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Epworth Dermatology

Epworth HealthCare

Recent advances in Melanoma and Non Melanoma Skin Cancer

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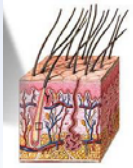

Research

Non-melanoma skin cancer in Australia

Abstract

Objectives: To report the burden and cost of non-melanoma skin cancer (NMSC) treatments in Australia and to project estimates of numbers and costs to 2015.

Design and setting: Retrospective study of data obtained from Medicare Australia for NMSC treated by excision, curettage, laser or cryotherapy between 1 January 1997 and 31 December 2010, by year, sex, age group and state or territory.

Main outcome measures: Total number, total Medicare Benefits Schedule (MBS) benefit and total cost in Australian dollars of NMSC treatments.

Results: The total number of NMSC treatments increased from 412 493 in 1997 to 767 347 in 2010, and we estimated that the number of treatments would increase to 938 991 (95% CI, 901 047–976 934) by 2015. The total MBS benefit for NMSC treatments in 2010 was $93.5 million, and we estimated that this will increase to $109.8 million (95% CI, $105.9–$113.7 million) by 2015, whereas the total cost with inflation (ie, cost which includes diagnosis, treatment and pathology) was $511.0 million in 2010, estimated to increase to $703.0 million (95% CI, $674.6–$731.4 million) by 2015.

Conclusion: NMSC treatments increased by 86% between 1997 and 2010. We anticipate that the number and the total cost without inflation of NMSC treatments will increase by a further 22% between 2010 and 2015. NMSC will remain the most costly cancer and place an increasing burden on the Australian health care system.

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Research

1 Total number of services, total MBS benefit and total cost of non-melanoma skin cancer treatment in Australia, 1997–2015

Year	Total no. of services (95% CI)	Population*	Age-standardised rate of services,† per 100 000 (95% CI)	Total MBS benefit, $millions (95% CI)	Total cost‡ without inflation, $millions in 2001 (95% CI)	Total cost‡ with health inflation, $millions (95% CI)
1997	412 493	18 514 747	2338 (2311–2366)	42.5	–	–
1998	443 701	18 708 571	2458 (2430–2486)	42.1	–	–
1999	452 914	18 923 236	2449 (2421–2477)	44.0	–	–
2000	467 669	19 153 840	2489 (2461–2517)	46.1	–	–
2001	510 590	19 413 240	2630 (2601–2659)	51.0	264.0	264.0
2002	544 028	19 662 781	2733 (2703–2762)	55.2	281.3	290.3
2003	591 179	19 895 435	[illegible]	61.1	305.7	325.2
2004	617 546	20 127 363	[illegible]	65.5	319.3	350.0
2005	635 959	20 328 609	[illegible]	69.6	328.8	370.9
2006	649 476	20 697 880	[illegible]	72.1	335.8	389.5
2007	667 647	21 015 042	[illegible]	75.8	345.2	411.5
2008	693 022	21 431 781	3020 (2990–3050)	80.7	368.3	438.6
2009	724 520	21 864 256	3076 (3046–3106)	86.1	393.5	470.5
2010	767 347	21 991 031	3174 (3143–3205)	93.5	426.9	511.0
2011	801 988 (776 814–827 162)	22 339 066	3271 (3240–3303)	93.6 (90.9–96.3)	[illegible]	547.4 (530.2–564.5)
2012	835 270 (807 079–863 461)	22 647 464	3334 (3303–3366)	976 (94.6–100.6)	[illegible]	583.9 (564.2–603.6)
2013	866 194 (837 864–900 524)	22 976 367	3398 (3366–3429)	101.7 (98.4–105.0)	449.4 (433.2–[illegible])	622.0 (599.6–644.4)
2014	903 766 (868 183–938 350)	23 305 898	3461 (3429–3493)	1057 (1023–1093)	467.3 (449.4–485.2)	661.7 (636.4–687.0)
2015	938 991 (901 047–976 934)	23 636 109	3524 (3492–3556)	109.8 (105.9–113.7)	485.5 (465.9–505.1)	703.0 (674.6–731.4)

