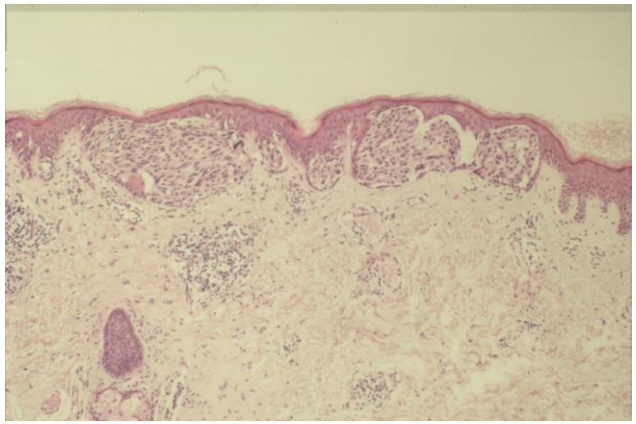
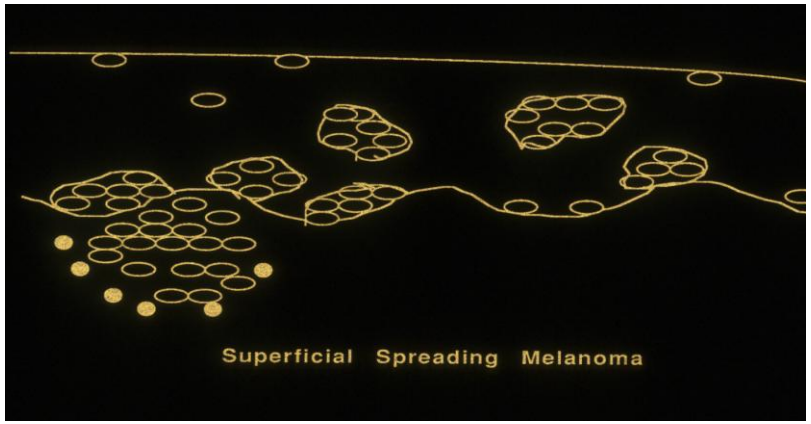
Determinants of outcome from melanoma

- The determinants of survival for melanoma
- Key clinical outcomes analyses for melanoma?
- What will we do with the data?
- The new proposed National Cancer Dataset, with site specific defined data items
- Making sure that staging is accurate

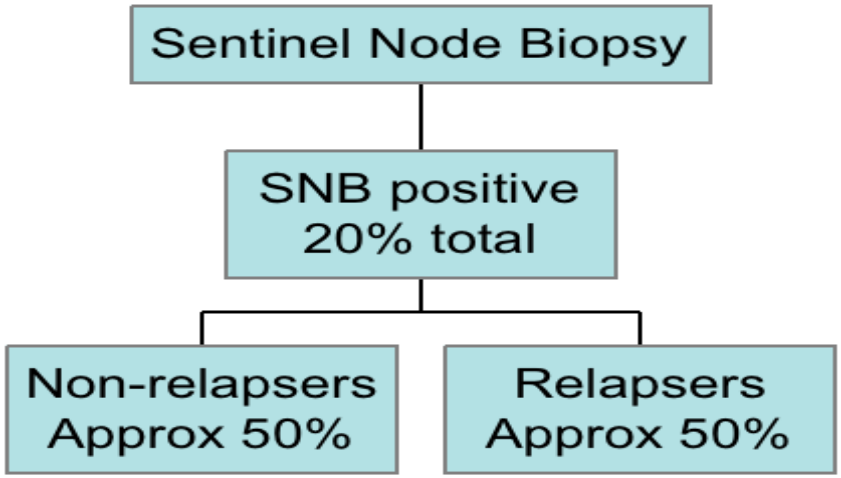
The determinants of survival for melanoma: pathology crucial

