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Medical Research Institute

The burden of keratinocyte cancer:

Occurrence, multiplicity and predicting risk

David Whiteman, Nirmala Pandeya, Bridie Thompson, Padmini Subramaniam, Jean Claude Dusingize, Rachel Neale, Adele Green, Catherine Olsen

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Background

- Keratinocyte cancers exceedingly common
- High disease burden *(morbidity, mortality, costs)*
- Very few population-based registries
- Population-based data on incidence, multiplicity and risk are scarce

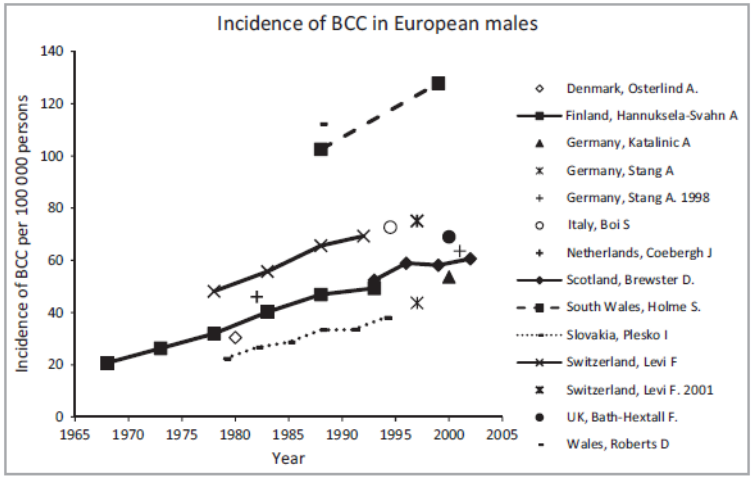
EPIDEMIOLOGY AND HEALTH SERVICES RESEARCH

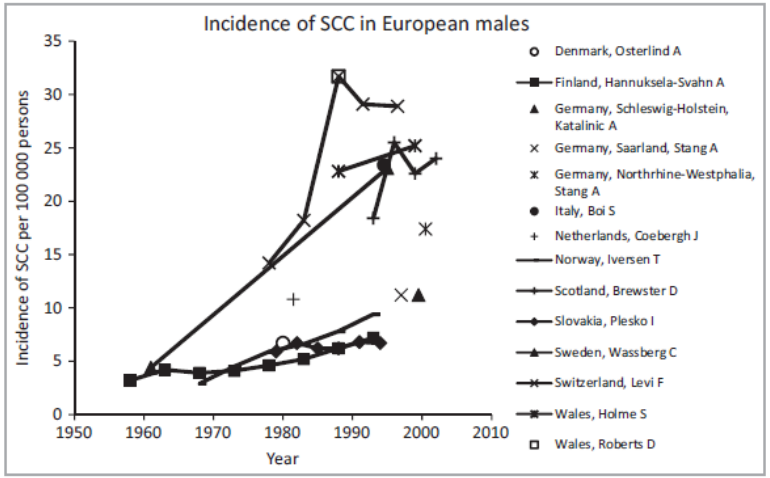
BJD
British Journal of Dermatology

A systematic review of worldwide incidence of nonmelanoma skin cancer

A. Lomas, J. Leonardi-Bee and F. Bath-Hextall*

*Epidemiology and Public Health, and *Centre for Evidence Based Dermatology, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UH, U.K.*





Background

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- High disease burden *(morbidity, mortality, costs)*
- Very few population-based registries
- Population-based data on incidence, multiplicity and risk are scarce

STUDY

Incidence Estimate of Nonmelanoma Skin Cancer in the United States, 2006

Howard W. Rogers, MD, PhD; Martin A. Weinstock, MD, PhD; Ashlynne R. Harris; Michael R. Hinckley, MD; Steven R. Feldman, MD; Alan B. Fleischer, MD; Brett M. Coldiron, MD

Table 1. Number of Procedures and of Age-Adjusted Procedures for All Skin Cancers in the Medicare Fee-for-Service Population

Year	Total Skin Cancer Procedures	Age-Adjusted Procedure Rate per 100 000 Beneficiaries	Procedures to Treat NMSC, %
1992	1 158 298	3514	NA
1996	1 377 741	4136	NA
1997	1 450 746	4400	NA
1998	1 473 728	4521	NA
1999	1 497 444	4647	NA
2000	1 577 165	4947	NA
2001	1 694 913	5173	NA
2002	1 785 136	5312	92.6
2003	1 834 443	5322	93.8
2004	1 905 121	5477	92.7
2005	2 007 826	5772	92.4
2006	2 048 517	6075	93.7

Abbreviations: NA, not available; NMSC, nonmelanoma skin cancer.

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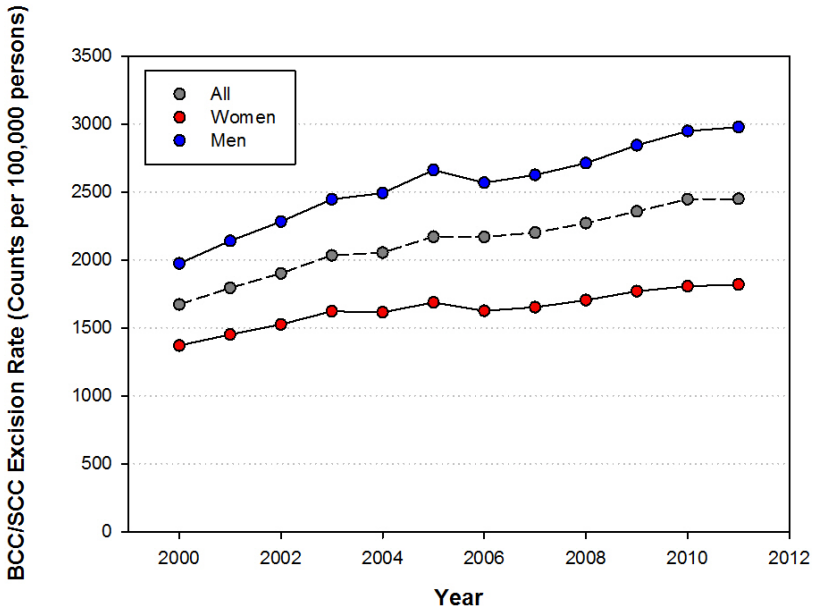
Background

ORIGINAL ARTICLE

Turning the tide? Changes in treatment rates for keratinocyte cancers in Australia 2000 through 2011

Catherine M. Olsen, PhD,[a] Patricia F. Williams, MD,[b] and David C. Whiteman, MBBS, PhD[a]
Queensland, Australia, and Richmond, Virginia



AIMS

For **melanoma** *and* **SCC** *and* **BCC,** to

- define causal pathways
- measure absolute risks associated with sun exposure, phenotype, demography & genotype
- develop and validate risk prediction tools
- measure the health burden / costs

