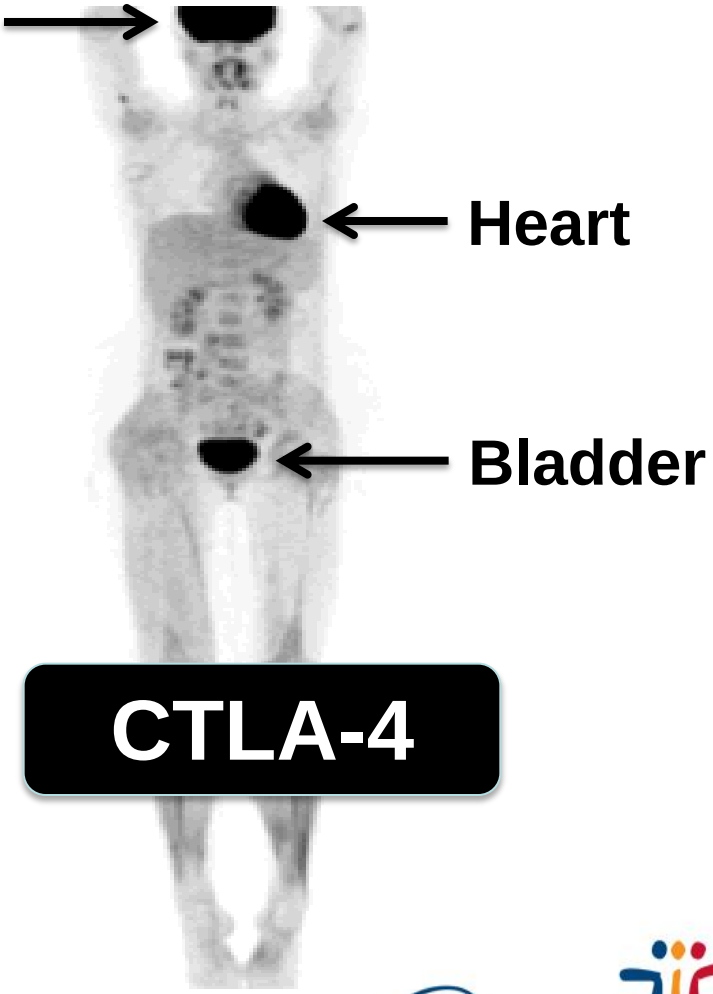
Dr Raowf Guirguis, National Cancer Institute, Scanning electron images

Unlocking the immune system



Feb 2012

June 2012



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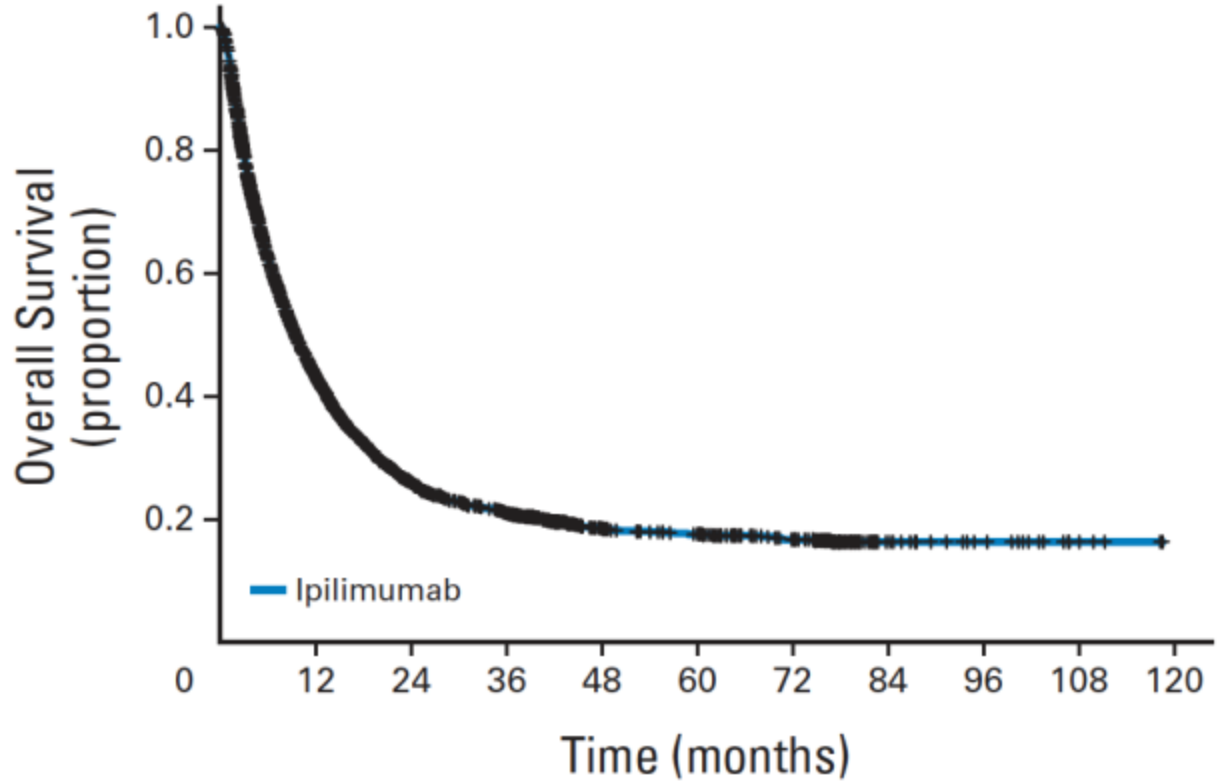
SHADE
SEEKERS

Long Term Responses in Advanced Melanoma after 4 doses of anti-CTLA4



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Schadendorf et al, *J Clin Oncol*, 2015

