Associate Professor Amanda Oakley

Dermatologist

Hamilton

Friday, June 9, 2017

14:15 - 14:30 Does Early Detection of Melanoma Do More Harm than Good?

Does Early Detection of Melanoma Do More Harm than Good?

Adjunct Associate Professor Amanda Oakley
Waikato DHB

I don't know the answer

• • •

And I am not an expert on this topic:
Some musings follow.

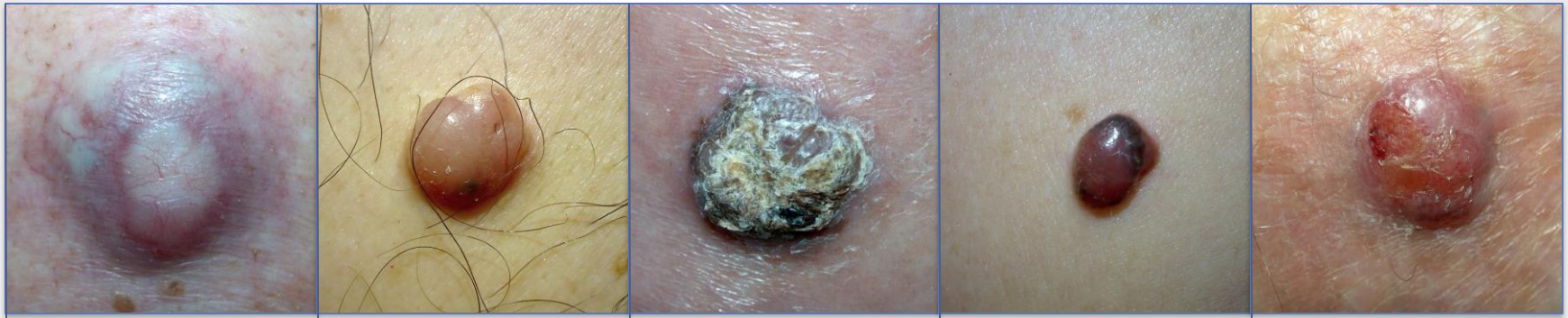
My conflicts

- I diagnose hundreds of skin lesions each week
- Consultant for MoleMap NZ
- Director of NZ Teledermatology
- Editor in chief DermNet New Zealand
  - Sponsored by Pharma

Thick melanomas are dangerous

- Nodular melanomas
- Amelanotic melanomas
- Melanomas in dark skin
- Non-cutaneous melanomas

Nodular melanomas



20 mm	7.2 mm	6 mm	5 mm	3 mm

Amelanotic melanoma

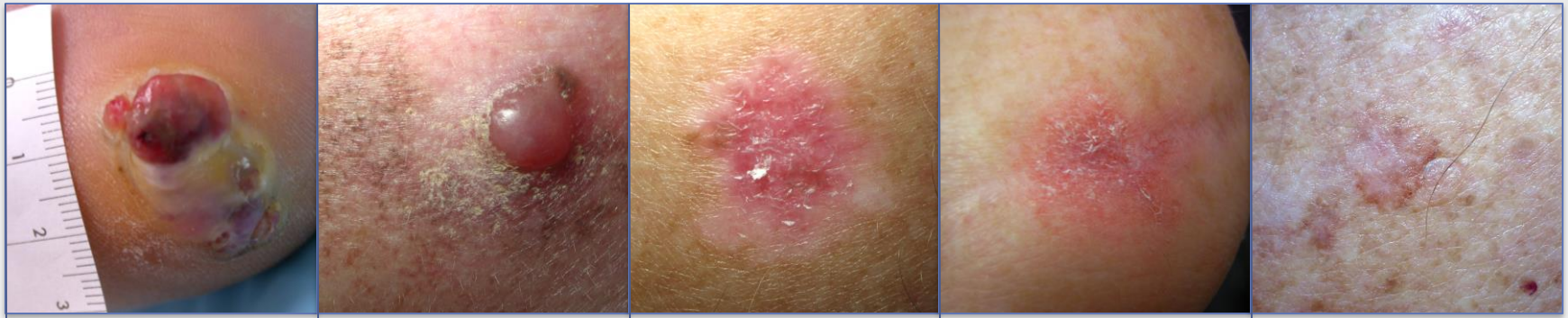
- Hard to diagnose
  - → Thick at diagnosis — often nodular subtype
  - → Possibly, more mitoses ie grow faster than pigmented melanomas
  - → Poor survival rates compared to pigmented melanomas [HR2]

JAMA Dermatol. 2014 Dec;150(12):1306-314.