QSKIN Sun & Health Study

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Overview

- Methods
- Incidence and multiplicity
- Risk Prediction
- Next steps

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QSKIN overview

Invite 200,000 people aged 40-69 years

AEC Australian Electoral Commission

Collect information at baseline

QSkin Survey
Paper
Online

Datatime

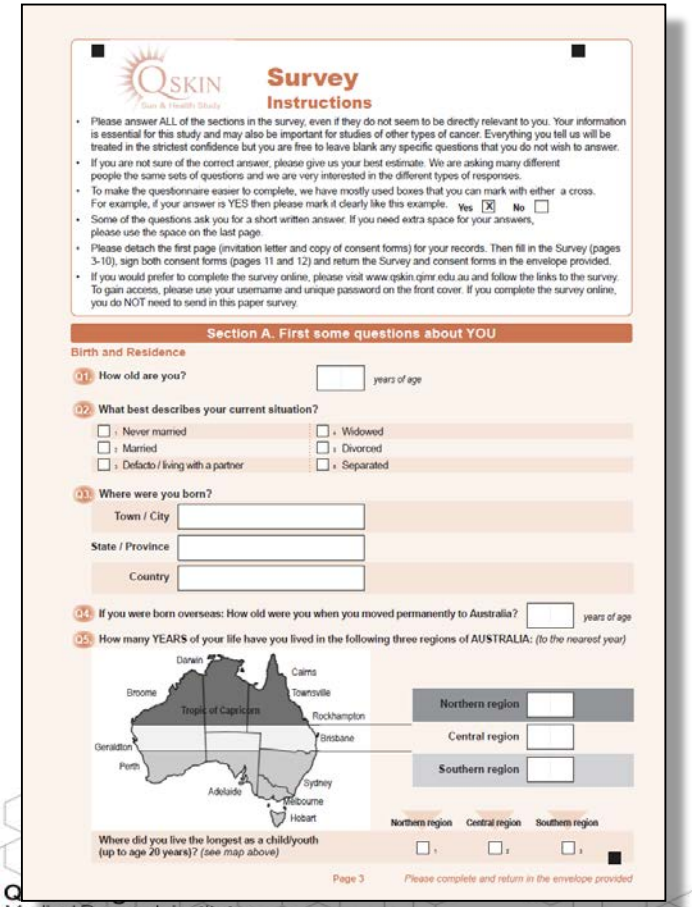
pathology
pharmacology
imaging
biospecimens
dermoscopy
health services
behaviours

Follow up
Data linkage

Australian Government
Medicare Australia

Australian Government
Australian Institute of Health and Welfare

Baseline data collection



QSKIN Sun & Health Study

Survey

Instructions

- Please answer ALL of the sections in the survey, even if they do not seem to be directly relevant to you. Your information is essential for this study and may also be important for studies of other types of cancer. Everything you tell us will be treated in the strictest confidence but you are free to leave blank any specific questions that you do not wish to answer.
- If you are not sure of the correct answer, please give us your best estimate. We are asking many different people the same sets of questions and we are very interested in the different types of responses.
- To make the questionnaire easier to complete, we have mostly used boxes that you can mark with either a cross. For example, if your answer is YES then please mark it clearly like this example. Yes ☒ No ☐
- Some of the questions ask you for a short written answer. If you need extra space for your answers, please use the space on the last page.
- Please detach the first page (invitation letter and copy of consent forms) for your records. Then fill in the Survey (pages 3-10), sign both consent forms (pages 11 and 12) and return the Survey and consent forms in the envelope provided.
- If you would prefer to complete the survey online, please visit www.qskin.qimr.edu.au and follow the links to the survey. To gain access, please use your username and unique password on the front cover. If you complete the survey online, you do NOT need to send in this paper survey.

Section A. First some questions about YOU

Birth and Residence

Q1 How old are you? ____ years of age

Q2 What best describes your current situation?

☐ 1 Never married ☐ 4 Widowed
☐ 2 Married ☐ 5 Divorced
☐ 3 Defacto / living with a partner ☐ 6 Separated

Q3 Where were you born?

Town / City
State / Province
Country

Q4 If you were born overseas: How old were you when you moved permanently to Australia? ____ years of age

Q5 How many YEARS of your life have you lived in the following three regions of AUSTRALIA: *(to the nearest year)*

Northern region ____
Central region ____
Southern region ____

Where did you live the longest as a child/youth (up to age 20 years)? *(see map above)*

Northern region ☐1 Central region ☐2 Southern region ☐3

Page 3 *Please complete and return in the envelope provided*

Demographics:

Age, Marital status, Place of birth, Residential history
Health insurance, Education, Occupation, Ancestry

Phenotype:

skin colour, burning, tanning, eye & hair colour, freckling & moles

Sun exposure and sun protection:

Sunburns, sunscreen use, time spent outdoors, tanning beds

Medical history:

self-rated health, history of skin cancers, medication use, family history of melanoma, self-rated melanoma risk

Skin checks:

history of skin examination

Height, weight and lifestyle:

trouser/dress size, smoking & alcohol, fruit, fruit juice, vegetables, hours of sleep, self-rated stress past year

Women only:

age at menarche/menopause, contraceptive & hormone use, number of children, endometriosis

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Medicare Benefits Schedule

Procedure		Item Numbers
Surgical Excision	**Benign Lesions** *(8 items)*	31205, 31210, 31215, 31220, 31225, 31230, 31235, 31240
	BCC & SCC First Surgical Excision *(8 items)*	31255, 31260, 31265, 31270, 31275, 31280, 31285, 31290
	BCC & SCC Residual and Recurrent previously treated surgically *(24 items)*	31256, 31261, 31266, 31271, 31276, 31281, 31286, 31291, 31257, 31262, 31267, 31272, 31277, 31282, 31287, 31292, 31258, 31263, 31268, 31273, 31278, 31283, 31288, 31293,
	BCC & SCC Residual and Recurrent previously treated non-surgically	31295
Biopsy		30071
Other treatment (cryotherapy or serial curettage)	**Benign Lesion**	30195
	Premalignant Lesion	30192
	Malignant Lesion *(5 items)*	30196, 30197, 30202, 30203, 30205

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Medicare Benefits Schedule

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Surgical Excision	**Benign Lesions** *(8 items)*	31205, 31210, 31215, 31220, 31225, 31230, 31235, 31240
	BCC & SCC First Surgical Excision *(8 items)*	**31255**, 31260, 31265, 31270, 31275, 31280, 31285, 31290
	BCC & SCC	31256, 31261, 31266, 31271, 31276, 31281, 31286,

31255	BASAL CELL CARCINOMA OR SQUAMOUS CELL CARCINOMA (including keratocanthoma), **removal from nose, eyelid, lip, ear, digit or genitalia, tumour size up to and including 10mm in diameter** - where removal is by therapeutic **surgical excision (other than by shave excision) and suture and** ***where the initial specimen removed is sent for histological examination and malignancy confirmed, and any subsequently excised specimen is sent for histological examination*** (Anaes.) *(See para T8.22 of explanatory notes to this Category)* **Fee:** $217.20 **Benefit:** 75% = $162.90 85% = $184.65

PATHOLOGY		PATHOLOGY
	GROUP P5 - TISSUE PATHOLOGY	
72813	Examination of complexity level 2 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions - 1 or more separately identified specimens (Item is subject to rule 13) **Fee:** $72.00 **Benefit:** 75% = $54.00 85% = $61.20	

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Concordance of outcomes data

- 97% MBS claims for **KC excision** had synchronous MBS claims for **anatomical pathology**
- 98% histologically-confirmed KCs had corresponding MBS claim for KC excision