MBS = Medicare Benefits Schedule. * Data from the Australian Bureau of Statistics,[3] using Series B projections. † Age-standardised to the 2001 Australian standard population. ‡ Total cost is based on the Australian Institute of Health and Welfare report from 2001, and estimates before 2001 are not available.[1]

86.5% increase

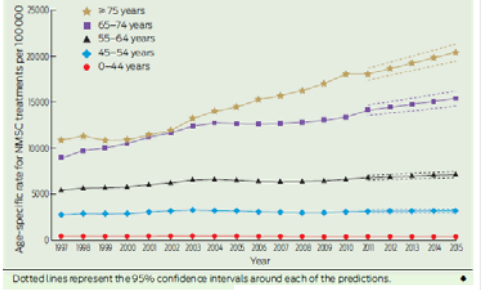
120% increase

37.5% increase

Research

Non-melanoma skin cancer in Australia

3 Age-specific rate for non-melanoma skin cancer (NMSC) treatments, 1997–2015



Dotted lines represent the 95% confidence intervals around each of the predictions.

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To ascertain incidence of NMSC

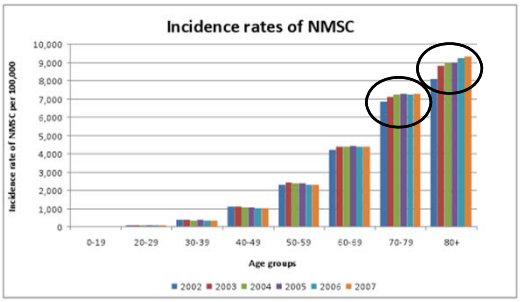
- **De identified patient specific data obtained directly from Commonwealth Department of Health and Ageing, Medicare Australia and Department of Veterans Affairs**

Incidence rates per 100,000

- Total Population

Persons	2002	2003	2004	2005	2006	2007
1(0-19)	8.3	7.9	8.1	8.0	7.1	6.2
2(20-29)	82.1	84.9	79.5	81.8	68.7	64.4
3(30-39)	369.3	371.6	361.2	371.9	348.6	341.5
4(40-49)	1,101.1	1,125.6	1,075.0	1,079.7	1,026.1	1,016.2
5(50-59)	2,308.0	2,414.9	2,394.0	2,381.3	2,302.7	2,285.4
6(60-69)	4,196.7	4,389.6	4,404.0	4,429.0	4,373.6	4,367.5
7(70-79)	6,833.4	7,124.1	7,224.2	7,266.9	7,225.4	7,264.6
8(80+)	8,080.3	8,827.4	8,974.4	8,981.1	9,248.3	9,310.1
Cases	295,572	316,280	323,003	333,696	334,488	343,667
ASR	980.2	1,023.0	1,018.5	1,022.7	1,001.4	998.1
Lower 95% CI	976.7	1,019.5	1,015.0	1,019.2	998.0	994.8
Upper 95% CI	983.7	1,026.6	1,022.1	1,026.1	1,004.8	1,001.5

Incidence rate 2002-2007



Ratio of BCC to SCC

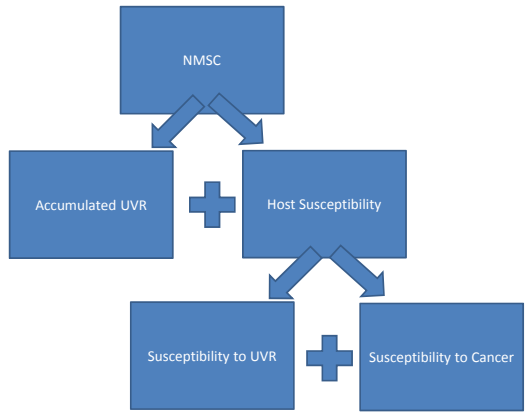
Analysis of 860, 697 consecutive lesions from 3 separate laboratories