Comparison of clinicopathologic features and survival of histopathologically amelanotic and pigmented melanomas: a population-based study.

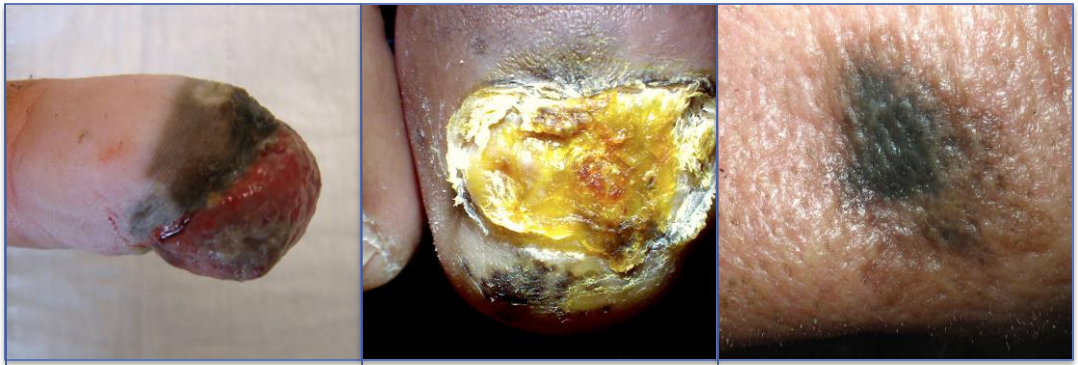
Thomas NE, Kricker A, Waxweiler WT, Dillon PM, Busman KJ, From L, Groben PA, Armstrong BK, Anton-Culver H, Gruber SB, Marrett LD, Gallagher RP, Zanetti R, Rosso S, Dwyer T, Venn A, Kanetsky PA, Orlow I, Paine S, Ollila DW, Reiner AS, Luo L, Hao H, Frank JS, Begg CB, Berwick M; Genes, Environment, and Melanoma (GEM) Study Group.

Amelanotic melanoma



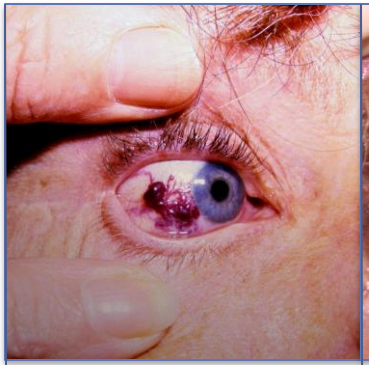
7.5 mm	4 mm	0.62 mm	In situ	In situ

Melanomas in dark skin

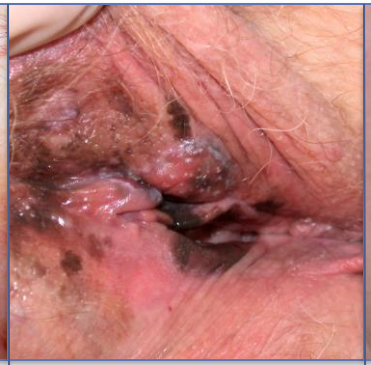


8 mm	0.9 mm	In situ

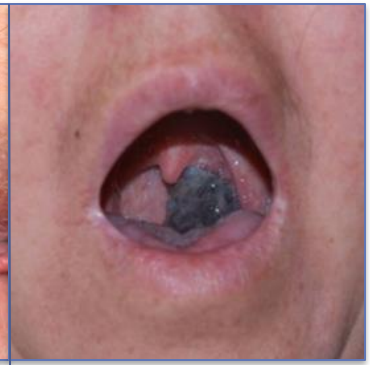
Non-cutaneous melanomas



Ocular



Vulval



Tonsillar

http://ispub.com/IJORL/7/2/7810

Thick melanomas are not found by screening

- No change in incidence over the years
- Often detected between screening visits
- 43% NM biopsied at first encounter vs 70% of SSM

