



QIMR Berghofer
Medical Research Institute

Melanoma screening: *the epidemiologic principles*

David Whiteman

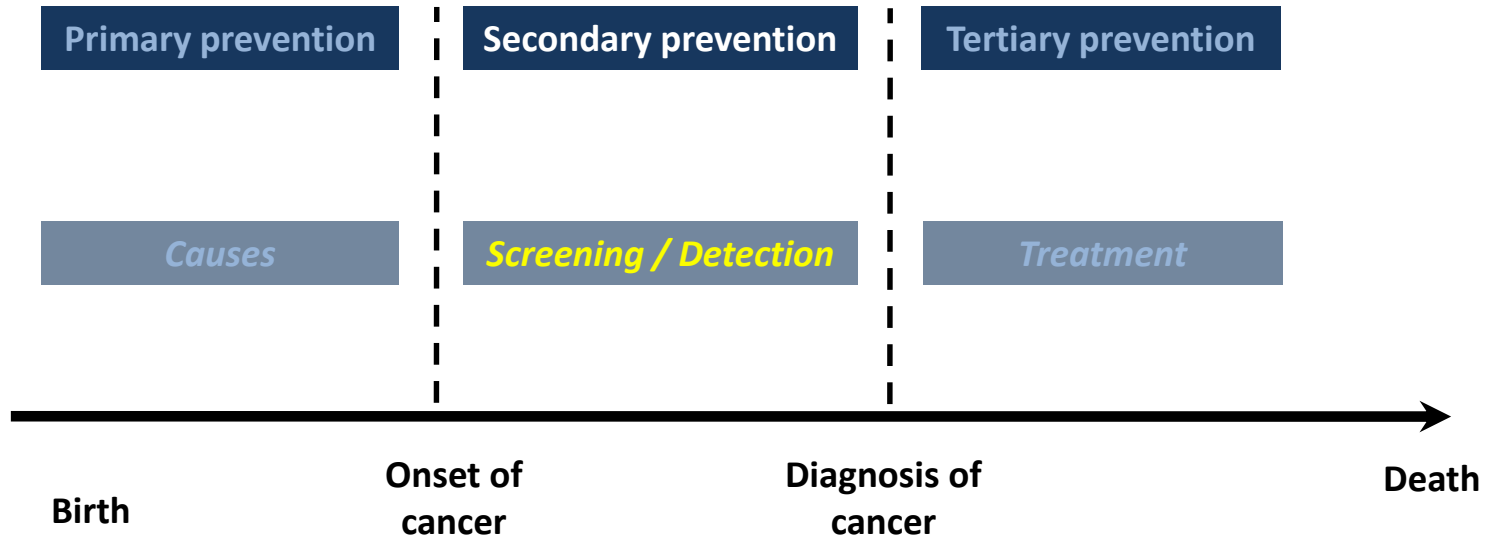
Deputy Director, QIMR Berghofer
Head, Cancer Control Group



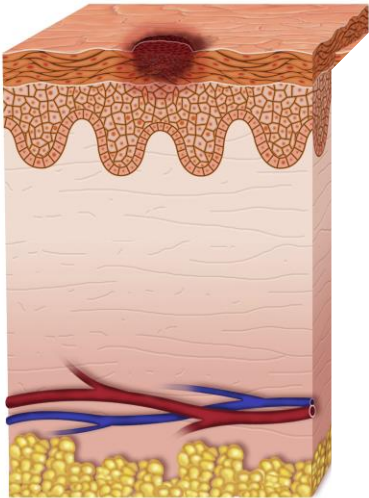
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Strategies for melanoma control



Aim of early detection = *reduce melanoma mortality*



Early detection options

1. **Population screening:** *breast, cervix, bowel*
2. **Targeted screening:** *'high-risk' patients*
3. **Opportunistic screening:** *'case finding'*



Population screening definition

“A screening test is performed on an asymptomatic individual to determine that cancer might be present and that further evaluation, including a biopsy and staging, is necessary.”