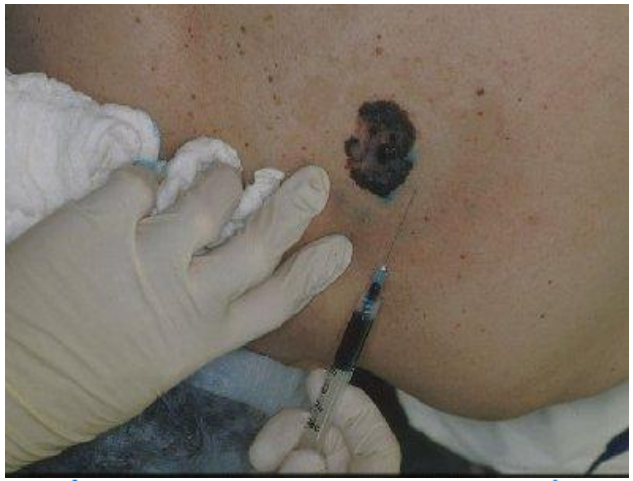




- Histopathological characteristics of the primary eg ulceration, mitotic rate
- Mirror of genetic changes

SNB





- Sentinel node biopsy is a good prognostic test for melanoma
- What does a positive sentinel node biopsy tell us?
  - Good prognostic indicator
  - No established effect on survival

Survival by AJCC stage basic requirement

Sub-stage		AJCC 10 year survival (Balch et al., 2001)	SEER 10 year survival in % (Gimotty et al., 2005a)
IA	≤1	87.9 +/- 1.0	97.4
IB	≤1 with ulceration	83.1 +/- 1.5	90.2
	1.01-2.0 no ulceration	79.2 +/-1.1	84.1
IIA	1.01-2.0 with ulceration	64.4 +/- 2.2	65.2
	2.01-4.0 no ulceration	63.8 +/- 1.7	67.3
IIB	2.01-4.0 with ulceration	50.8 +/- 1.7	62.1
	>4 no ulceration	53.9 +/- 3.3	56.3
IIC	>4 with ulceration	32.3 +/- 2.1	47.5
IIIA	1 node	62.0 +/-4.4	
	2-3 nodes	56.9 +/- 6.8	
IIIB	Micromets and ulcerated primary	37.8 +/- 4.8	
	1 node	35.9 +/- 7.2	49.7
	2-3 nodes	47.7 +/- 5.8	43.6
	Satellites no nodes	39.2 +/- 5.8	59.2
IIIC	1 node and ulcerated primary	24.4 +/- 5.3	36.6
	2-3 nodes and ulcerated primary	15.0 +/- 3.9	32.9
	≥4 nodes	18.4 +/- 2.5	22.4
IV	Overall		14.1
	Skin and SC	15.7 +/- 2.9	
	Lung	2.5 +/- 1.5	
	Other visceral or any organ with raised LDH	6.0 +/- 0.9	

Usi

New AJCC Nov 2009

- T1 $\leq$ 1.00 mm thickness
  - a: Without ulceration and mitosis 1/mm2
  - B. With ulceration or mitoses 1/mm2

- Stage IA
  - T1a N0 M0 IA T1a N0 M0
- Stage IB
  - T1b N0 M0 IB T1b N0 M0
  - T2a N0 M0 T2a N0 M0

Minimal data

- Thickness
- Ulceration
- Mitotic rate
- Nodal status
- Visceral involvement
- LDH x2

Leeds Cohort Study: Determinants of relapse free and overall survival in 822 patients recruited at least 2 years (median 4.7 years)

Parameter	HR (95% CI) for RFS	HR (95% CI) for OS
Age: per year	1.01 (0.99, 1.02)	**1.04 (1.02, 1.06)**
Gender: male vs female	**1.66 (1.10, 2.49)**	1.01 (0.68, 1.56)
Site: head and neck vs trunk	0.69 (0.39, 1.24)	0.59 (0.34, 1.05)
Site: limbs vs trunk	0.77 (0.49, 1.22)	**0.61 (0.38, 0.98)**
Site: others vs trunk	0.87 (0.44, 1.73)	**0.46 (0.22, 0.97)**
Breslow thickness: per mm	**1.32 (1.23, 1.41)**	**1.28 (1.21, 1.35)**