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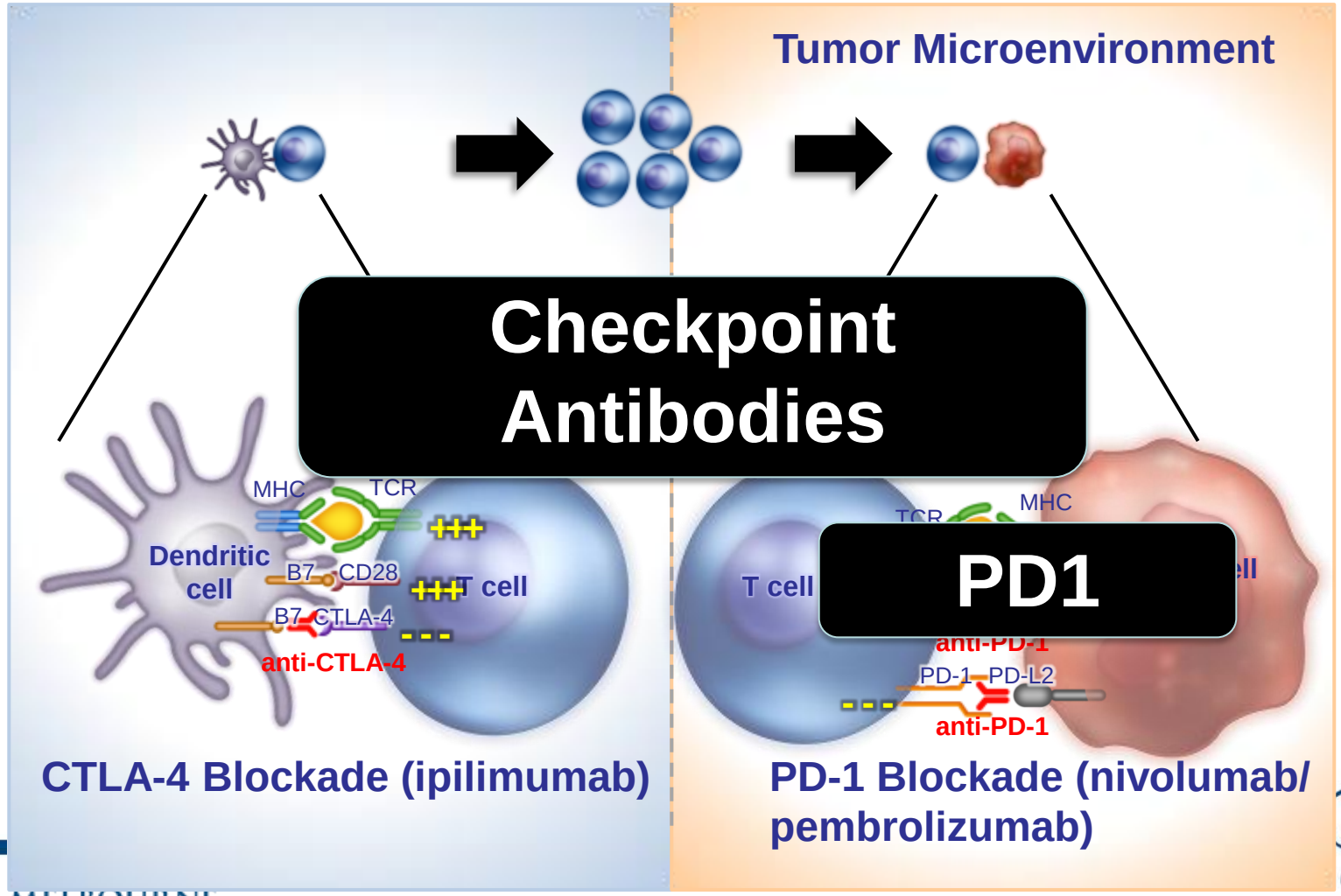
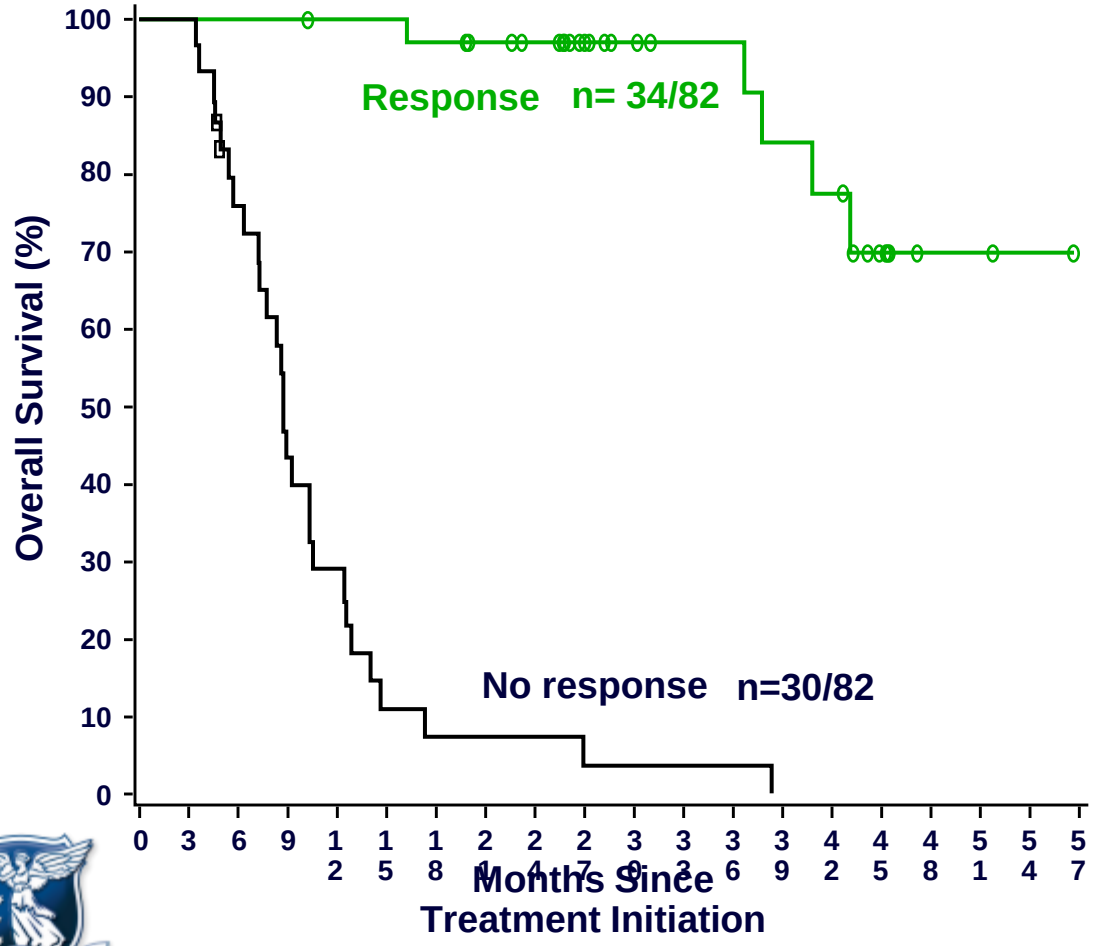
Unlocking the immune system