Thompson *et al, Aust NZ J Public Health.* 2016; 40:154-8

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Overview

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Risk Prediction

Next steps

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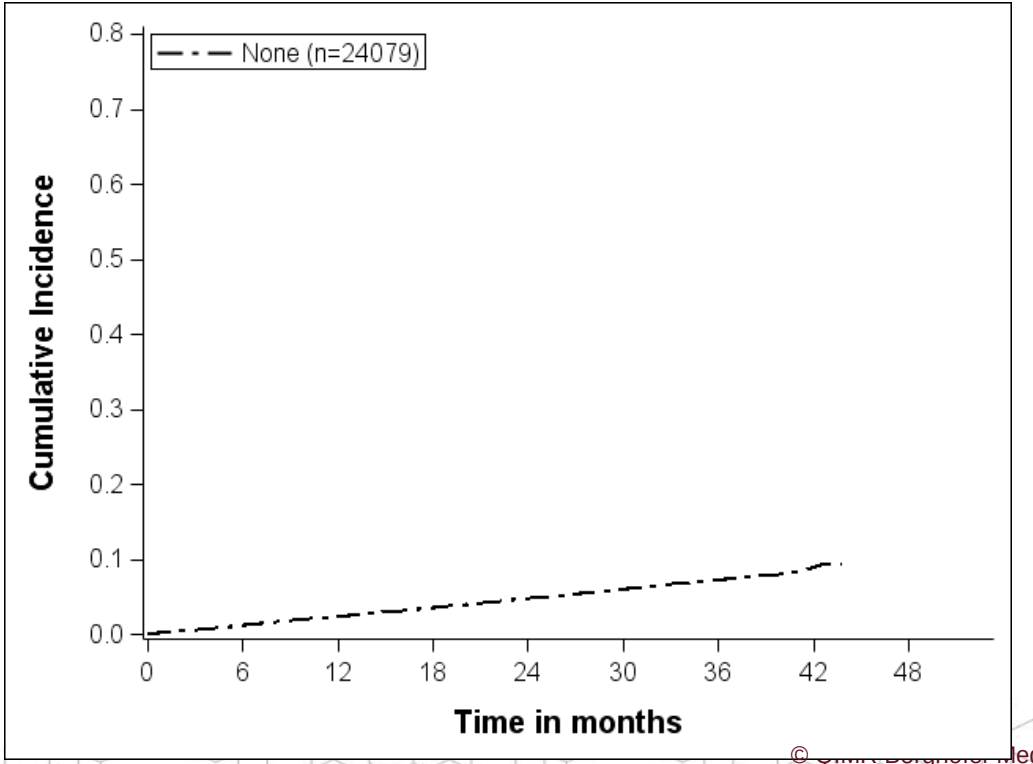
Cumulative incidence of KC *(MBS data)*

Q24. About how many separate SKIN CANCERS (but *not* moles or warts) have you ever had CUT OFF your skin?

20+ skin cancers	10-20 skin cancers	2-10 skin cancers	1 skin cancer	None
☐ 1	☐ 2	☐ 3	☐ 4	☒ 5



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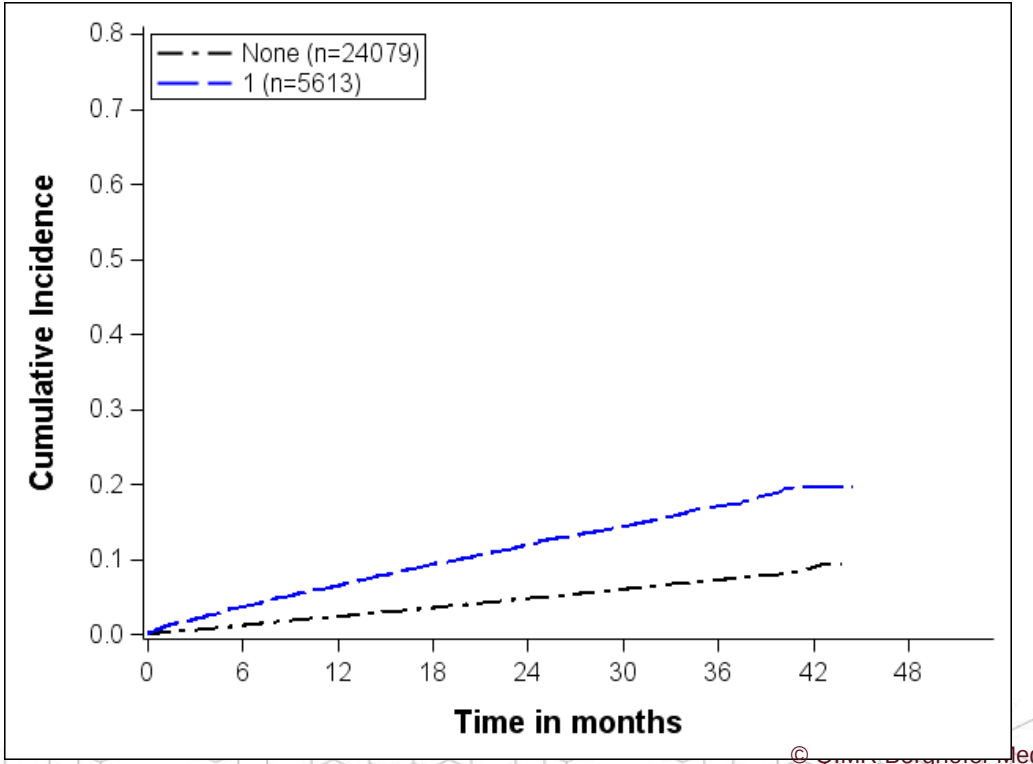

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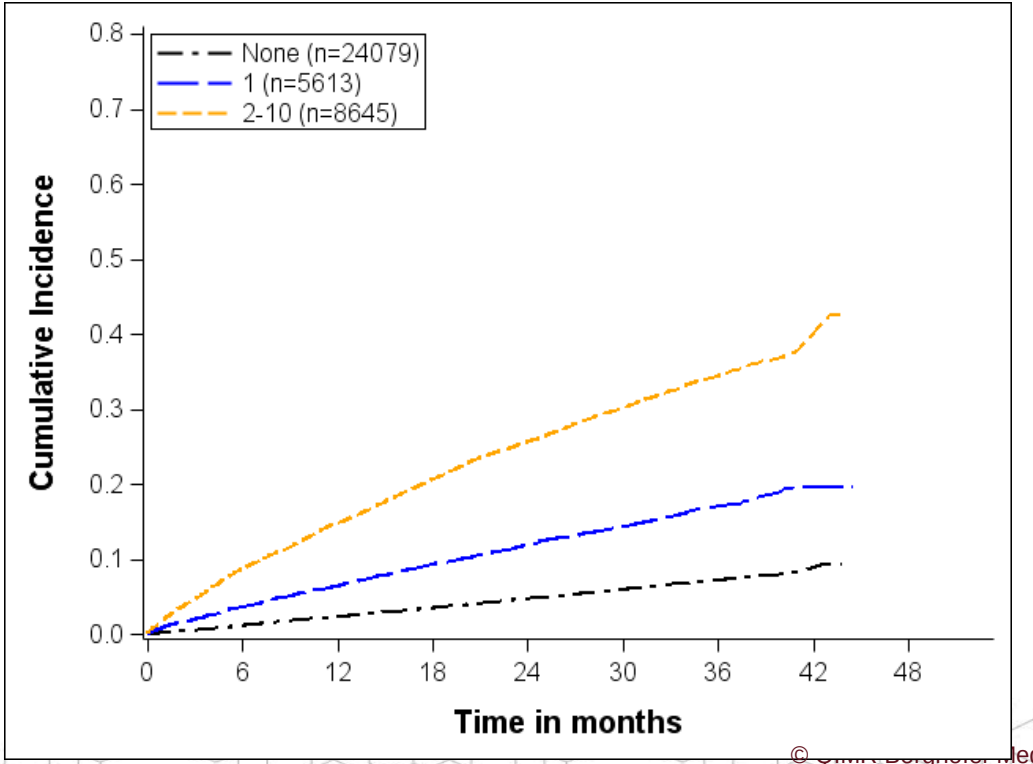