Determinants of survival

- Breslow thickness
- Ulceration
- Mitotic rate
- Site
- Sex
- Age
- SNB positivity
- Biomarkers

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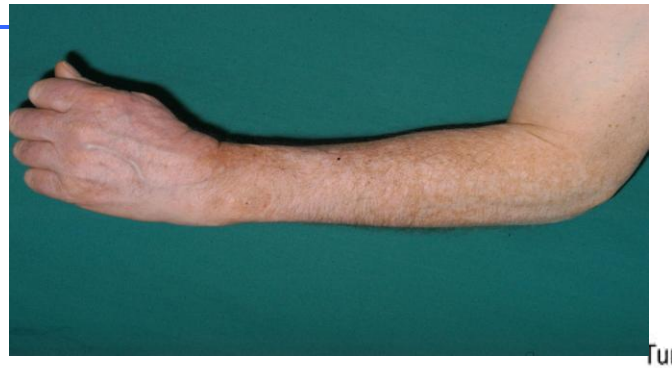
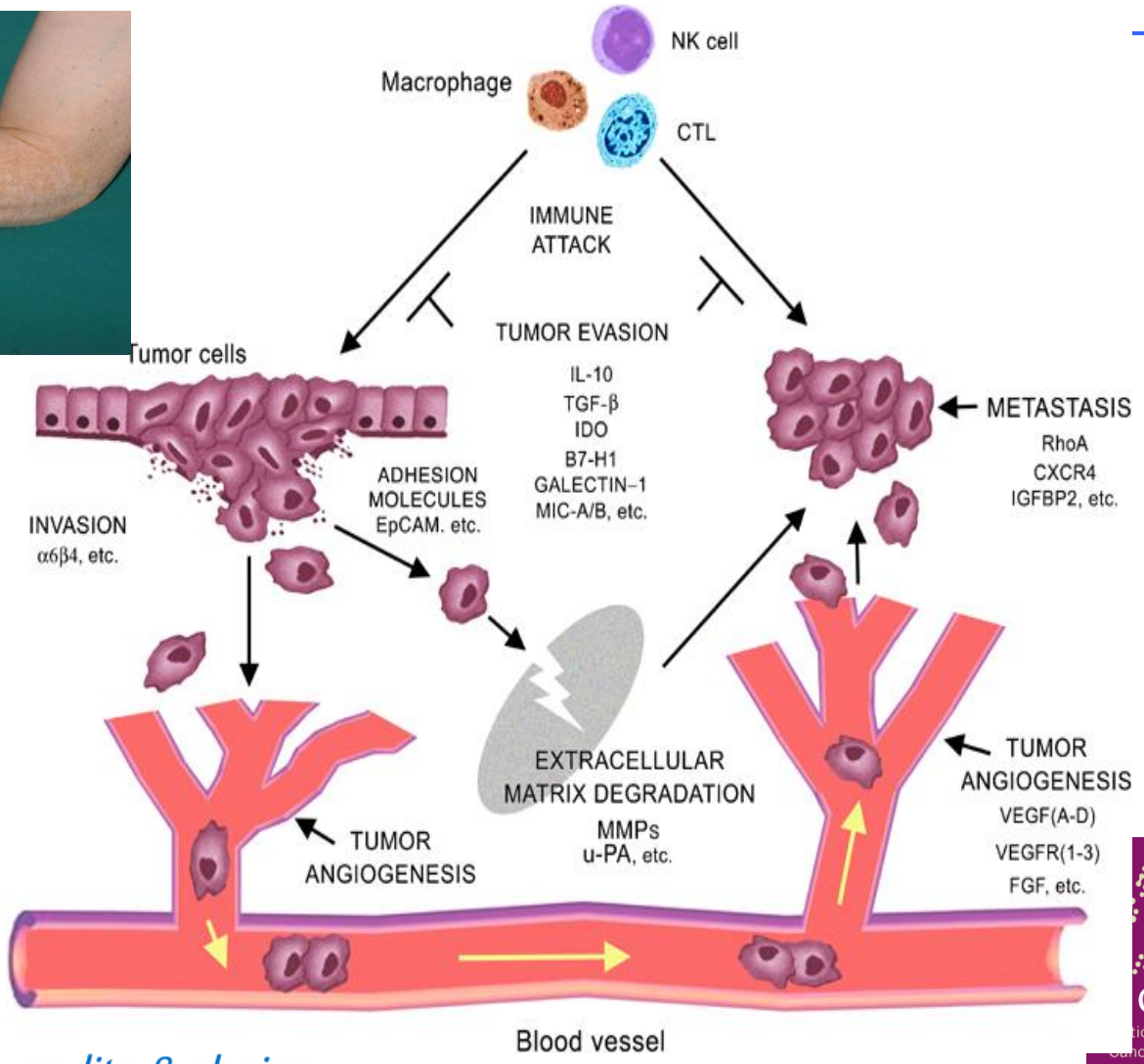
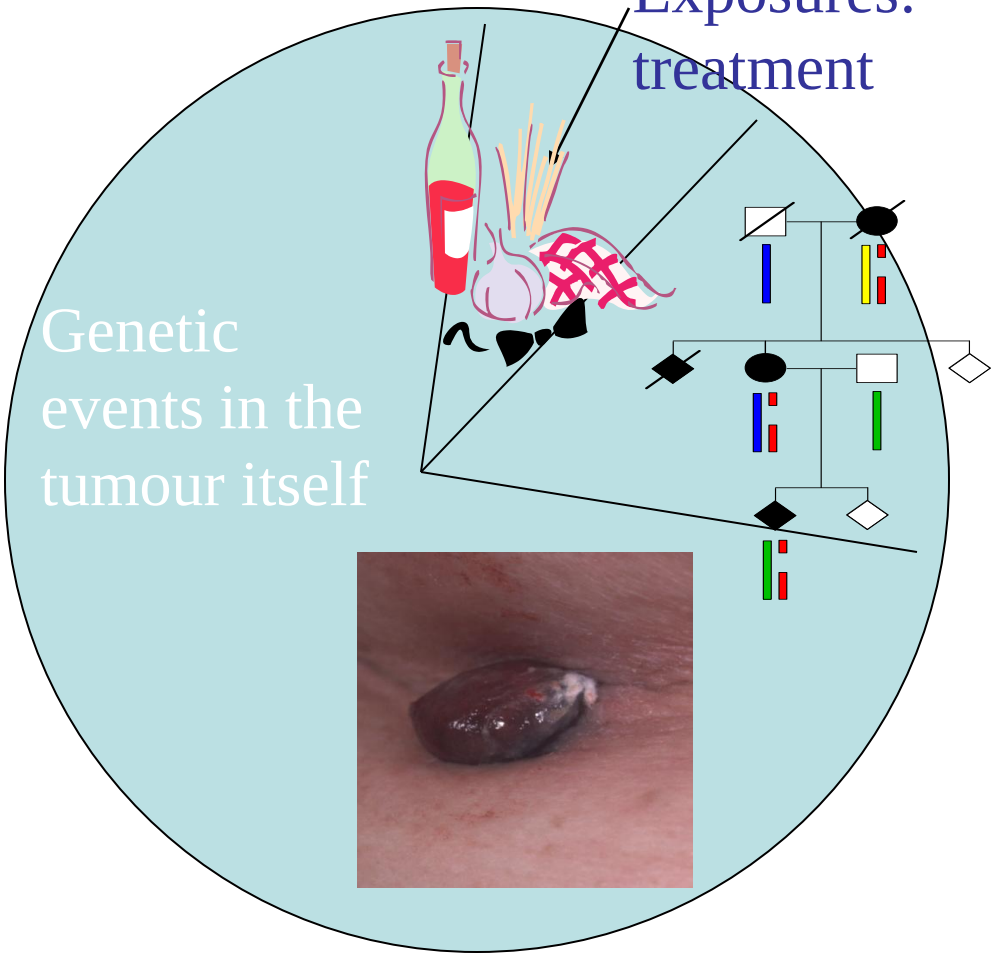
Host/ tumour interaction