	BCC	SCC	KA
2001	118231	57519	7081
2002	131405	56801	7456
2004	100124	41240	2352
2007	100133	44015	3391
2010	155477	64605	3710

SCC in situ excluded from analysis

New NMSC Statistics

- Number of NMSC increased by 87% in 14 years (population growth over that time was 22%).
- Prevalence of NMSC increased by 200% in those aged 65 years and older (while their population grew 60%)
- NMSC accounts for 7 out of every 8 new cancers diagnosed in Australia (87.5%)
- NMSC is rising at 2.5 times the rate of all other cancers combined
- Australia with 22.6 million people estimated to have 11,200 melanoma and 950,000 NMSC in 2012



Risk of subsequent cancer

- We performed a national record-linkage study using English Hospital Episode Statistics from 1999 to 2011 to determine the risk of other primary malignancies in a cohort of people with NMSC compared with a control cohort
- cohort of 502,503 NMSC cases
- the relative risk (RR) for all cancers excluding subsequent NMSC was 1.30 (95% CI 1.29-1.31).
- the relative risk for all cancers excluding all skin cancers was 1.21 (95% CI 1.20-1.22)

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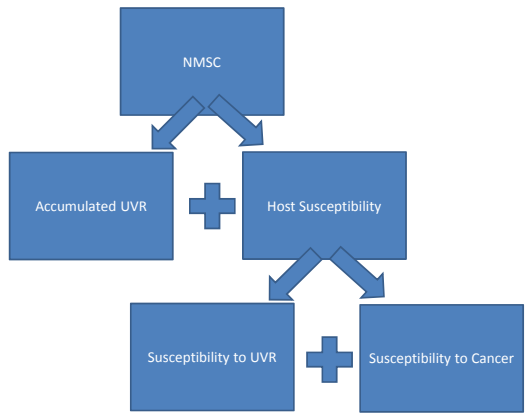
Heart Foundation

Position Statement on lipid management - 2005 National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand

- Relative risk of AMI associated with a cholesterol of 9 with no other risk factors is 1.12 for a man ≥ 55yo man and 1.05 for a woman ≥ 55yo