Brawley and Kramer, J Clin Oncol, 2005

Population screening criteria

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognised disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognisable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case finding should be a continuing process and not a 'once and for all' project.

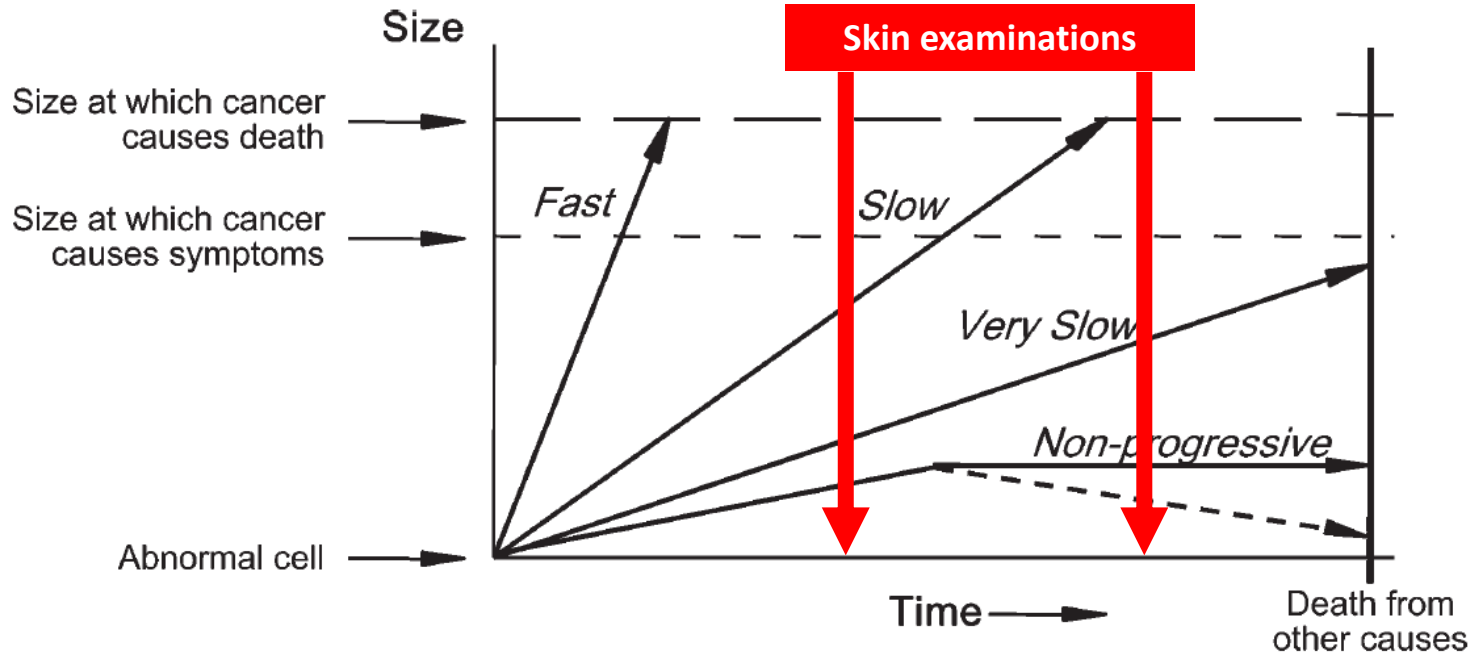
Melanoma screening criteria

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The heterogeneity of cancer



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*Whole-body skin examination
vs
technology*

Key metrics for screening tests

- 1. Sensitivity**
- 2. Specificity**
- 3. Positive Predictive Value**
- 4. Negative Predictive Value**
- 5. Number needed to screen**

How the metrics are calculated

SCREENING RESULT

DISEASE STATUS

	Melanoma	Not Melanoma	
Screen positive	True +ve (+/+)	False +ve (+/-)	<i>Total screen positive</i>
Screen negative	False -ve (-/+)	True -ve (-/-)	<i>Total screen negative</i>
	<i>Total melanoma</i>	<i>Total not melanoma</i>	