Pai et al Gene Therapy 2006

Survival from melanoma:hypothesis

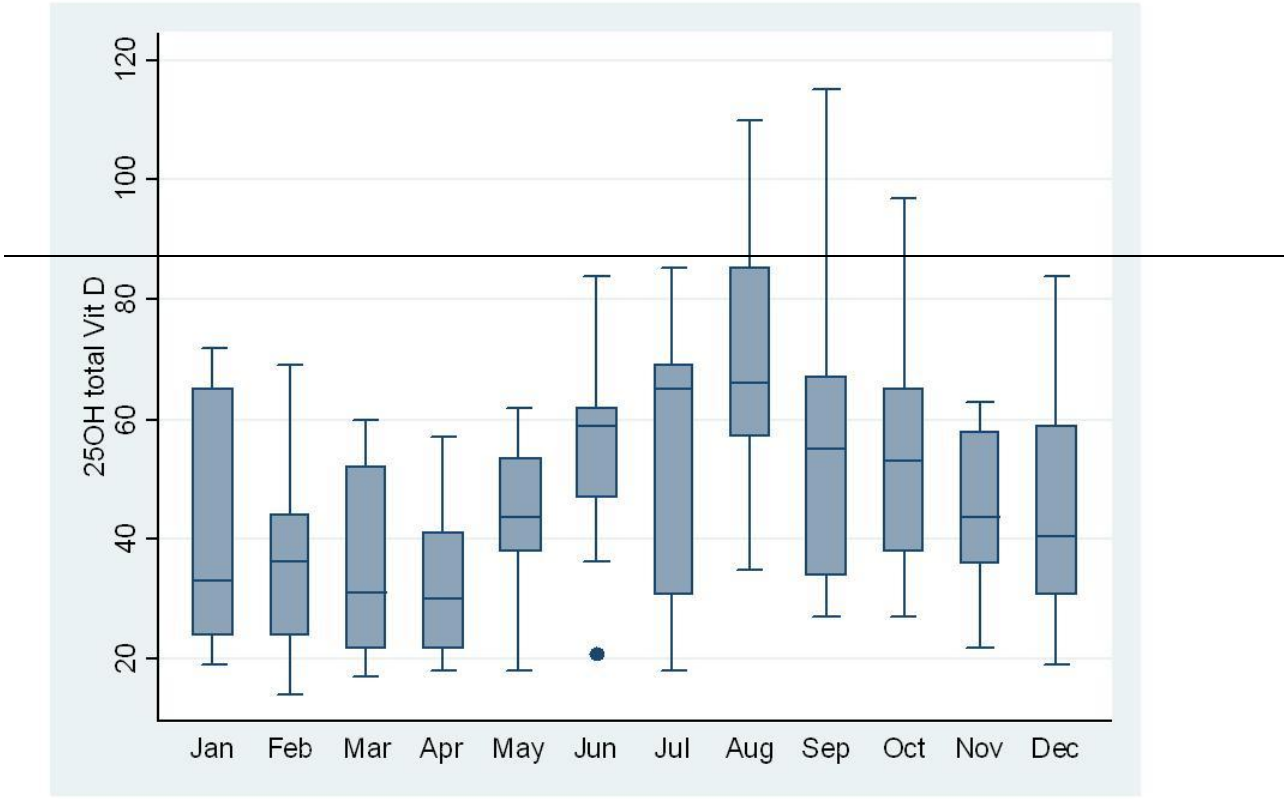


Host factors

- such as site
- sex
- deprivation
- age
- hereditary variation in immune response genes or genes governing angiogenesis