Australas J Dermatol. 2016 May;57(2):97-101. doi: 10.1111/ajd.12416. Epub 2015 Nov 12.

An assessment of clinical pathways and missed opportunities for the diagnosis of nodular melanoma versus superficial spreading melanoma.

Cicchiello M[1], Lin MJ[1], Pan Y[1], McLean C[1,2], Kelly JW[1].

True or false?

1. Early detection saves lives.
2. Excisions of benign lesions are justified, so as not to miss even a single melanoma.
3. Self-skin examination leads to early diagnosis.
4. White-skinned patients >50 should have skin checks.
5. A dermatologist should triage all suspicious lesions.
6. Every doctor should be trained in skin examination.
7. Machines can diagnose melanoma.

1. Early detection saves lives.

Unproven.

The theory is:

- Thick melanomas → greater risk of death
- Thin melanomas are less likely to cause death
- Therefore, detect and remove thin melanomas

What is cancer screening?

- Population screening
  - Asymptomatic adults in organised programme
- Opportunistic screening
  - Patient examined for another reason or on request
- Case finding
  - Patient presents with lesion of concern that proves to be cancer
- Surveillance programme
  - Patient at high risk

US Preventive Services Skin Cancer Screening*

- Concludes that current evidence is insufficient to assess the balance of benefits and harms of visual skin cancer screening in adults
- Insufficient evidence on morbidity and mortality
- Evidence for harm: misdiagnosis, overdiagnosis, cosmetic and functional adverse effects

*USPSTF Screening for Skin Cancer. American Family Physician 2016;94:581

SCREEN

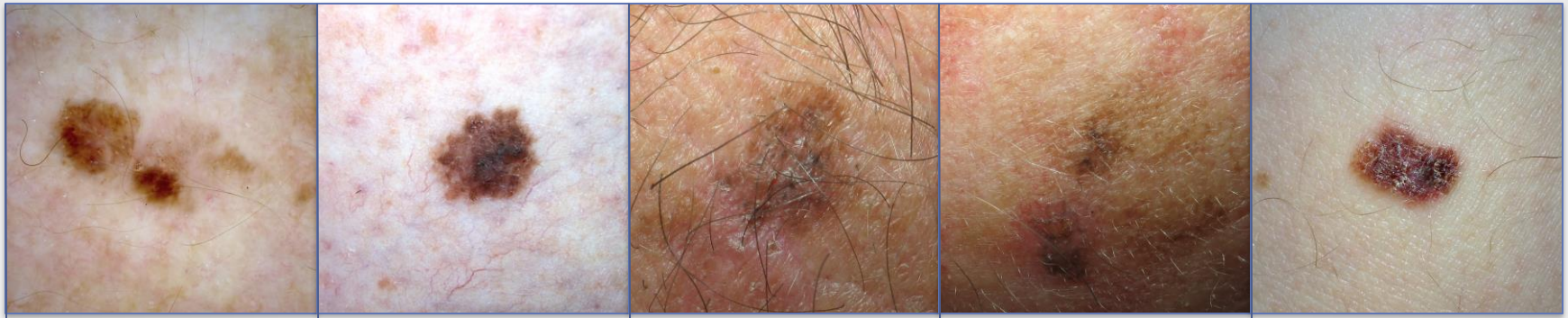
- **S**kin **C**ancer **R**esearch to provide **E**vidence for **E**ffectiveness of screening in **N**orthern Germany
  - Methodological limitations
- At most, **one** fewer melanoma death per 100,000 persons screened over a decade
  - 4.4% of screened individuals had an excision
  - 20–55 excisions performed for every melanoma detected
  - >4000 excisions needed to prevent one death from melanoma

J Invest Dermatol. 2014 Jan;134(1):43-50. doi: 10.1038/jid.2013.304. Epub 2013 Jul 22.