Risk of subsequent cancer

Site (ICD-10 code)	NMSC before other cancer			Other cancer before NMSC		
	Observed (O)	Expected (E)	RR (95% CI)	Observed (O)	Expected (E)	O/E (95%
Any Malignant primary cancer* excluding nmsc* (C00-C97)	641265498	48733.146525.3	1.307 (1.3629-	375653812	306472648.9	1.330 (1.3
Any Malignant primary cancer* excluding all skin* (C00-C44, C47-C97)	6175254316	483824.645831.6	1.32 21 (1.3120-	3340931262	2920528106.7	1.20 15 (1.
Bladder (C67)	4684	4276.1	1.11 (1.08-1.15)	4837	4736.7	1.02 (0.99
Bone (C40-C41)	509	204.2	2.91 (2.63-3.21)	252	63.8	3.96 (3.49
Brain (C71)	697	609.6	1.16 (1.07-1.25)	107	122.7	0.87 (0.71
Breast (C50)	5337	4568.9	1.19 (1.15-1.22)	4870	4214.4	1.16 (1.13
Cervix (C53)	162	175.5	0.92 (0.78-1.08)	129	136.7	0.94 (0.79
Colon (C18-C19)	6268	5636.3	1.13 (1.10-1.16)	3443	3563.5	0.96 (0.93
GI - upper (C00-C06.8, C09-C10, C12-C14)	1720	847.6	2.26 (2.15-2.39)	1627	459.2	3.59 (3.41
Kidney (C64-C66)	1624	1442.8	1.14 (1.09-1.21)	673	627.1	1.07 (0.99
Larynx (C32)	573	455.9	1.30 (1.19-1.42)	476	324.4	1.47 (1.34)
Leukaemia - lymphoid (C91)	1851	1213.2	1.64 (1.56-1.73)	916	269.2	3.43 (3.21
Leukaemia - myeloid (C92)	992	847.8	1.20 (1.12-1.28)	256	179.5	1.43 (1.26
Liver (C22)	913	857.1	1.07 (1.00-1.15)	90	110.1	0.82 (0.66
Lung (C33-C34)	9496	7643.1	1.28 (1.26-1.31)	1124	1406	0.80 (0.75
Lymphoma - Hodgkins (C81)	266	172.7	1.60 (1.41-1.82)	140	86.5	1.62 (1.36
Lymphoma - non-Hodgkins (C82-C85)	3118	2153.3	1.53 (1.47-1.59)	2147	1055	2.04 (1.92
Melanoma - malignant (C43)	5760	1525.3	5.54 (5.36-5.73)	4908	796.6	6.44 (6.2
Meningeal - benign (D32-D33)	662	665.7	0.99 (0.92-1.08)	359	315	1.14 (1.03
Multiple Myeloma (C90)	1028	1004.5	1.03 (0.96-1.10)	504	397.4	1.27 (1.16
Nasopharynx (C11)	89	63.8	1.44 (1.14-1.80)	77	21.6	3.57 (2.83
Nervous system - other (C70)	56	31.4	1.95 (1.44-2.61)	17	9.2	1.86 (1.08
Oesophageal (C15)	1965	1826.5	1.09 (1.04-1.14)	443	538.9	0.82 (0.75
Ovary (C56)	769	736.6	1.05 (0.97-1.13)	298	358.8	0.83 (0.74
Pancreas (C25)	1663	1634.6	1.02 (0.97-1.07)	94	209.8	0.45 (0.36
Prostate (C61)	10117	10033.2	1.01 (0.99-1.03)	5066	4904.8	1.04 (1.01
Rectum (C20-C21)	3076	2292.2	1.40 (1.35-1.46)	1997	1688	1.19 (1.13
Salivary gland (C07-C08)	783	211.2	5.88 (5.34-6.46)	281	68.4	4.12 (3.63
Stomach (C16)	1953	1840.2	1.07 (1.02-1.12)	391	602.9	0.65 (0.58
Testis (C62)	61	49.3	1.25 (0.95-1.61)	61	60.2	1.01 (0.77
Thyroid (C73)	186	157.9	1.19 (1.02-1.39)	171	134.6	1.27 (1.0
Uterus - body of (C54)	714	684.2	1.05 (0.97-1.13)	714	682.5	1.05 (0.97



Risk of subsequent cancer

- Cancer susceptibility was much higher in younger than older people.

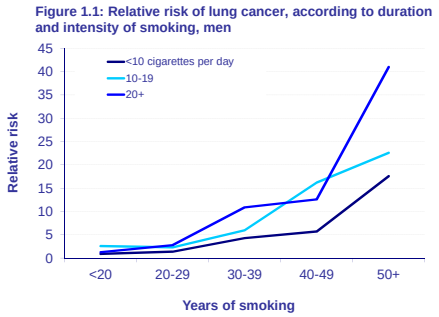
Age	RR
<25	22.99
25-44	3.55
45-59	1.75
60+	1.25

(all p<0.001).

Risk of subsequent cancer in people treated for NMSC <25 yo

		Ages 0-24		
Site (ICD-10 code)		Observed (O)	Expected (E)	RR (95% CI)
Malignant primary cancer excluding nmsc*		75	3.3	22.99 (18.05-28.88)
Malignant primary cancer excluding all skin†		42	3.0	14.07 (10.13-19.06)
Bone (C40-C41)		9	0.1	72.88 (32.90-140.81)
Brain (C71)		6	0.3	18.82 (6.88-41.20)
Leukaemia – lymphoid (C91)		5	0.2	23.55 (7.62-55.27)
Melanoma - malignant (C43)		36	0.4	98.56 (67.50-140.11)
Meninges - benign (D32-D33)		4	0.2	21.81 (5.90-56.58)

Smoking and lung cancer



Doll and Hill, BMJ 1954

Risk of subsequent cancer

Conclusions

NMSC is strongly associated with a broad spectrum of other primary cancers, particularly at certain sites and, very strikingly, in younger age-groups.