Environmental factors and relapse

Variation in serum vitamin D measures by month: late relapsing study



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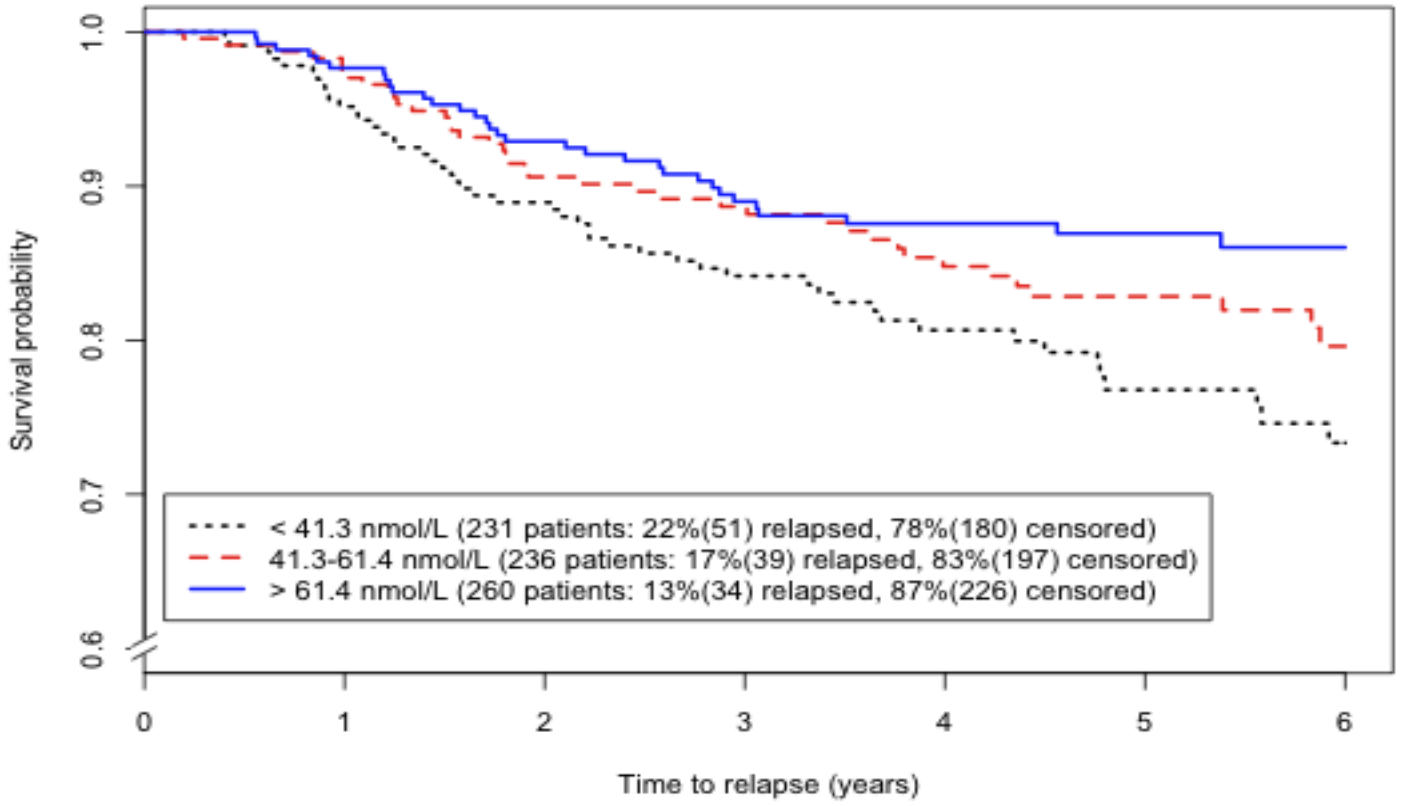
Newton-Bishop et al, JCO 2009

Thinner tumors were associated with higher vitamin D levels at diagnosis

Breslow thickness	N	Crude mean (95% CI)	Adjusted mean (95% CI)
< 0.75 mm	152	57.2 (53.5, 61.0)	55.8 (52.5, 59.0)
0.75 – 1 mm	259	54.1 (51.3, 56.9)	54.9 (52.0, 57.8)
1 – 2 mm	381	52.4 (50.2, 54.5)	53.7 (51.3, 56.2)
2 – 3 mm	156	50.8 (47.1, 54.4)	51.6 (47.8, 55.4)
> 3mm	182	49.6 (46.3, 52.9)	48.5 (44.8, 52.2)