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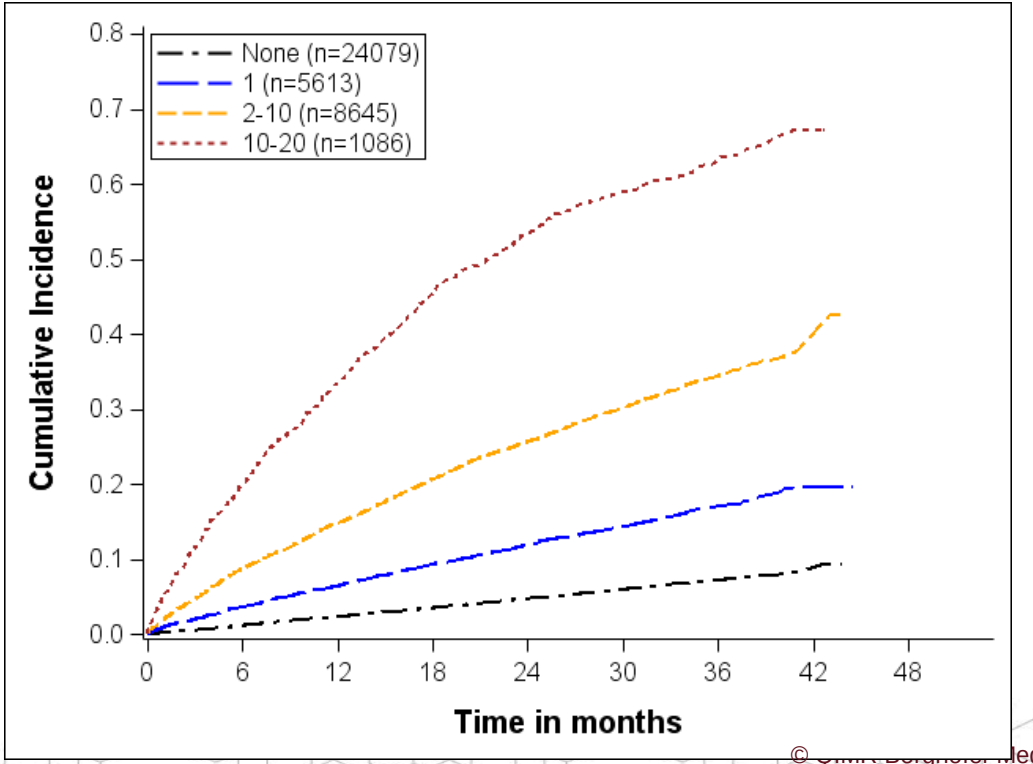
☐ 1	☒ 2	☐ 3	☐ 4	☐ 5



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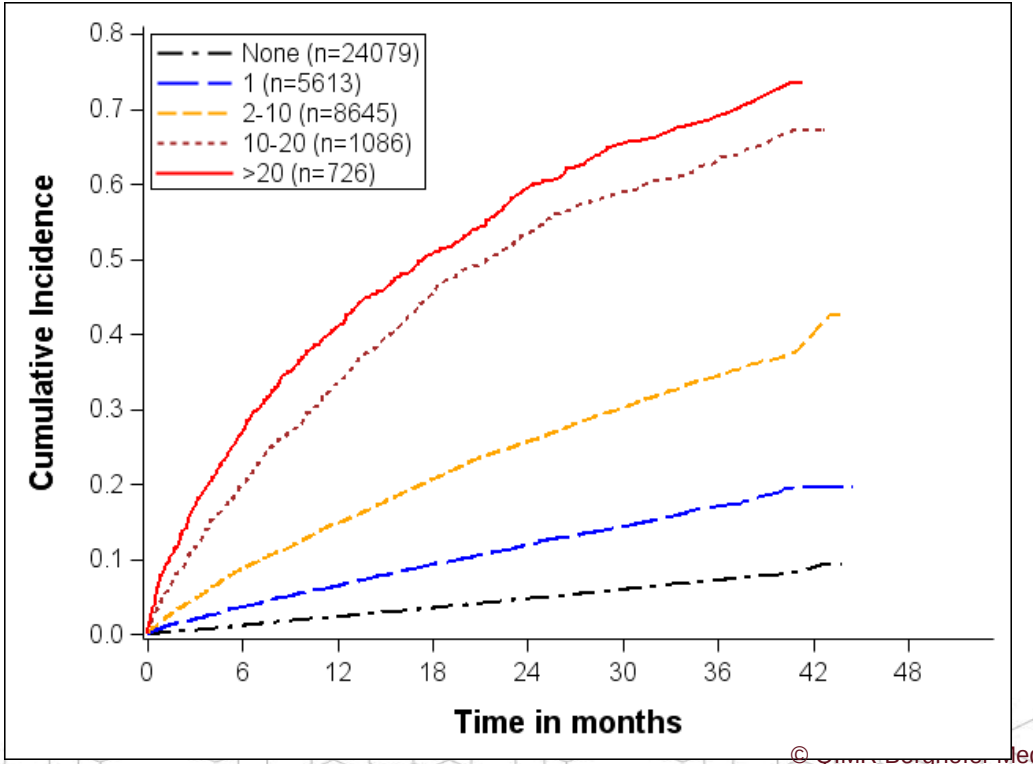

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Multiplicity of KC *(3 years of follow-up)*

Medicare data
'All comers'
N=40,383

Number of KC excisions	Females	Males	Total
None	86%	79%	**83%**
1	9%	11%	**10%**
2	2%	4%	**3%**
3-5	3%	5%	**4%**
6+	<1%	1%	**<1%**

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KC incidence *("all comers")*

EARLY DATA

	Person-based ($x10^{-5}$ pyar)*	Lesion-based ($x10^{-5}$ pyar)*
KC ASR (Medicare data)	5,794	11,670
BCC ASR (histology data)	3,282	6,915
SCC ASR (histology data)	1,262	1,991

*Standardised to the US 2000 Standard Population

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KC incidence *("cleanskins")*

Q24. About how many separate SKIN CANCERS (but *not* moles or warts) have you ever had CUT OFF your skin?