This pattern of cancer susceptibility cannot be explained by conventional risk factors, and indicates genetic rather than acquired causes.

Implications in management of patients of NMSC

- I tell my young NMSC patients that they are at increased risk of melanoma
- And increased risk of cancer in general and they need to diligently adhere to recommendations for cancer screening and stop smoking

Cancer Council Victoria

Prof Graham Giles
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Emily Karahallos

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Dr Nicholas Rufaut
Dr Niyati Sharma
Dr Marloes Fransen

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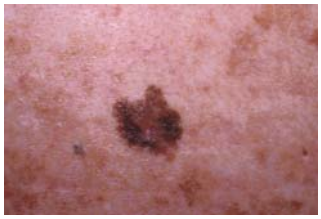
Dr Eugene Ong
Prof Michael Goldacre
Prof Raph Goldacre
Dr Uy Hoang

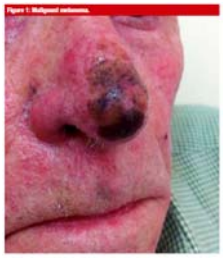
Melanoma

- In 2008 the incidence of melanoma in Australia was 11,442 and 1224 people died from melanoma.
- Survival at five years following newly diagnosed invasive melanoma (Clark's level 2-5) has increased from 85% in 1986 to 90% in 2010.



Melanoma

- In the absence of any new significant chemotherapy in that period, this improvement has been attributed to public education, early diagnosis and excision.



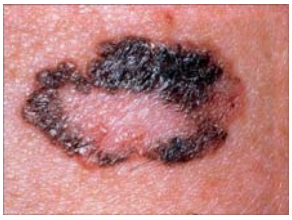
Melanoma

Scar re-excision, sentinel nodebiopsy, elective lymph node dissection, chemotherapy, radiotherapy and immunotherapy may improve survival at one year but have not been shown to improve five-year survival.

Adjuvant therapy with interferon may improve five-year survival by 10% but is associated with significant toxicity.

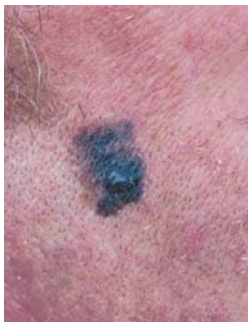
Melanoma

Macroscopic loco-regional lymph node metastasis reduces five-year survival to 50%. Distant visceral or bone metastasis (stage IV disease) has a one-year survival of about 25% and a five-year survival of less than 2.5%.



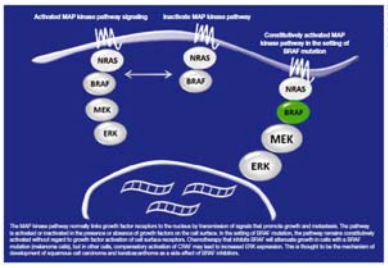
Melanoma

Following successful surgical resection of metastasis, the median disease-free time to relapse is six weeks.



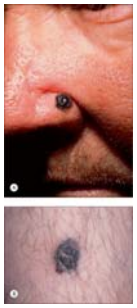
Melanoma

Functional mutations in genes in the mitogen-activated protein (MAP) kinase pathway are commonly detected in melanoma and these mutations influence growth control (figure 1).



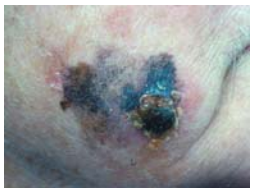
Melanoma

In 2009, these discoveries led to the development of the first new effective chemotherapy medication for metastatic disease in almost 40 years.



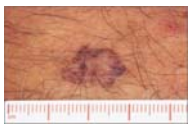
Melanoma

Several agents based on molecular understanding of this pathway have been approved for stage IV disease and additional agents are currently being evaluated in clinical trials.