The perfect test

SCREENING RESULT

DISEASE STATUS

	Melanoma	Not Melanoma	
Screen positive	True positive	0	<i>Total screen positive</i>
Screen negative	0	True negative	<i>Total screen negative</i>
	<i>Total melanoma</i>	<i>Total not melanoma</i>	

How the metrics are calculated

$$\text{Sensitivity} = \frac{\text{True +ve}}{(\text{True +ve} + \text{False -ve})}$$

*The proportion of all people with **true melanomas** who are correctly identified by the screening test*

How the metrics are calculated

$$\text{Sensitivity} = \frac{\text{True +ve}}{(\text{True +ve} + \text{False -ve})}$$

DISEASE STATUS

SCREENING RESULT

	Melanoma	Not Melanoma
Screen positive	True +ve (+/+)	False +ve (+/-)
Screen negative	False -ve (-/+)	True -ve (-/-)
	Total melanoma	Total not melanoma

**INDEPENDENT OF
MELANOMA
PREVALENCE**

Total screen positive

Total screen negative

How the metrics are calculated

$$\text{Specificity} = \frac{\text{True -ve}}{(\text{False +ve} + \text{True -ve})}$$

*The proportion of all people **who do not have melanoma** for whom the screening test is negative*

How the metrics are calculated

$$\text{Specificity} = \frac{\text{True -ve}}{(\text{False +ve} + \text{True -ve})}$$

DISEASE STATUS

SCREENING RESULT

	Melanoma	Not Melanoma	
Screen positive	True +ve (+/+)	False +ve (+/-)	Total screen positive
Screen negative	False -ve (-/+)	True -ve (-/-)	Total screen negative
	Total melanoma	Total not melanoma	

How the metrics are calculated

$$\text{PPV} = \frac{\text{True +ve}}{(\text{True +ve} + \text{False +ve})}$$

*The proportion of all people who are told
“you might have melanoma” who actually
do have melanoma*

How the metrics are calculated

DISEASE STATUS

SCREENING RESULT

Screen
positive

"Provisional diagnosis"

"High index of suspicion"

"Suspicious"

"Ruling it out"

"...cannot be excluded"

"Second opinion"

"Not sure"

"Difficult lesion"

"Don't know"

How the metrics are calculated

$$\text{PPV} = \frac{\text{True +ve}}{(\text{True +ve} + \text{False +ve})}$$

DISEASE STATUS

SCREENING RESULT

	Melanoma	Not Melanoma
Screen positive	True +ve (+/+)	False +ve (+/-)
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	Total melanoma	Total not melanoma

**DEPENDENT ON
MELANOMA
PREVALENCE**

Total screen
positive

Total screen
negative

How the metrics are calculated

$$\text{NPV} = \frac{\text{True -ve}}{(\text{False- ve} + \text{True -ve})}$$

The proportion of all people who are told “you don’t have melanoma” who actually do not have melanoma

How the metrics are calculated

$$\text{NPV} = \frac{\text{True -ve}}{(\text{False- ve} + \text{True -ve})}$$

SCREENING RESULT

		DISEASE STATUS		
		Melanoma	Not Melanoma	
SCREENING RESULT	Screen positive	True +ve (+/+)	False +ve (+/-)	Total screen positive
	Screen negative	False -ve (-/+)	True -ve (-/-)	Total screen negative
		Total melanoma	Total not melanoma	

Units of analysis: *people vs lesions*

Multiplicity of skin cancer endpoints



THE
REAL
WORLD

What are the screening metrics for melanoma?