Durable responses to checkpoint antibodies



PD-1

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Hodi et al, ASCO, 2014

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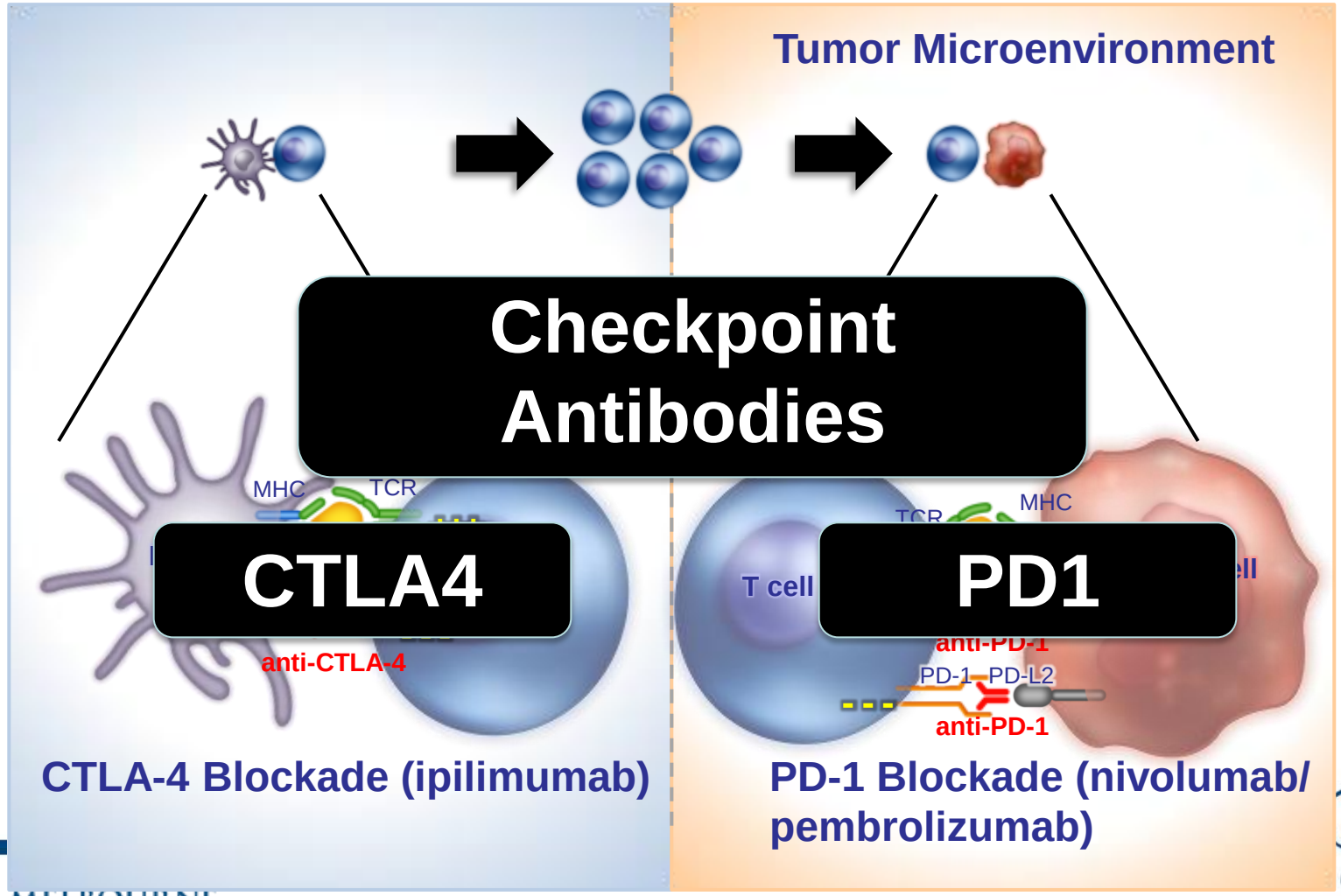
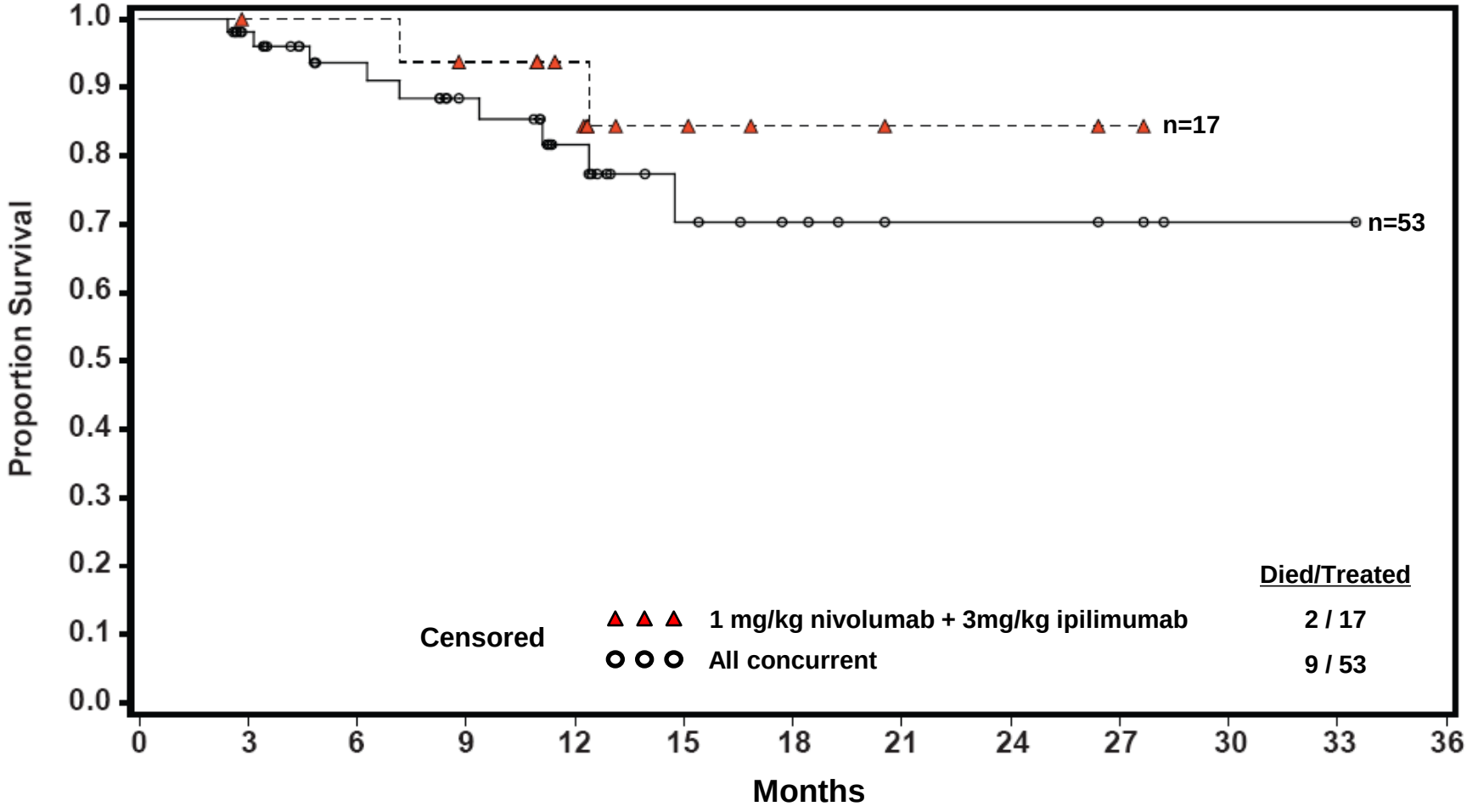
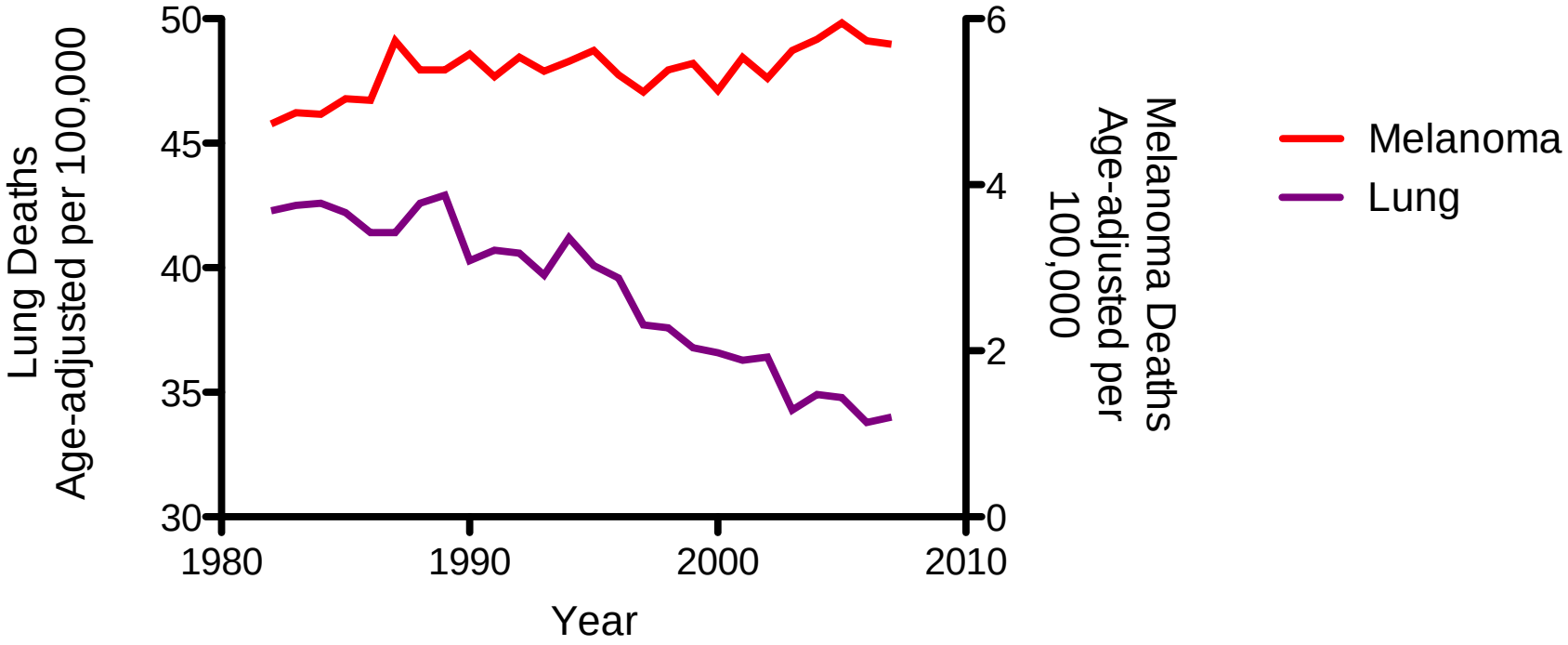
Unlocking the immune system



Ongoing Survival of Patients Treated Anti-PD-1 and anti-CTLA4



Recent reductions in cancer mortality - not in all cancers



Source of data Australian Institute of Health and Welfare (AIHW) 2011. ACIM (Australian Cancer Incidence and Mortality) books. AIHW

Melanoma – making advances

- A team approach
- A global coordinated approach
  - community
  - scientists/healthcare professionals
  - industry
  - government.