Adjusted for age, sex, BMI, month blood taken using a general linear model.
P-value for trend was 0.002

Kaplan Meier survival curves showed furthermore that higher vitamin D levels at diagnosis were associated with better survival



Determinants of relapse free and overall survival in 872 patients recruited at least 2 years (median 4.7 years) showed that vitamin D levels were independently predictive of outcome (multivariable analysis)

Parameter	HR (95% CI) for RFS	HR (95% CI) for OS
Age: per year	**1.01 (1.00, 1.03)**	**1.04 (1.02, 1.05)**
Gender: male vs female	**1.69 (1.10, 2.61)**	1.27 (0.81, 2.00)
Townsend score: per quartile increase	1.06 (0.89, 1.26)	1.11 (0.92, 1.33)
Site: head and neck vs trunk	0.90 (0.50, 1.62)	0.85 (0.47, 1.53)
Site: limbs vs trunk	0.92 (0.56, 1.51)	0.72 (0.43, 1.20)
Site: others vs trunk	1.10 (0.52, 2.32)	0.43 (0.18, 1.04)
Breslow thickness: per mm	**1.35 (1.236 1.44)**	**1.29 (1.21, 1.38)**
BMI: 24.9-29.9 vs <24.9	0.63 (0.39, 1.03)	0.82 (0.50, 1.33)
BMI: >29.9 vs 24.9	1.21 (0.75, 1.96)	1.18 (0.71, 1.96)
Vitamin D level (per 20 nmol/L increase)		
January to March	**0.72 (0.56, 0.96)**	**0.72 (0.54, 0.96)**
April to June	0.85 (0.67, 1.08)	0.80 (0.62, 1.06)
July to September	**0.77 (0.63, 0.96)**	0.85 (0.70, 1.04)
October to December	**0.77 (0.60, 0.98)**	0.82 (0.64, 1.04)

Determinants of survival

- Breslow thickness
- Ulceration
- Mitotic rate
- Site
- Sex
- Age
- SNB positivity

AJCC stage

Vitamin D

Other things

BMI

Deprivation index

Biomarkers

Key clinical outcomes analyses for melanoma

NCIN national cancer intelligence network

- Stage at diagnosis
- Cancer treatment times
- Adequacy of surgery
- Proportion offered/participated in clinic trials
- Proportion treated with first line/second line chemo
- Relapse free survival
- Overall survival

So how useful are the data we have now?

- And are the data we have now open to mis-interpretation?

3 year relative survival for males with melanoma 1999-2003

- Merseyside and Cheshire
  - 82.7% (95% CI 78.0, 87.4)
- Yorkshire
  - 93.7% (95% CI 90.7, 96.7)
- Humber and Yorkshire Coast
  - 83.9% (95% CI 77.2, 90.7)

What will be done with the data?

- Track changes over time in incidence, stage at diagnosis and outcome
- Understand the differences in determinants of outcome between networks
- Identify changes which will result in improved outcome for all networks
- Commissioners will use the data