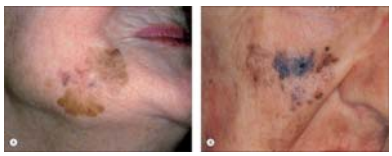
Melanoma

Various combinations of these agents are also being evaluated for stage IV disease and the BRAF inhibitor, dabrafenib, and the immune modulator ipilimumab are currently being evaluated in the US in Phase II clinical trials as adjuvant therapy for high risk primary melanoma.



Melanoma

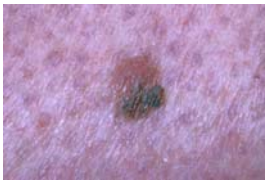
The availability of adjuvant treatment, even in a trial setting, would necessitate a review of the current management of high-risk primary melanoma, and in particular the role of sentinel node biopsy.



Sentinel node Biopsy

Sentinel node biopsy is a technique performed immediately before surgical re-excision of the scar.

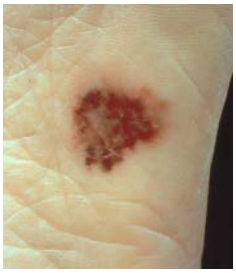
It involves lymphatic mapping by lymphoscintigraphy and intraoperative injection of radioisotope and/or blue dye to identify the lymph node immediately downstream from the primary tumour.



Sentinel node Biopsy

Histological examination of the first ('sentinel') lymph node(s) identified with this technique has been demonstrated to identify the presence or absence of metastatic
cells in the entire lymph node basin.

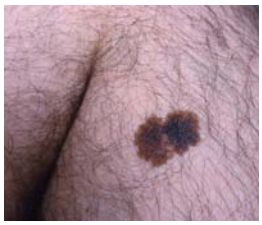
This procedure is considered the most sensitive and specific staging test for the detection of micrometastatic melanoma in regional lymph nodes.



Sentinel node Biopsy

Sentinel lymph node status is the most important prognostic factor for disease-specific survival of patients with melanoma greater than 1mm in thickness.

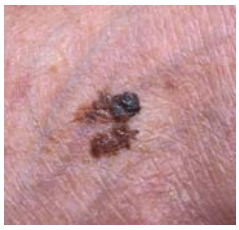
In this group, 15-20% will have micrometastasis on sentinel node biopsy.



Sentinel node Biopsy

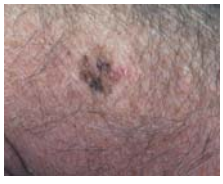
Identification of micro-metastatic disease in the sentinel lymph node is often followed by completion lymph node dissection.

While there is some evidence to suggest this procedure achieves local control, the available data do not show a survival advantage.



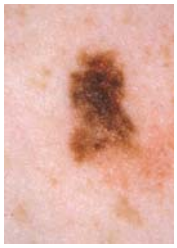
Sentinel node Biopsy

In view of this outcome and the significant potential morbidity associated with completion lymph node dissection, sentinel node biopsy has received only limited support in Australia.



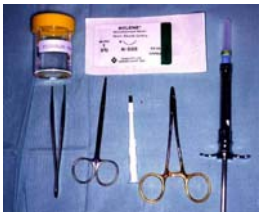
Sentinel node Biopsy

In anticipation of adjuvant chemotherapy becoming an alternative to completion lymph node dissection for patients with a micrometastasis in the sentinel node, we suggest that patients with invasive melanoma on excision biopsy are referred to a rapid-access specialist multidisciplinary clinic for clinical staging (including sentinel node biopsy where indicated) and simultaneous re-excision of the scar.



Diagnosis

- Clearly Benign
- Clearly Malignant
- Too close to call



Or

Refer to rapid access clinic

- If you are only 99% sure that the lesion is benign, a definitive diagnosis is required. Options include diagnostic biopsy, excisional biopsy or referral to a dermatologist. Access to specialists varies and patients usually find it disconcerting to wait weeks or months for a definitive diagnosis for a 'suspicious lesion'. Hence, GPs often