“Melbourne Melanoma Project- Update”

- 60% have experienced severe sunburn with blistering
- 9.4% have used a solarium
- 3.2% have had a SCC
- 9.3% have had a BCC

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Olivia Newton-John
Cancer Wellness & Research Centre

VMS Victorian Melanoma Service

BORDER MEDICAL ONCOLOGY

MELBOURNE MELANOMA PROJECT

"Melbourne Melanoma Project- Update"

- 18.6% patients reported a family history of melanoma
  - 265 reported first degree relatives
  - 26 reported first and second degree relatives
  - 80 reported second degree relatives

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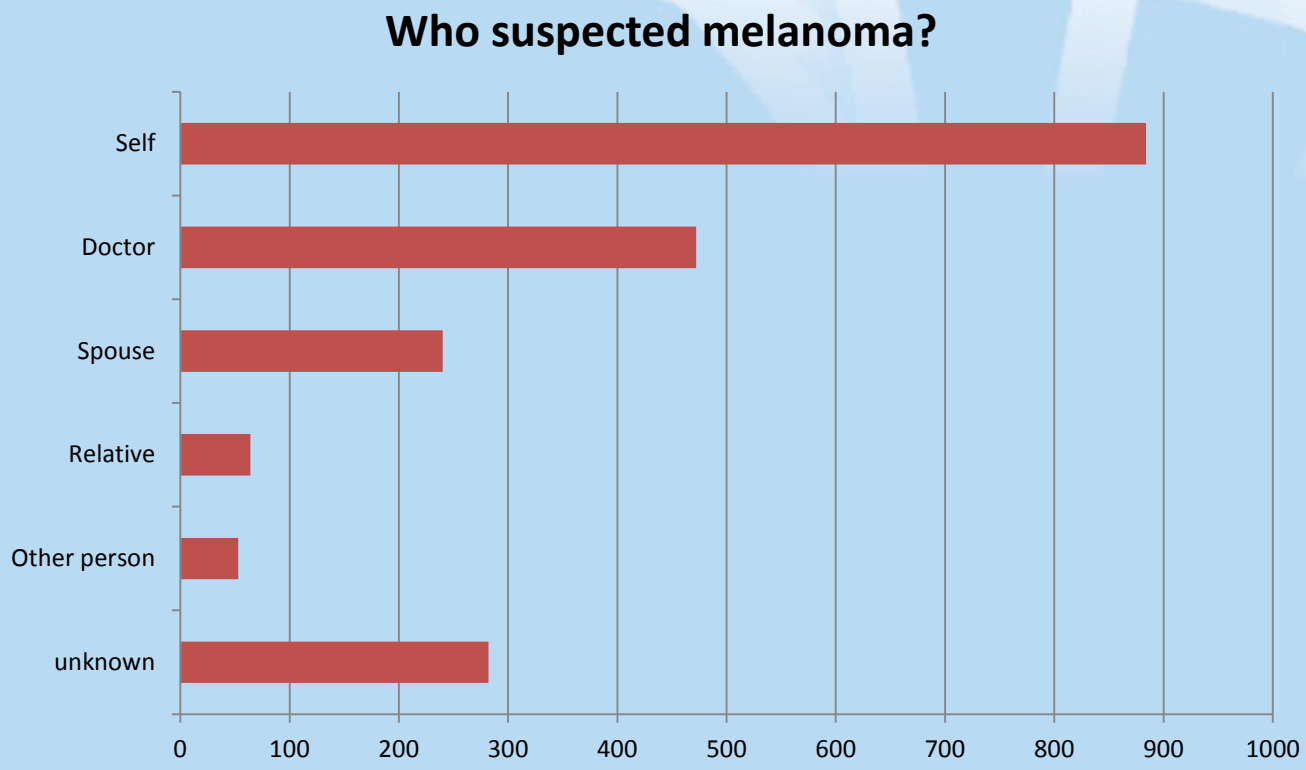

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“Staging in Melanoma- contributions from the Melbourne Melanoma Project”

Professor Grant McArthur

Director Melanoma & Skin Service Peter MacCallum Cancer Centre

Lorenzo Galli Chair in Melanoma & Skin Cancer University of Melbourne

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Olivia Newton-John
Cancer Wellness & Research Centre

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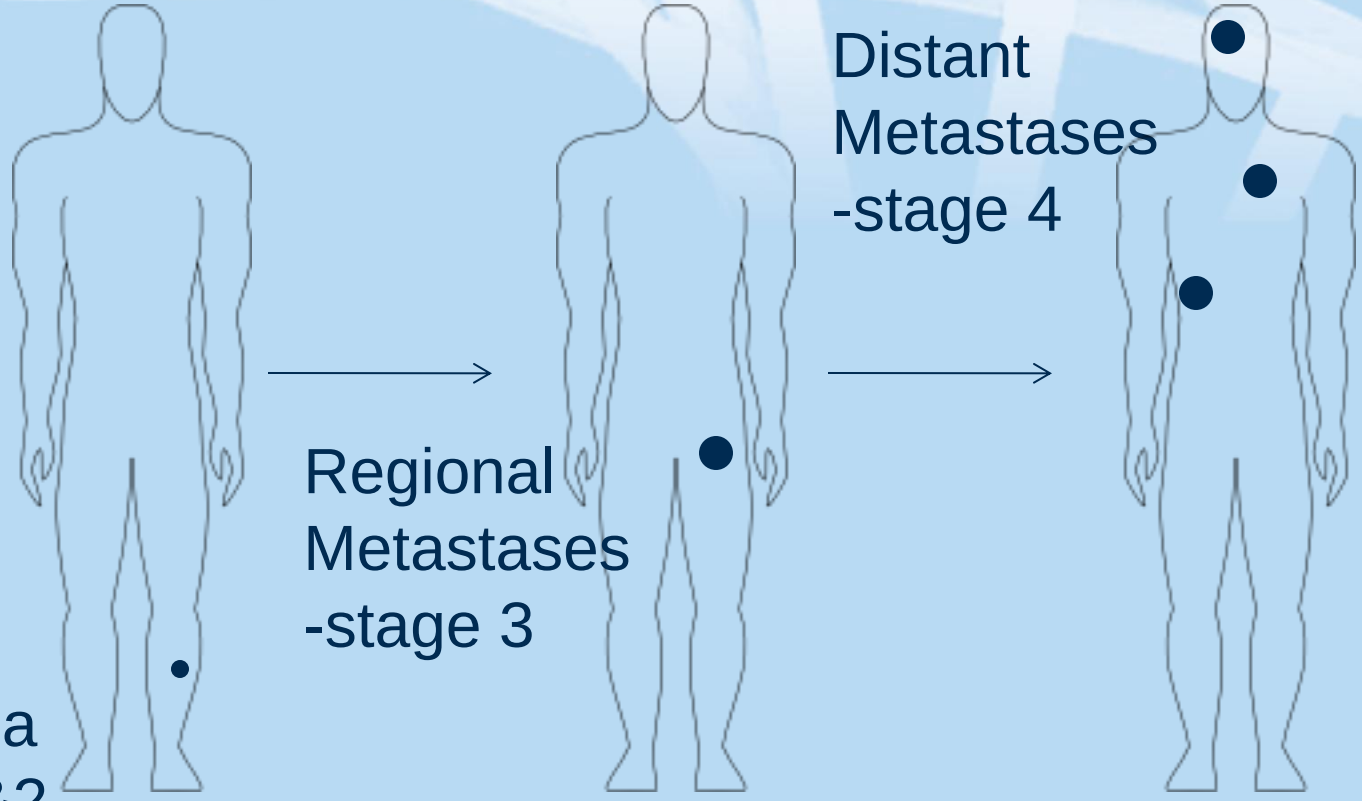
MELBOURNE MELANOMA PROJECT