20+ skin cancers	10-20 skin cancers	2-10 skin cancers	1 skin cancer	None
☐ 1	☐ 2	☐ 3	☐ 4	☒ 5

EARLY DATA

	Person-based (x10^{-5} pyar)*	Lesion-based (x10^{-5} pyar)*
KC ASR (Medicare data)	2,039	3,396
BCC ASR (histology data)	1,288	2,125
SCC ASR (histology data)	429	594

*Standardised to the US 2000 Standard Population

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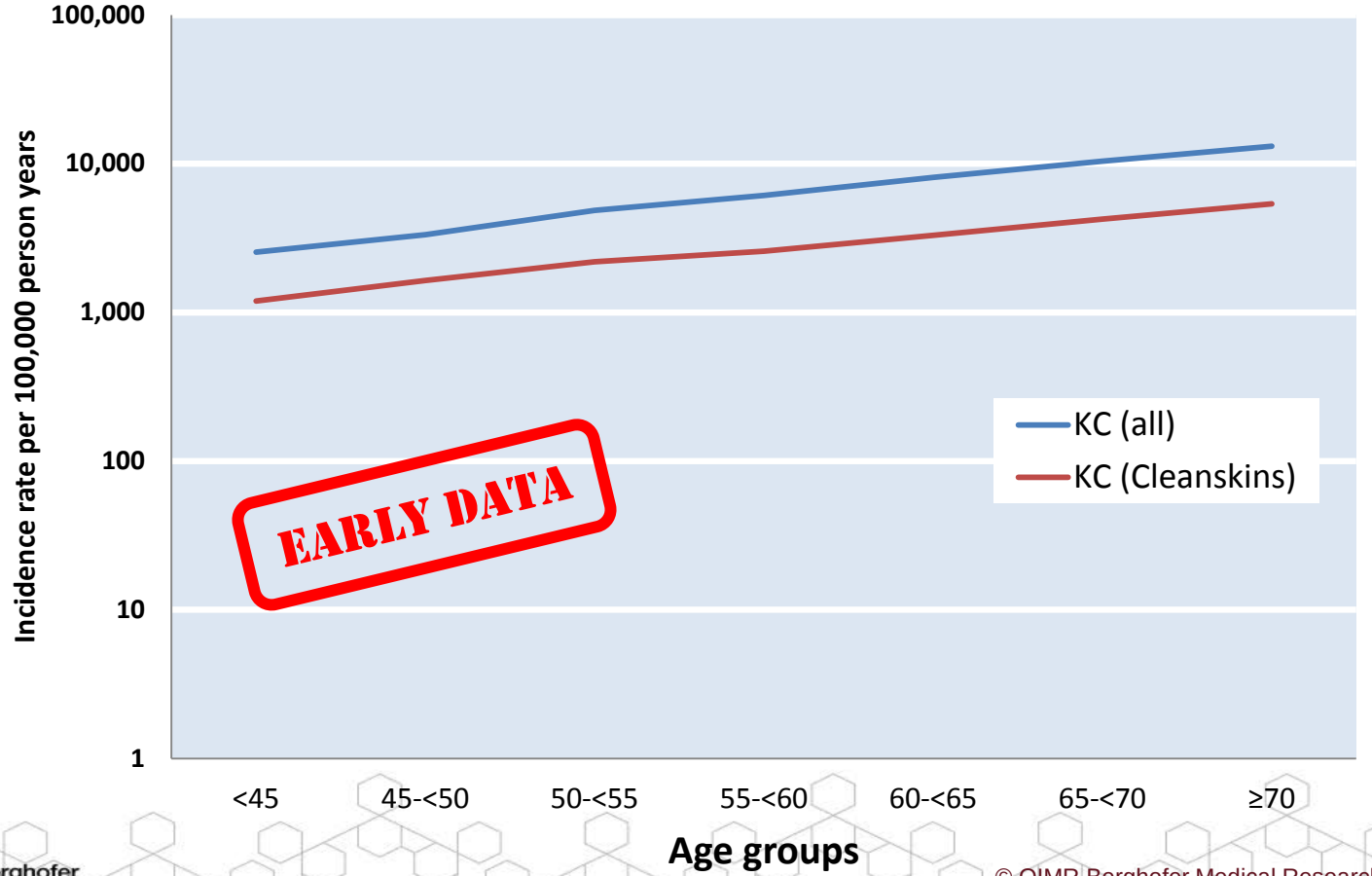
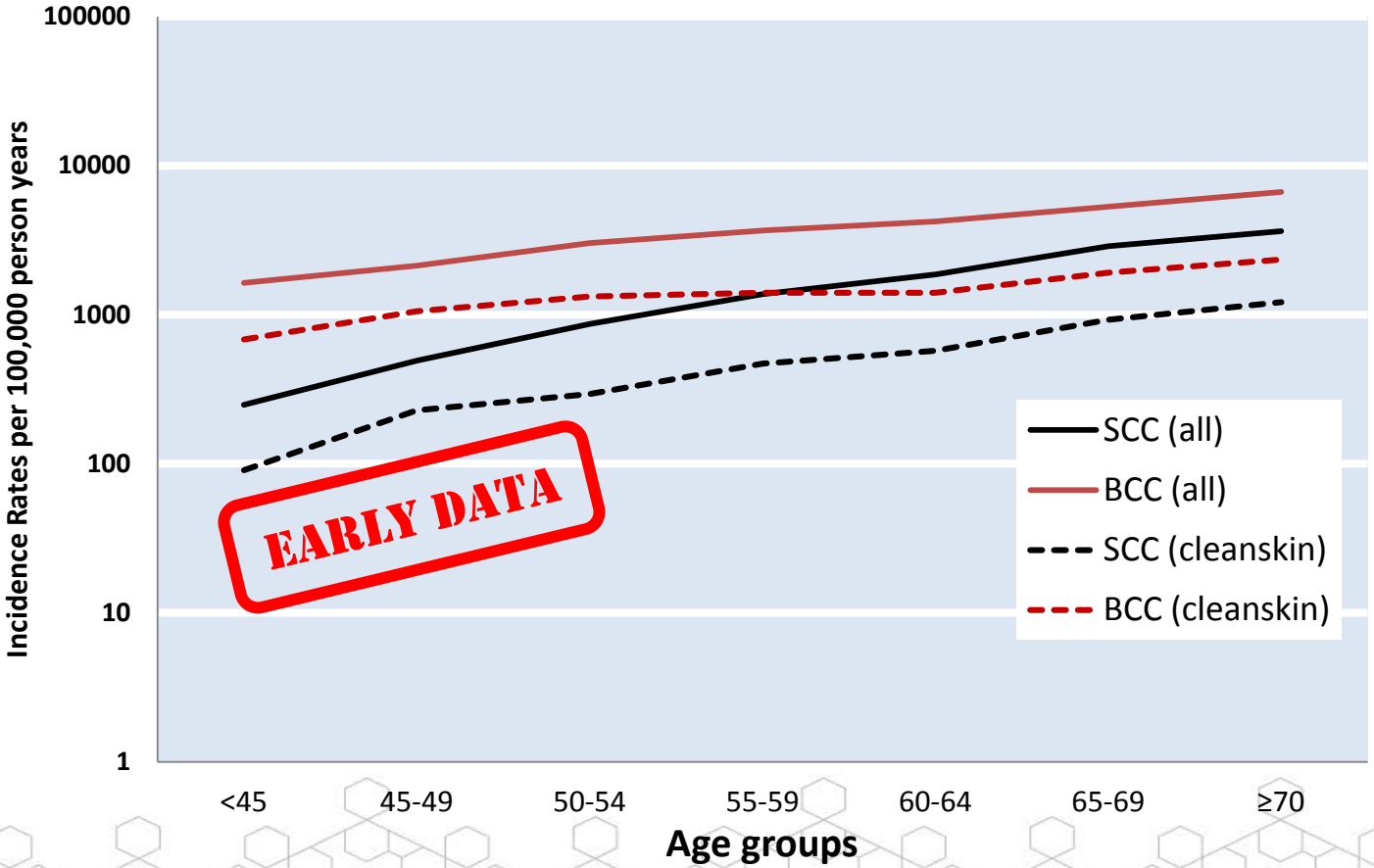
Age-specific incidence of KC *(Medicare data)*



Age-specific incidence of BCC & SCC *(histology data)*



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Overview

Methods

Incidence and multiplicity

Risk Prediction

Next steps

Why predict risk of skin cancer?