Non-melanoma skin cancer incidence and impact of skin cancer screening on incidence.

Eisemann N[1], Waldmann A[2], Geller AC[3], Weinstock MA[4], Volkmer B[5], Greinert R[5], Breitbart EW[6], Katalinic A[7].

Thin melanomas < 0.8 mm



0.4 mm	0.5 mm	0.6 mm	0.6 mm	0.75 mm

Deaths from melanoma

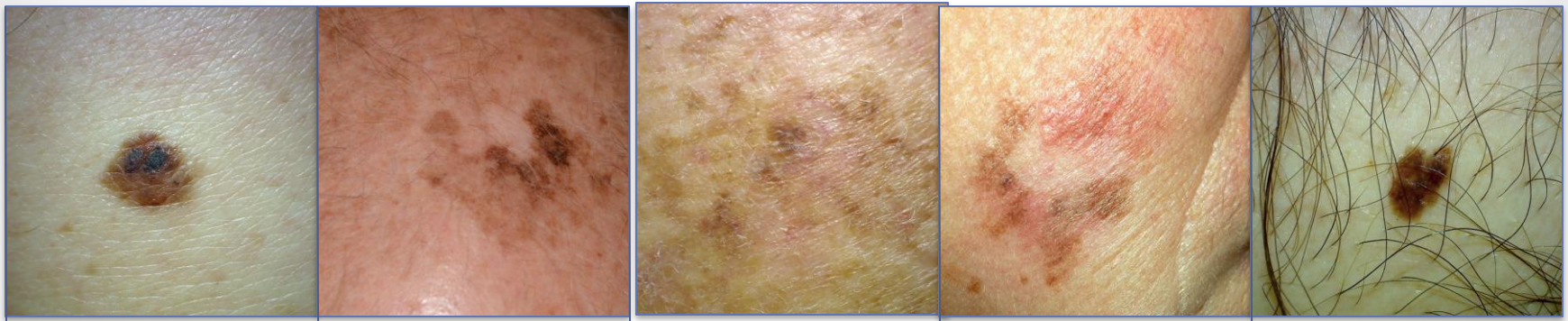
- >30% deaths are in patients with thin melanomas
- So, aim to diagnose melanoma while it's in situ
  - But aggressive melanomas may not have an in-situ phase
  - And aggressive melanomas generally present at an advanced stage

J Am Acad Dermatol. 2011 Nov;65(5 Suppl 1):S17-25.e1-3. doi: 10.1016/j.jaad.2011.04.032.

Recent trends in cutaneous melanoma incidence and death rates in the United States, 1992-2006.

Jemal A[1], Saraiya M, Patel P, Cherala SS, Barnholtz-Sloan J, Kim J, Wiggins CL, Wingo PA.

In situ melanomas



2. Excisions of benign lesions are justified, so as not to miss even a single melanoma.

- No figures available for New Zealand
- NNT* = 1 is 100% specificity
  - Poor sensitivity (ie melanomas are missed)
- NNT for melanoma probably ranges from 2 to 100
  - >500 in children
- NNT by dermatologist is lower than other groups
  - Probable range 2 to 10
- NNT lower with the use of dermatoscopy
  - Now reported by many studies

* NNT: number needed to treat a lesion suspicious of melanoma to find one

Aim to reduce:

- Number needed to treat NNT
- Benign: malignant ratio B:M
- Invasive melanoma: melanoma in situ ratio MM:MIS

Clin Exp Dermatol. 2014 Mar;39(2):129-34. doi: 10.1111/ced.12223.