Clinical outcomes from skin screening clinics within a community-based melanoma screening program

Joanne F. Aitken, PhD,^{a,b} Monika Janda, PhD,^{a,c} Mark Elwood, MD,^d Philippa H. Youl, MPH,^a
 Ian T. Ring, FAFPHM,^c and John B. Lowe, DrPH^f
Brisbane, Queensland, Carlton, Victoria, and Wollongong, New South Wales, Australia; and Iowa City, Iowa



Table II. Histopathological diagnosis for lesions excised or biopsied*

Suspected diagnosis	Total (n = 1343)	Histopathological diagnosis									
		Melanoma (n = 33)	BCC (n = 259)	SCC (n = 97)	HMF (n = 1)	Benign nevus (n = 433)	Dysplastic nevus (n = 96)	Lentigo (n = 103)	Seborrheic keratosis (n = 85)	Solar keratosis (n = 87)	Other (n = 149)
Melanoma	161	15	7	3	1	68	18	19	12	4	14
BCC	371	1	200	51	0	19	2	5	12	28	53
SCC	87	1	21	28	0	1	0	1	8	16	11
HMF	5	0	0	0	0	1	0	2	1	1	0
Benign nevus	171	0	4	0	0	101	21	23	4	3	15
Dysplastic nevus	368	10	8	2	0	211	51	39	28	4	15
Lentigo	11	1	0	0	0	4	0	4	0	0	2
Seborrheic keratosis	52	3 [†]	2	1	0	19	2	5	11	3	6
Solar keratosis	47	0	13	6	0	2	0	0	3	17	6
Other	70	2 [‡]	4	6	0	7	2	5	6	11	27

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POSITION STATEMENT

Screening and early detection of skin cancer



* Endorsed by the Australasian College of Dermatologists

- Do ***not*** recommend mass or population-based screening for melanoma or NMSC
- Do recommend GPs to identify **high-risk patients**
- Do recommend GPs to counsel **high-risk patients**

Rationale

- there is insufficient evidence that population screening offers reduced morbidity and mortality

Clinical Practice Guidelines
for the
Management of Melanoma
in Australia and New Zealand



Recommendation

	Grade
1. In the absence of substantive evidence as to its effectiveness in reducing mortality from melanoma, population-based skin screening cannot be recommended	C

Recommendation

	Grade
2. Individuals at high risk of melanoma and their partner or carer be educated to recognise and document lesions suspicious of melanoma, and to be regularly checked by a clinician with six-monthly full body examination supported by total body photography and dermoscopy as required	C

Early detection options

1. Population screening: *breast, cervical, colorectal*
2. Targeted screening: *'high-risk' patients*
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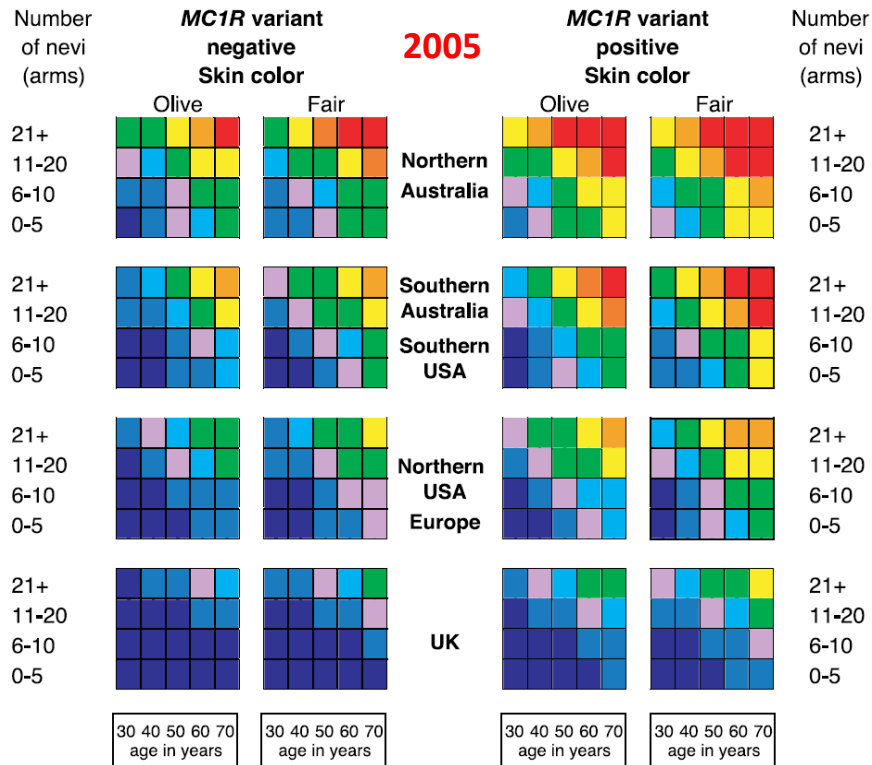


Can we identify patients at high risk of melanoma?