Melanoma - stage defines treatment



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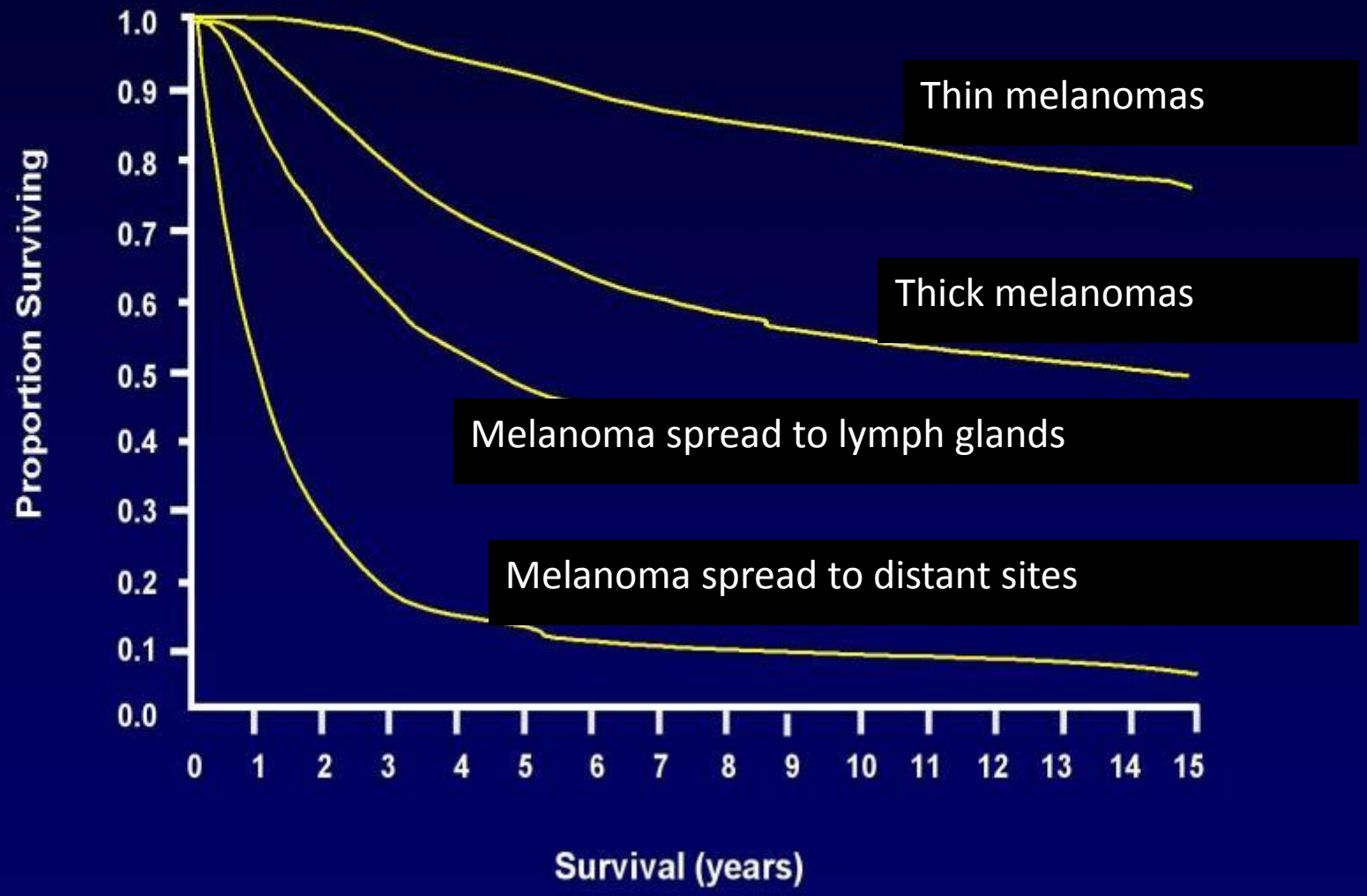
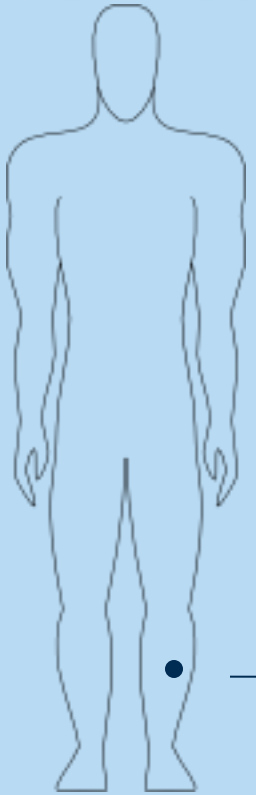
Fifteen-Year Survival of Patients in AJCC Melanoma Staging Database

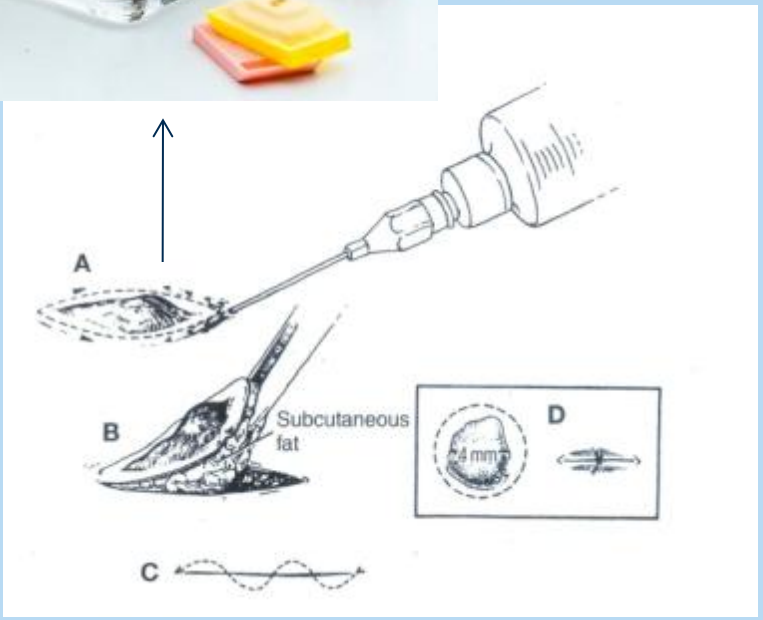


Journal of Clinical Oncology, Vol 19, No 16 (August 15), 2001: pp 3635-3648

Stage 1 & 2 – Surgery the Path to Cure



Primary
Melanoma
-stage 1&2



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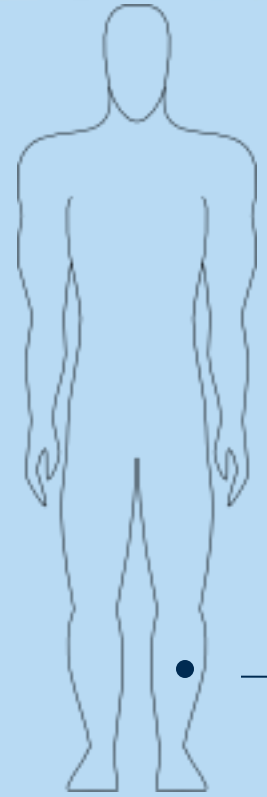
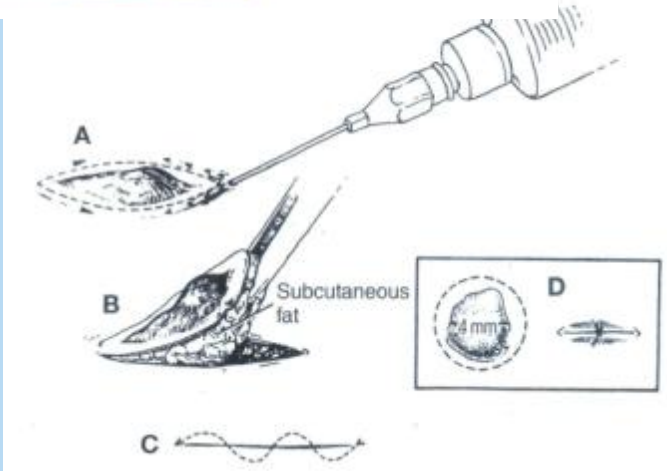