NCIN national cancer intelligence network

The new proposed National Cancer Dataset, with site specific defined data items

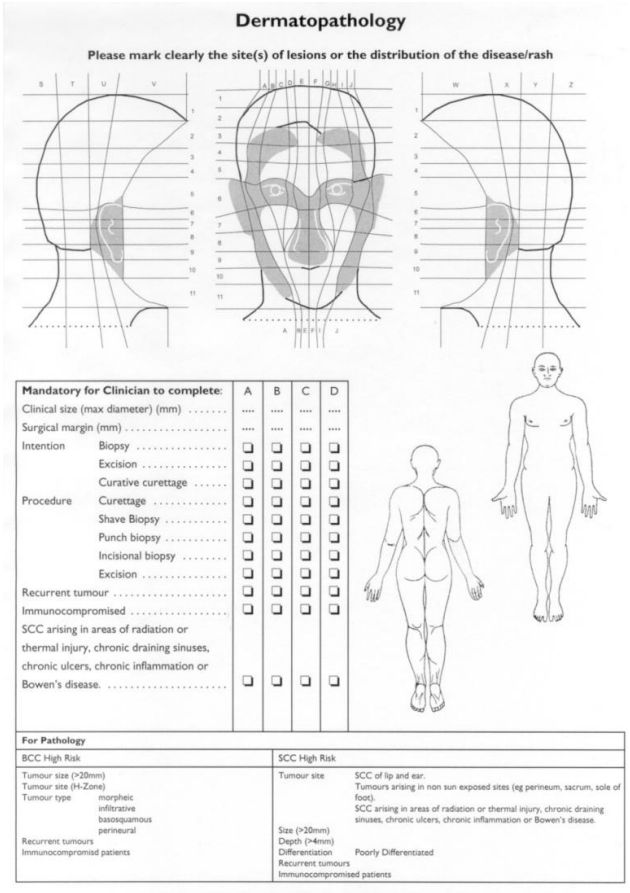
NCRI National Cancer Research Institute

Melanoma Data Set

- Data which are important but will be collected anyway as part of the common data set
  - Age at diagnosis
  - Sex
  - Postcode derived deprivation measure
  - BMI
- Data which could be entered on a stylized pathology request form (as developed in prototype form by the Leeds group)
  - Tumour site trunk/limb
  - Immunosuppressed yes/no
  - Clinical diameter of the tumour

Stylised dermatopathology request form

NCIN national cancer intelligence network



Dermatopathology

Please mark clearly the site(s) of lesions or the distribution of the disease/rash

Mandatory for Clinician to complete:		A	B	C	D
Clinical size (max diameter) (mm)		....	....	....	....
Surgical margin (mm)		....	....	....	....
Intention	Biopsy	❑	❑	❑	❑
	Excision	❑	❑	❑	❑
	Curative curettage	❑	❑	❑	❑
Procedure	Curettage	❑	❑	❑	❑
	Shave Biopsy	❑	❑	❑	❑
	Punch biopsy	❑	❑	❑	❑
	Incisional biopsy	❑	❑	❑	❑
	Excision	❑	❑	❑	❑
Recurrent tumour		❑	❑	❑	❑
Immunocompromised		❑	❑	❑	❑
SCC arising in areas of radiation or thermal injury, chronic draining sinuses, chronic ulcers, chronic inflammation or Bowen's disease.		❑	❑	❑	❑

For Pathology			
BCC High Risk		SCC High Risk	
Tumour size (>20mm)		Tumour site	SCC of lip and ear. Tumours arising in non sun exposed sites (eg perineum, sacrum, sole of foot). SCC arising in areas of radiation or thermal injury, chronic draining sinuses, chronic ulcers, chronic inflammation or Bowen's disease.
Tumour site (H-Zone)		Size (>20mm)	
Tumour type	morpheic infiltrative basosquamous perineural	Depth (>4mm)	
Recurrent tumours		Differentiation	Poorly Differentiated
Immunocompromisd patients		Recurrent tumours	
		Immunocompromised patients	

Using information to improve quality & choice

NCRI National Cancer Research Institute

Pathology reports

- Tick box data fields
  - Growth phase
    - In situ
    - Radial
    - Vertical
  - Breslow thickness in mm
  - Mitotic rate in mm^2
  - etc

Data to be collected by the MDT at entrance to the service

- Sentinel node biopsy status
  - Positive
  - Negative
  - Not done
- Final margin of excision (after wide local excision)
- WHO performance status
- Height
- Weight
- AJCC stage at diagnosis
- Offered adjuvant clinical trial?
  - Yes
    - Name
    - Accepted
  - No

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- Date last known to be alive
- Date of death
- Cause of death

- Treatment details for stage IV melanoma

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Summary

- Important that we ensure that appropriate data collection occurs
- Crucial that we ensure that we collect data which might influence outcome
  - Site, age, etc
- Must be feasible

Data collection

- Use data already available
- Collect crucial data only
- Build into MDTs
- Use electronic short cuts: pathology data fields