SKIN CANCER COLLEGE AUSTRALASIA

Triage

Higher

Lower

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Why predict risk of skin cancer?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention

Andrew C. Chen, M.B., B.S., Andrew J. Martin, Ph.D., Bonita Choy, M.Med., Pablo Fernández-Peñas, Ph.D., Robyn A. Dalziell, Ph.D., Catriona A. McKenzie, M.B., B.S., Richard A. Scolyer, M.D., Haryana M. Dhillon, Ph.D., Janette L. Vardy, M.D., Anne Kricker, Ph.D., Gayathri St. George, M.Sc.Med., Niranthari Chinniah, M.B., B.S., Gary M. Halliday, D.Sc., and Diona L. Damian, Ph.D.

CONCLUSIONS

Oral nicotinamide was safe and effective in reducing the rates of new nonmelanoma skin cancers and actinic keratoses in high-risk patients. (Funded by the National Health and Medical Research Council; ONTRAC Australian New Zealand Clinical Trials Registry number, ACTRN12612000625875.)

Risk prediction

Basal cell cancers

Squamous cell cancers

Objective

To derive and validate a risk stratification tool for keratinocyte cancers using data from a prospective Australian study.

Methods

- **Participants**
  - 43,794 consented participants (24%)
    - *Exclude 1657 with prior melanoma history*
  - 38,726 participants with link to Medicare data
  - ⅔ random sample for derivation (n=25,842)
  - ⅓ random sample for validation (n=12,884)
- **Risk factors**
  - Self-reported demographics, phenotype, sun exposure collected at baseline
- **Outcome**
  - Data linkage to Medicare over 3 yrs
  - First surgical excision of keratinocyte cancer **(Medicare data, n=6,348)**

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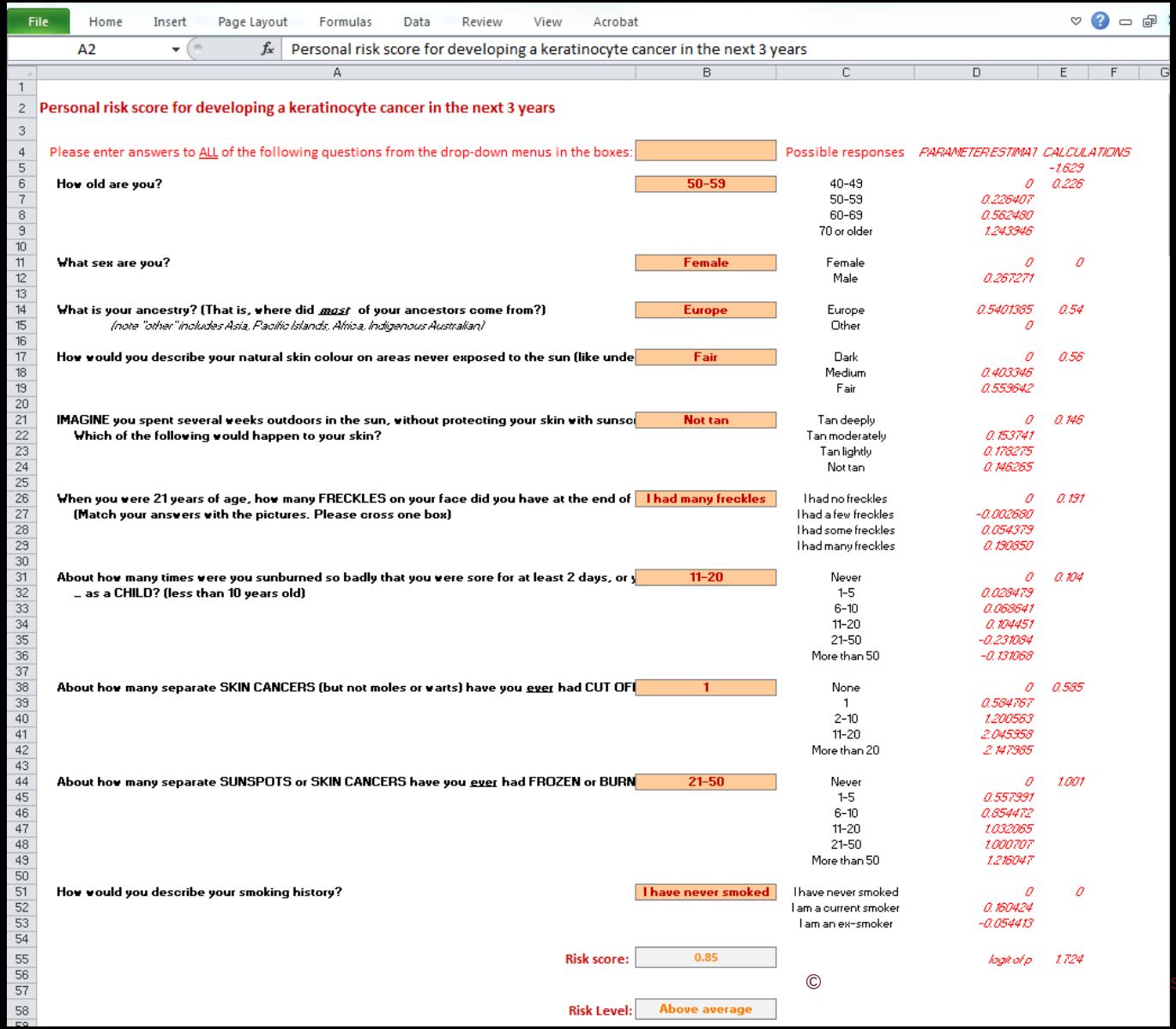
Model development

Univariate associations	PRIMARY ANALYSIS
• Age	p<0.001
• Sex	p<0.001
• Ethnicity	p<0.001
• Place of birth	p<0.001
• Unexposed skin colour	p<0.001
• Skin burning	p<0.001
• Skin tanning	p<0.001
• Eye colour	p<0.001
• Hair colour	p<0.001
• Freckles	p<0.001
• Moles	p<0.001
• Sunburns in childhood	p<0.001
• Sunburns in adolescence	p<0.001
• Sunburns in adulthood	p<0.001
• Sunbeds	p<0.006
• Time outdoors on weekdays	p<0.001
• Time outdoors on weekends	p=0.021
• Number of excised skin cancers	p<0.001
• Number of destroyed skin lesions	p<0.001
• Family history melanoma	p<0.001
• Aspirin frequency	p<0.001
• Smoking status	p=0.484