Primary Melanoma -stage 1&2

Wide Local Excision



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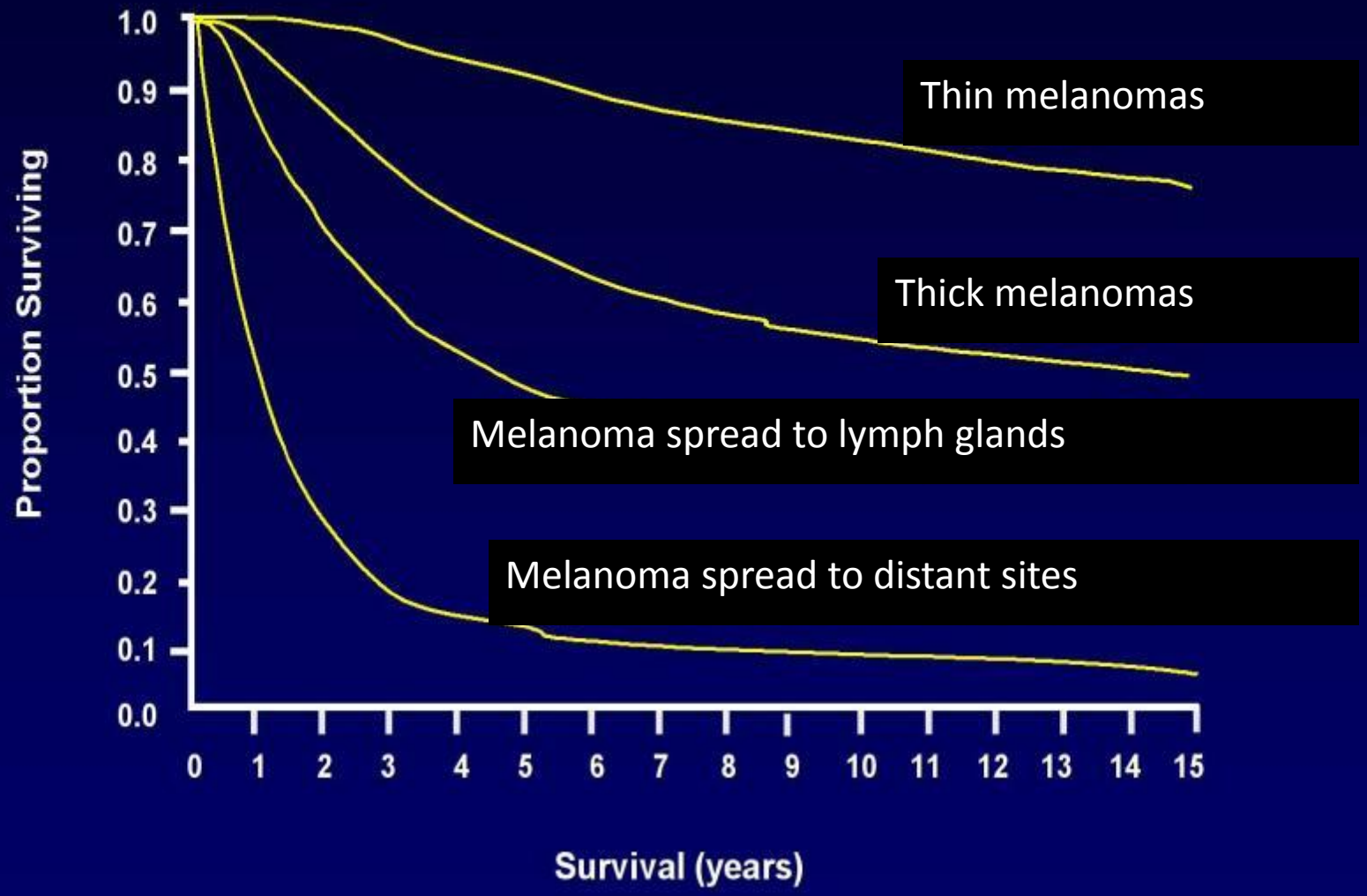
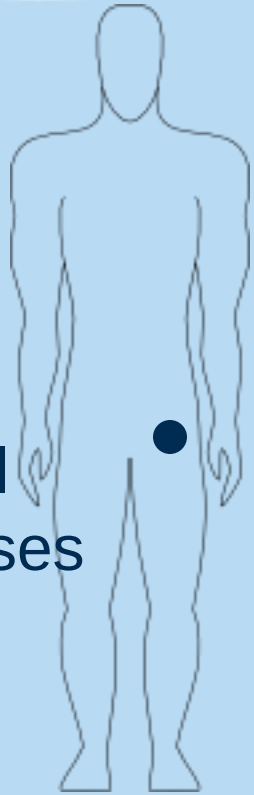
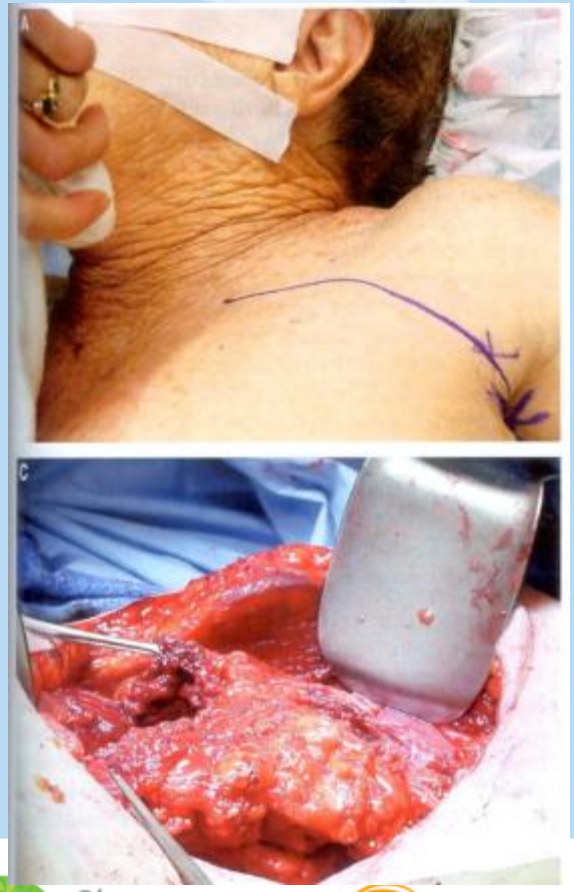


Journal of Clinical Oncology, Vol 19, No 16 (August 15), 2001: pp 3635-3648

Stage 3 melanoma- Surgery + Other Treatment

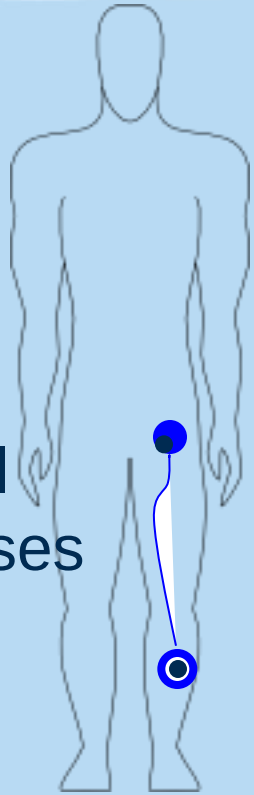
Regional Metastases -stage 3





Balch et al – Cutaneous Melanoma, QMP, 2009

Stage 3 melanoma- Surgery + Other Treatment

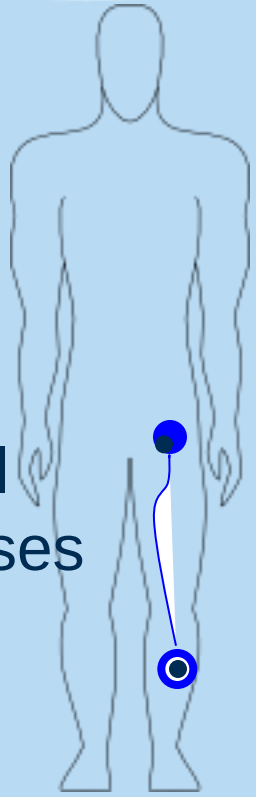


Regional Metastases -stage 3

Sentinel Lymph Node Biopsy

Balch et al – Cutaneous Melanoma, QMP, 2009

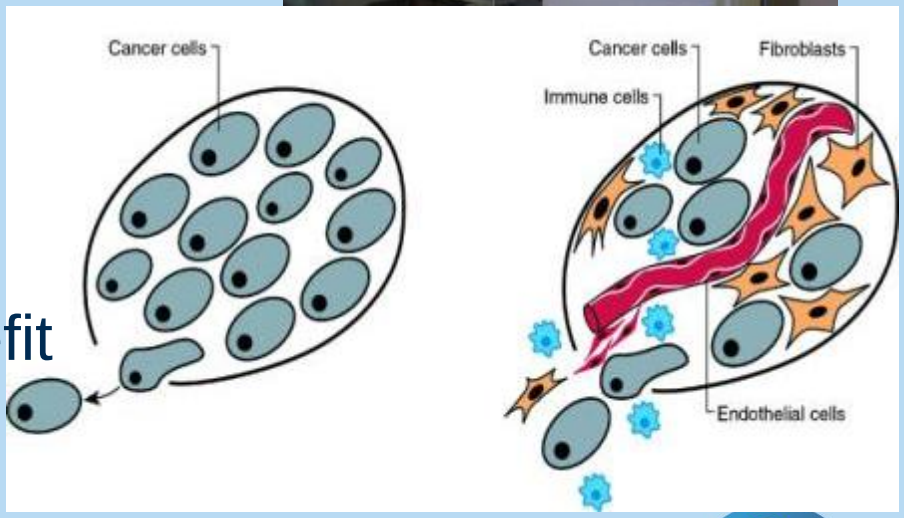
Stage 3 melanoma- Surgery + Other Treatment