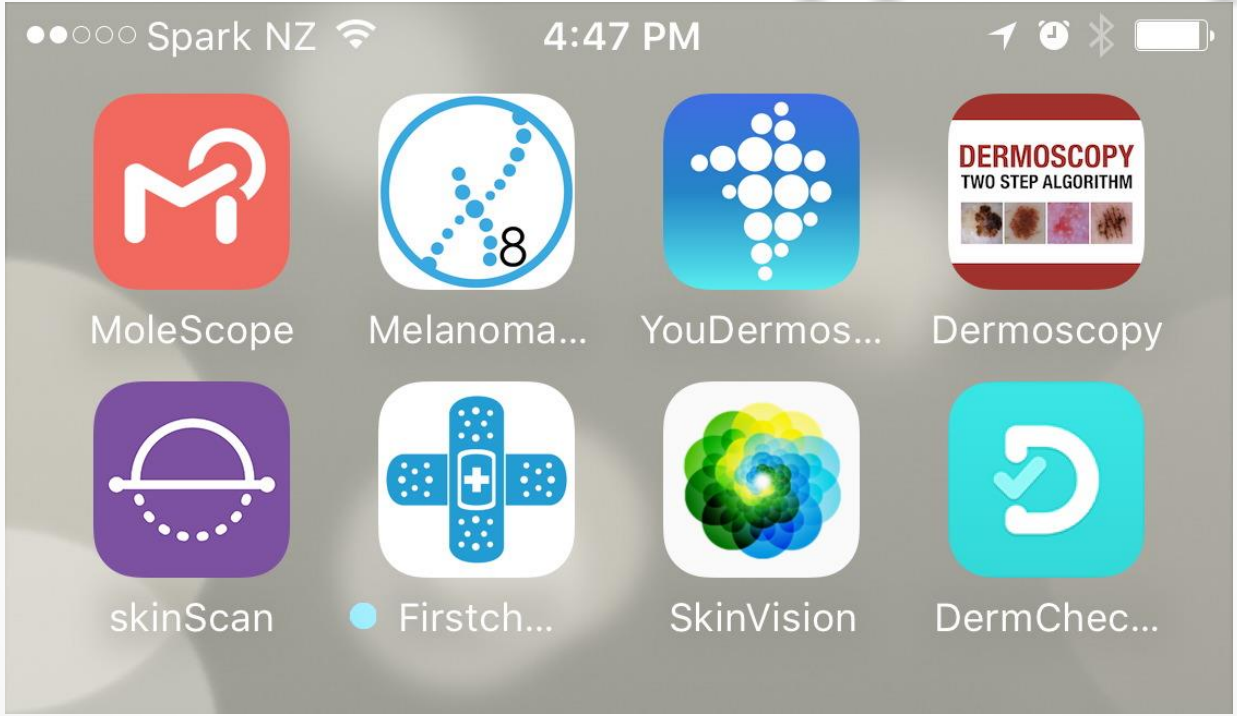
Diagnosing melanoma: how do we assess how good we are?

Esdaile B[1], Mahmud I, Palmer A, Bowling J.

3. Self-skin examination → early diagnosis

- Melanomas dx by HPs are thinner than those dx by patients
- SSE not shown to reduce mortality
- SSE is not cost effective (→ more excisions)
- Rates of SSE are low
- SSE may be warranted in high-risk patients

Do melanoma apps help?



Perhaps …

4. Patients >50 should have skin checks.

- Skin checks → More excisions
- Cancer Society does not recommend skin checks outside medical practice setting*
- Surveillance warranted for patients at high risk
- Remain alert for lesions with malignant features