©

Model development

Multivariate associations	PRIMARY ANALYSIS
• Age	p<0.0001
• Sex	p<0.0001
• Ethnicity	p<0.0001
• Place of birth	
• Unexposed skin colour	p<0.0001
• Skin burning	
• Skin tanning	p=0.0186
• Eye colour	
• Hair colour	
• Freckles	p=0.0557
• Moles	
• Sunburns in childhood	p=0.0148
• Sunburns in adolescence	
• Sunburns in adulthood	
• Sunbeds	
• Time outdoors on weekdays	
• Time outdoors on weekends	
• Number of excised skin cancers	p<0.0001
• Number of destroyed skin lesions	p<0.0001
• Family history melanoma	
• Aspirin frequency	
• Smoking status	p=0.0052



File Home Insert Page Layout Formulas Data Review View Acrobat

A2 fx Personal risk score for developing a keratinocyte cancer in the next 3 years

Personal risk score for developing a keratinocyte cancer in the next 3 years

		Possible responses	PARAMETER ESTIMATE	CALCULATIONS
Please enter answers to ALL of the following questions from the drop-down menus in the boxes:				-1.629
How old are you?	50-59	40-49	0	0.226
		50-59	0.226407	
		60-69	0.562480	
		70 or older	1.243946	
What sex are you?	Female	Female	0	0
		Male	0.267271	
What is your ancestry? (That is, where did *most* of your ancestors come from?) *(note "other" includes Asia, Pacific Islands, Africa, Indigenous Australian)*	Europe	Europe	0.5401385	0.54
		Other	0	
How would you describe your natural skin colour on areas never exposed to the sun (like unde	Fair	Dark	0	0.56
		Medium	0.403346	
		Fair	0.559642	
IMAGINE you spent several weeks outdoors in the sun, without protecting your skin with sunsc	Not tan	Tan deeply	0	0.146
Which of the following would happen to your skin?		Tan moderately	0.153741	
		Tan lightly	0.178275	
		Not tan	0.146265	
When you were 21 years of age, how many FRECKLES on your face did you have at the end of	I had many freckles	I had no freckles	0	0.191
(Match your answers with the pictures. Please cross one box)		I had a few freckles	-0.002680	
		I had some freckles	0.054379	
		I had many freckles	0.190850	
About how many times were you sunburned so badly that you were sore for at least 2 days, or y	11-20	Never	0	0.104
_ as a CHILD? (less than 10 years old)		1-5	0.039479	
		6-10	0.068641	
		11-20	0.104451	
		21-50	-0.231084	
		More than 50	-0.131068	
About how many separate SKIN CANCERS (but not moles or warts) have you ever had CUT OFI	1	None	0	0.585
		1	0.594767	
		2-10	1.200563	
		11-20	2.045358	
		More than 20	2.147985	
About how many separate SUNSPOTS or SKIN CANCERS have you ever had FROZEN or BURN	21-50	Never	0	1.001
		1-5	0.557991	
		6-10	0.854472	
		11-20	1.032065	
		21-50	1.000707	
		More than 50	1.216047	
How would you describe your smoking history?	I have never smoked	I have never smoked	0	0
		I am a current smoker	0.160424	
		I am an ex-smoker	-0.054413	
Risk score:	0.85		logit of p	1.724
Risk Level:	Above average			

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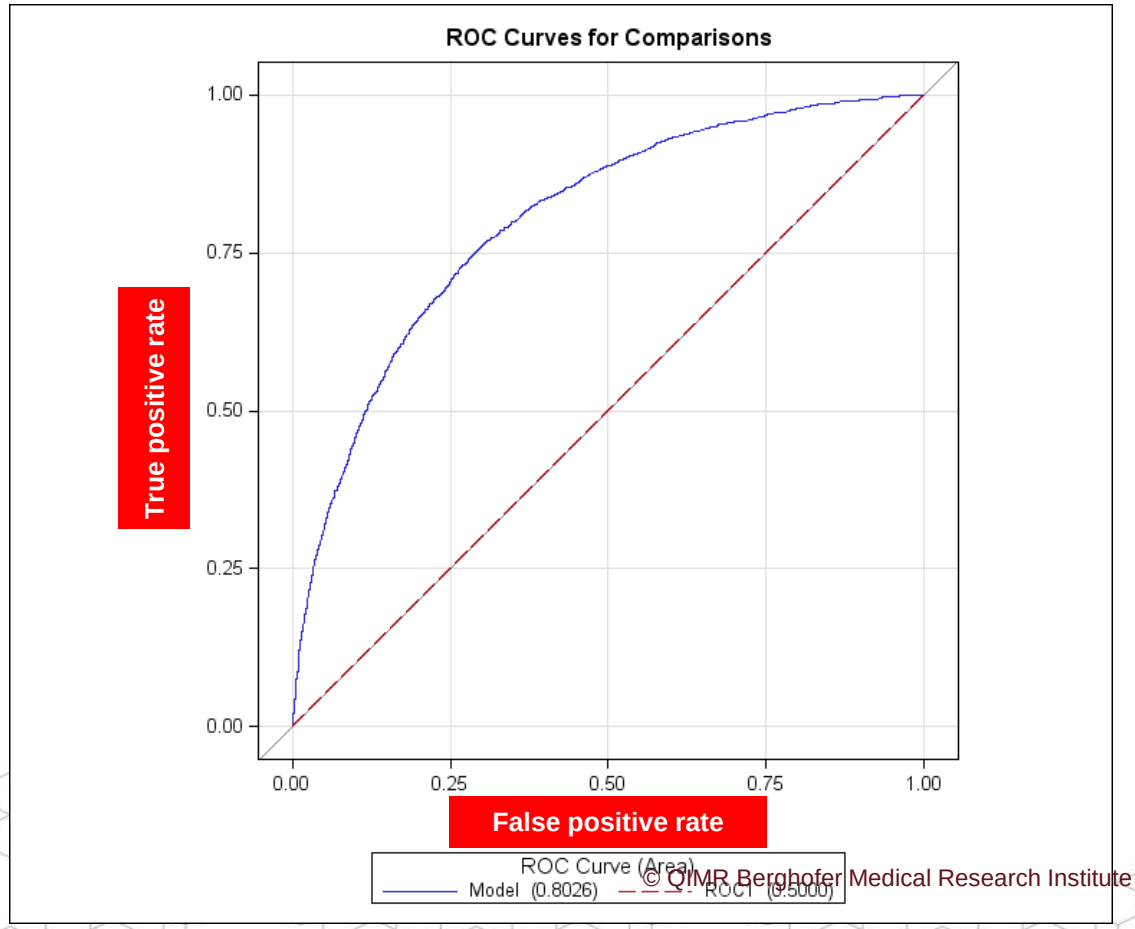
Discrimination