Regional Metastases -stage 3

Radiotherapy- Some patients

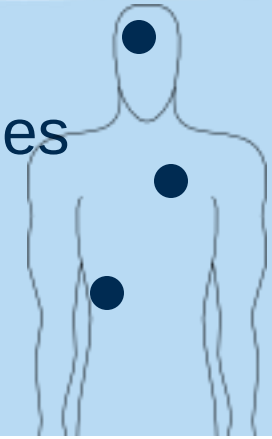
Interferon
- Side effects
- Modest Benefit



From Hanahan & Weinberg, Cell, 100:57, 2000

Stage 4 melanoma – drug treatment ± radiotherapy (sometimes surgery)

Distant Metastases -stage 4



Surgery
- Brain
- Bowel
-≤ 3 lumps

Radiotherapy
- Local Treatment at Specific sites

Drug Therapy
- Main Approach

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MELBOURNE MELANOMA PROJECT

"The 8th edition of the AJCC staging system- what may change"

- Measure melanoma thickness 0.1mm rounding not 0.01mm
- Change in cut point for very good prognosis melanomas to 0.8mm
- Sub-classify positive sentinel lymph node by size >1mm
- Include LDH/brain metastases in subclassification stage 4

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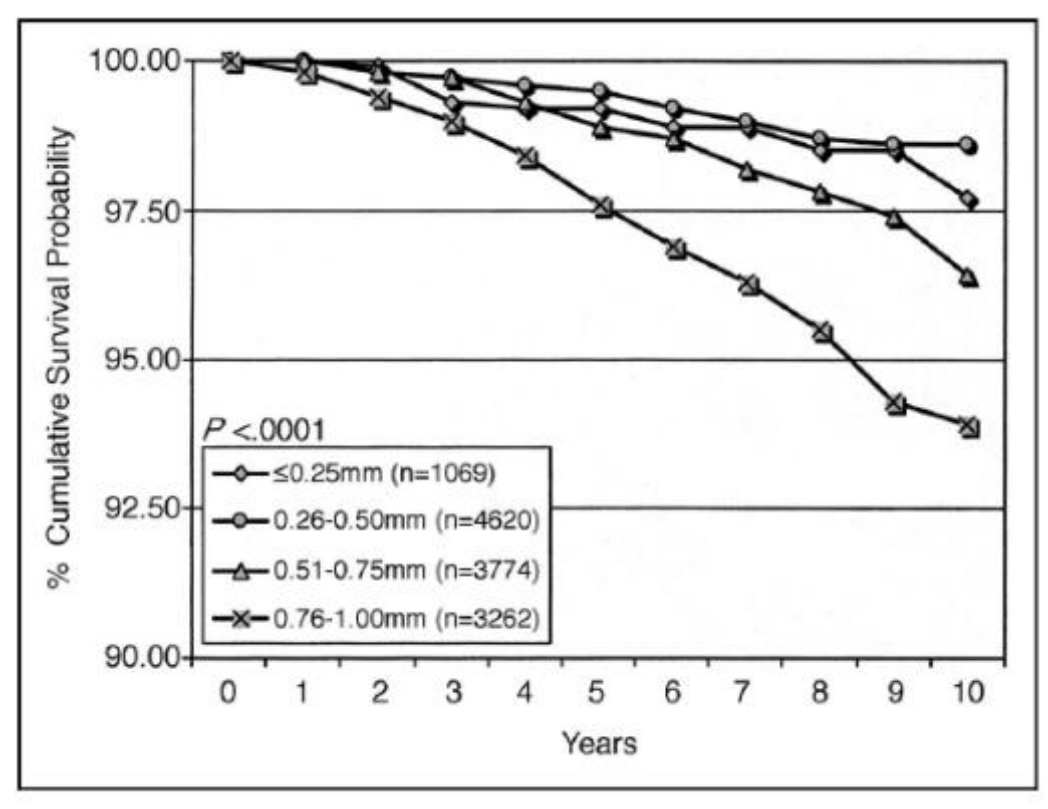

Leiter et al – J Clin Oncol, 2004

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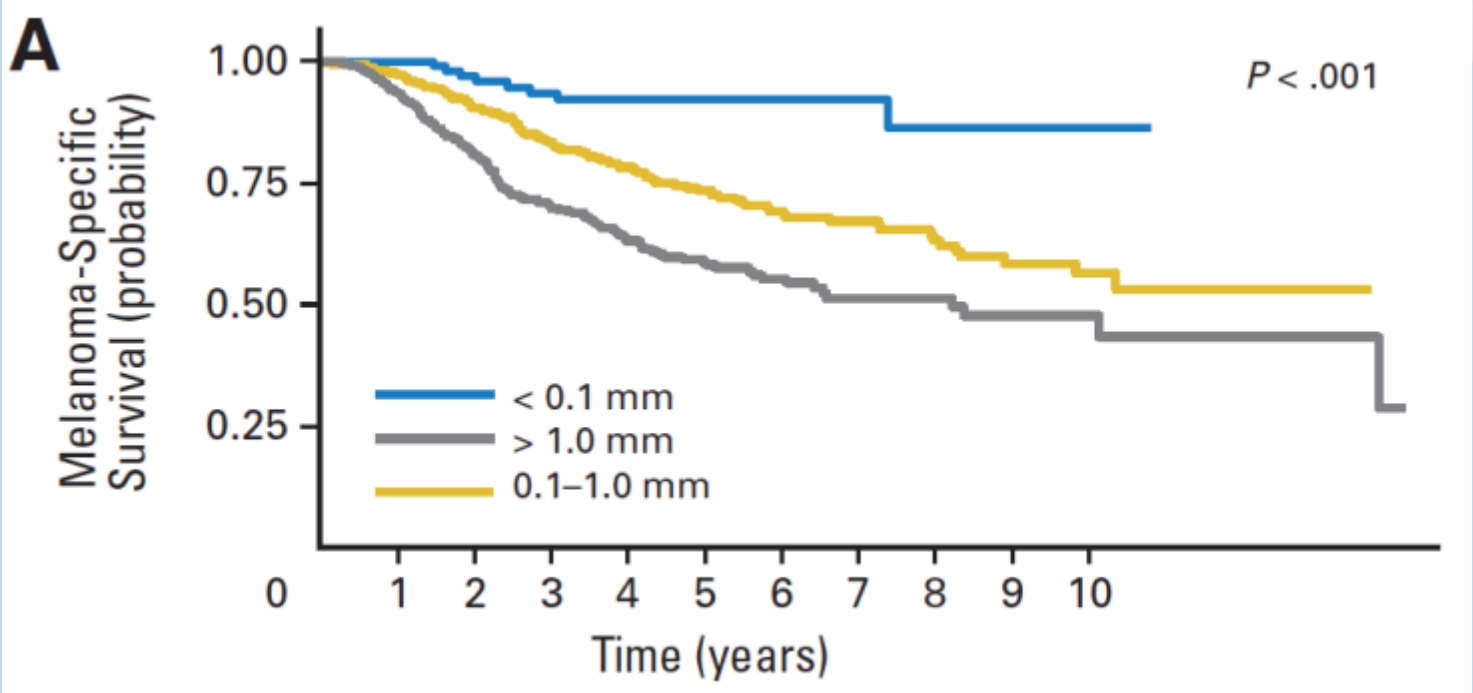