A Risk Prediction Tool for Melanoma?

David C. Whiteman and Adèle C. Green

Queensland Institute of Medical Research, Brisbane, Queensland, Australia



PERSONAL RISK FACTORS FOR CUTANEOUS MELANOMA

PETER BAADE 1989

RONA M. MACKIE
T. C. ...

Risk Factors and Individual Probabilities of Melanoma for Whites

2005

Eunyoung Cho, Bernard A. Rosner, Diane Feskanich, and Graham A. Colditz

Identifying Individuals at High Risk of Melanoma: A Practical Predictor of Absolute Risk

2006

Thomas R. Fears, DuPont Guerry IV, Ruth M. Pfeiffer, Richard W. Sagebiel, David E. Elder, Allan Halpern, Elizabeth A. Holly, Patricia Hartge, and Margaret A. Tucker

Predicting melanoma risk for the Australian population

2011

Victoria Mar,¹ Rory Wolfe² and John W Kelly¹

JAMA Dermatology | Original Investigation

Development and External Validation of a Melanoma Risk Prediction Model Based on Self-assessed Risk Factors

2016

Kylie Vuong, MBBS, MPH, FRACGP; Bruce K. Armstrong, MBBS (Hons), PhD, FAFPHM; Elisabete Weiderpass, MD, MSc, PhD; Eiliv Lund, PhD; Hans-Olov Adami, PhD; Marit B. Veierod, PhD; Jennifer H. Barrett, PhD; John R. Davies, PhD; D. Timothy Bishop, PhD; David C. Whiteman, MBBS(Hons), PhD; Catherine M. Olsen, PhD; John L. Hopper, PhD; Graham J. Mann, PhD; Anne E. Cust, MPH(Hons), PhD; Kevin McGeochan, PhD; and the Australian Melanoma Family Study Investigators

The early detection conundrum



Overdiagnosis

“INCIDENTALOMAS”

The diagnosis of a [*cancer*] that
would otherwise not go on to
cause symptoms or death

Overdiagnosis \neq false positive

Overdiagnosis \neq “overcalling”

Overdiagnosis \neq misdiagnosis

KATY BELL

Overdiagnosis in melanoma?

Journal of Surgical Oncology 1998;67:73-76

Non-Metastasizing Melanoma?

ROBERT C. BURTON, MD, PhD,^{1*} AND BRUCE K. ARMSTRONG, MBBS, DPHIL²

¹Anti-Cancer Council of Victoria, Victoria, Australia

²New South Wales Cancer Council, New South Wales (NSW), Australia

Melanoma Research 1994, 4, pp. 107-113

Recent incidence trends imply a non-metastasizing form of invasive melanoma

R. C. Burton* and B. K. Armstrong

Newcastle Melanoma Unit, PO Box 119, Wallsend, NSW 2287, Australia. Tel (+61) 49 236169; Fax (+61) 49 236984 (R. C. Burton); International Agency for Research on Cancer, Lyons, France (B. K. Armstrong).

Acta Derm Venereol 2011; 91: 499-503

REVIEW ARTICLE

Are All Melanomas Dangerous?

Carsten NØRGAARD¹, Martin GLUD¹ and Robert GNIADZECKI^{1,2}

KATY BELL

Summary and conclusions

- **Population screening for melanoma**
 - the metrics are not good..
 - the challenge of all the other non-lethal skin pathology
 - currently not recommended by Australian policy-makers
- **Targeted screening for melanoma**
 - Feasible, at least in theory
 - Mortality gains unknown
- **Balancing the benefits and harms of screening**
 - more research needed...