Validation dataset

- AUC = 0.8026
- 10,773 controls
- 2,111 cases



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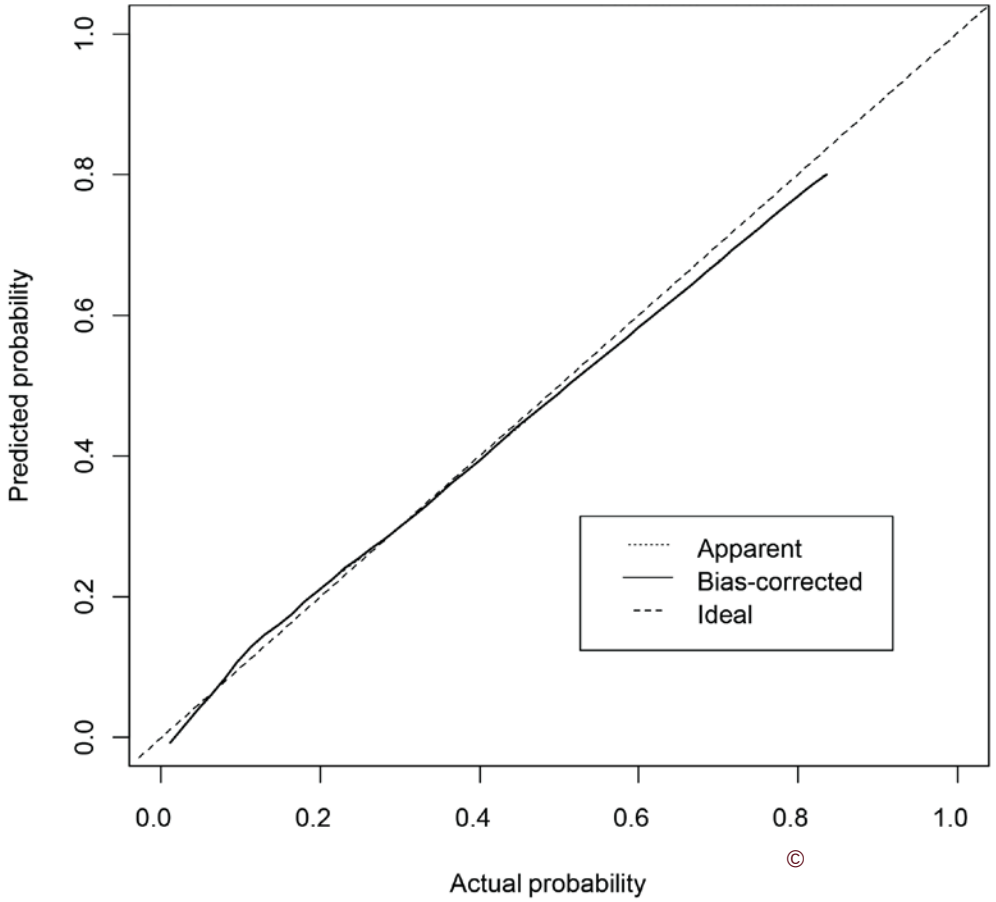
Calibration



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About the study | Results and news | FAQs | Confidentiality and privacy | Genetics of skin cancer | Funding and partners

QSKIN Sun & Health Study

QSkin

QSkin is the largest medical research study ever conducted in Queensland. The QSkin study will provide long-term information about the burden of skin cancer in Queensland. By comparing the information from people with and without skin cancer, we will also gain a better understanding of how skin cancers develop.

What is so important about skin cancer?

Queenslanders have the highest rates of melanoma and skin cancer in the world. With better knowledge of the causes, we can work towards better methods for preventing and treating these cancers.

Personal risk score for developing a keratinocyte cancer in the next 3 years

Please enter answers to ALL of the following questions from the drop-down menus in the boxes:

How old are you?

50 - 59

What sex are you?

Male

What is your ancestry? (That is, where did most of your ancestors come from?)
note: "other" includes Asia, Pacific Islands, Africa, Indigenous Australian

Europe

Risk Level:

About average

Compared to another male in your age group, your risk of skin cancer in the next 3 years is average.

Even though your risk of skin cancer is not 'high' compared with others of the same age and sex, this does not mean that you will not get skin cancer. To minimise your risk of developing skin cancer it is important to protect yourself from the harmful effects of sunlight. When outdoors and exposed to the sun, remember to wear sun protective clothing (including hats and sunglasses), apply broad-spectrum sunscreen to exposed skin, and seek shade.

More information about sun protection can be found at the SunSmart website.

Note: The information provided by the tool is to be used as a general guide and not to be solely relied upon. It is highly recommended that you discuss your personal risk factors and results of this risk assessment with your doctor. If you have a specific question about technical aspects of the risk tool please contact Professor David Whiteman (email: david.whiteman@qimrberghofer.edu.au)

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  recommended that you discuss your personal risk factors and results of this risk assessment with your doctor.

I HAVE READ AND ACKNOWLEDGED THE INFORMATION ABOVE.

Proceed to Skin cancer risk assessment tool

following

(less than 10

1 - 5

How would you describe your smoking history?

I have never smoked

Risk Level:

About average

QIMR Berghofer Medical Research Institute

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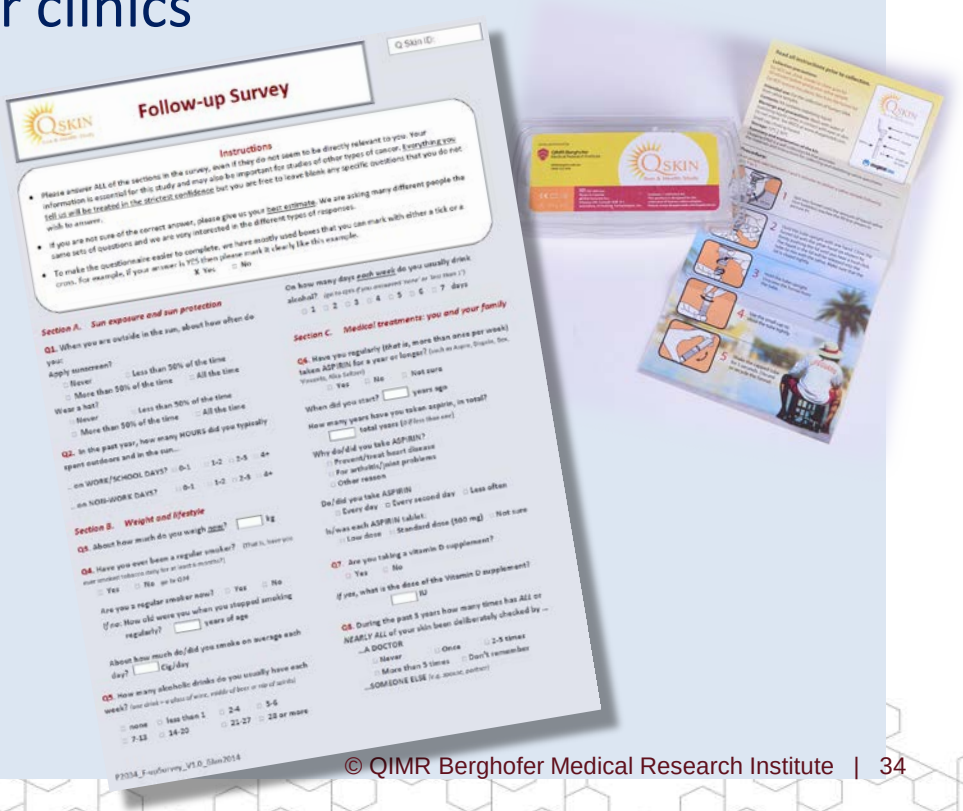
Next steps in QSKIN

- Validate tool in skin cancer clinics
- Add genetic data



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