van der Ploeg, et al – J Clin Oncol, 2011

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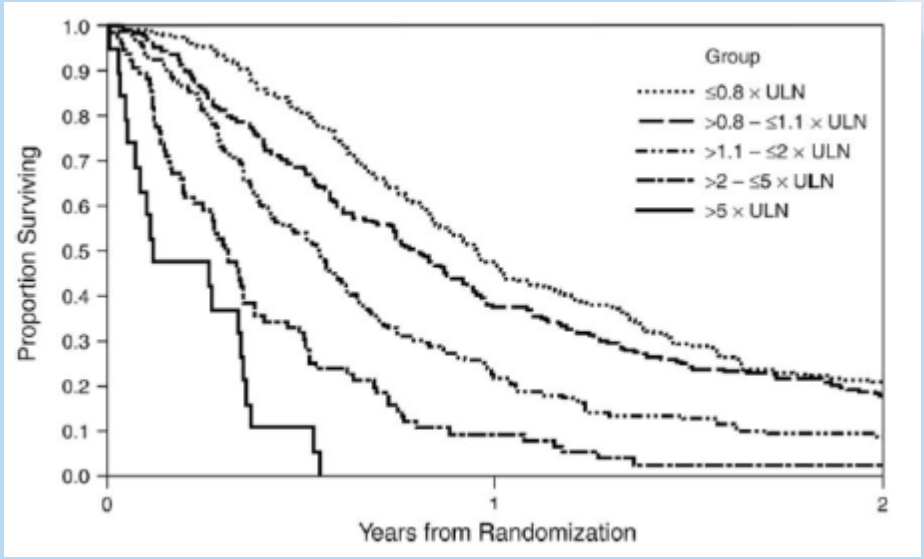
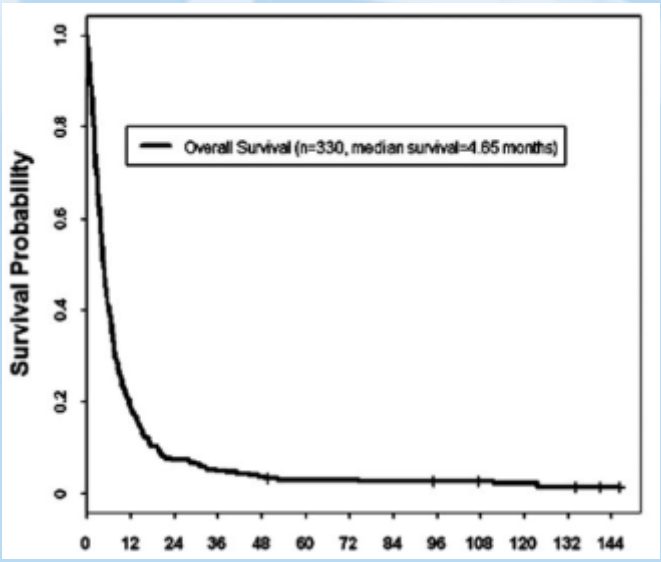


Agarwala et al – Eur J Cancer, 2009



Davies et al – Cancer, 2011

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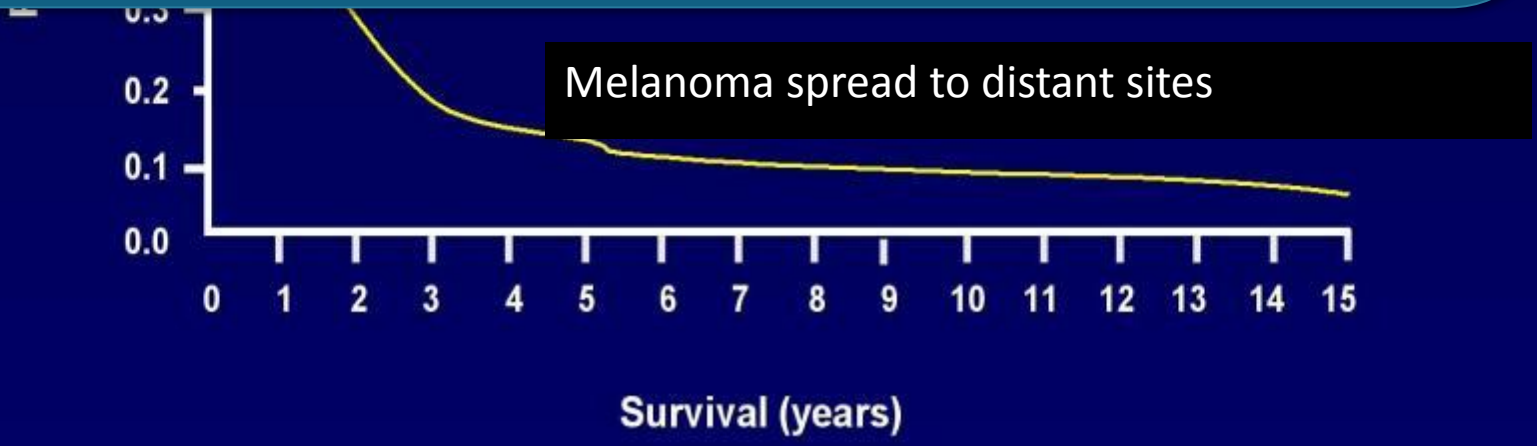
Fifteen-Year Survival of Patients in AJCC Melanoma Staging Database

"The Melbourne Melanoma Project has contributed data from *1409* participants to revision of the staging system (8th edition)"



Journal of Clinical Oncology, Vol 19, No 16 (August 15), 2001: pp 3635-3648

"The 8th edition of the AJCC staging system- what we have provided"

Stage	Patients
IA	308
IB	411
IIA	227
IIB	152
IIC	62
IIIA	104
IIIB	82
IIIC	62

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- 22.7% have ulceration
- 2.8% have microsatellites
- 2.7% have intransit disease
- 72.2% have mitoses
- 10.9% had a positive SLNB
- 30% had a negative SLNB
- 58% are male

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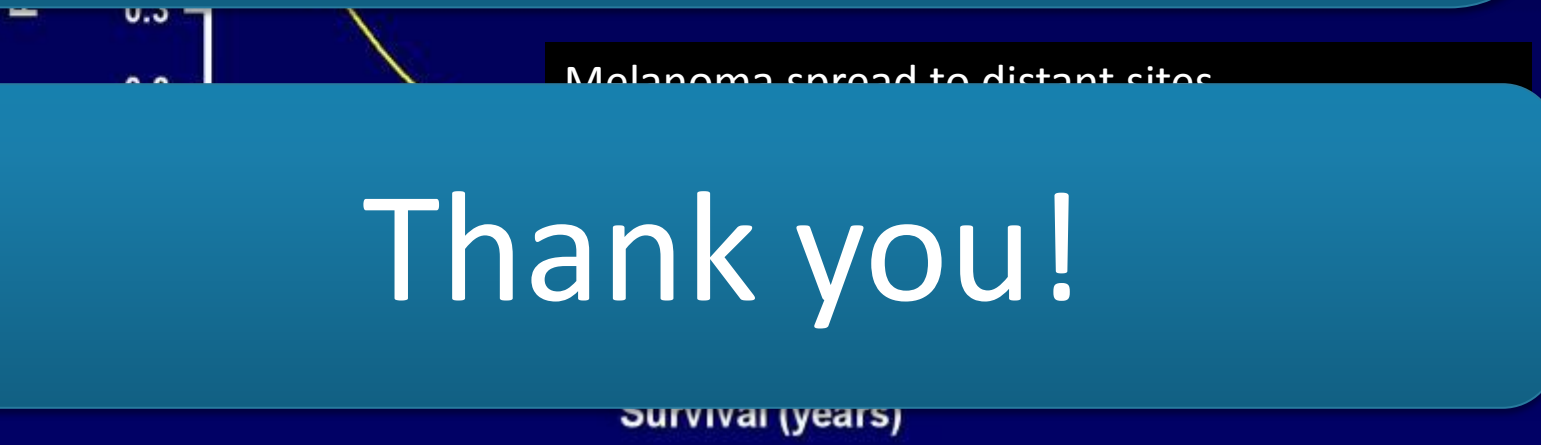

Thank you!

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