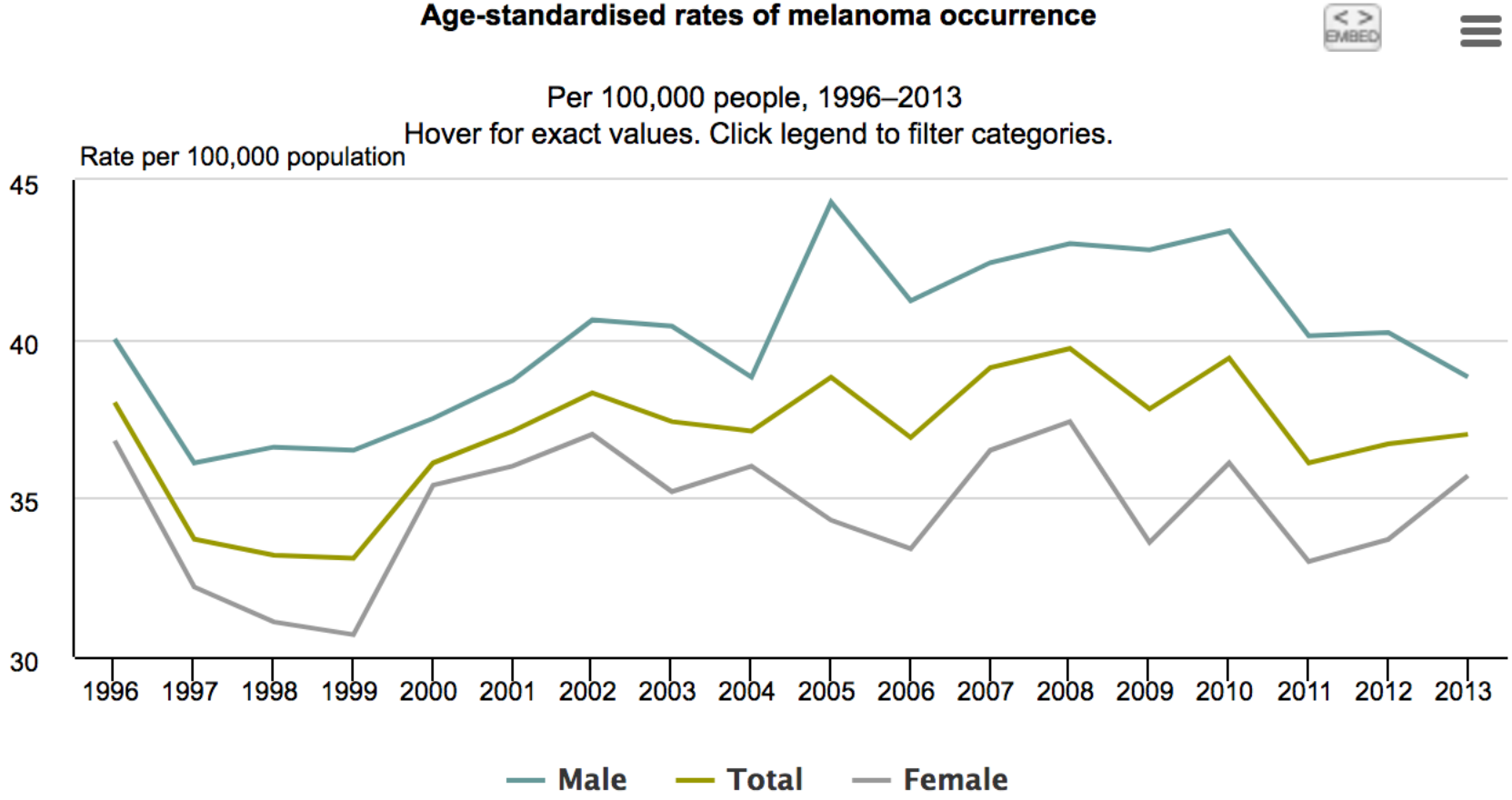
* Cancer Society of NZ Position Statement screening and early detection of skin cancer

Benefits of screening

- More thin melanomas are diagnosed
- More melanomas in situ are diagnosed
- Patients are reassured

Good: advanced disease may be prevented

Bad: MIS is harmless – unnecessary surgery


Age-standardised rates of melanoma occurrence
EMBED
Per 100,000 people, 1996–2013
Hover for exact values. Click legend to filter categories.
Rate per 100,000 population
45
40
35
30
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
Male
Total
Female

Who does screening?

- Mainly, undertrained health practitioners

→

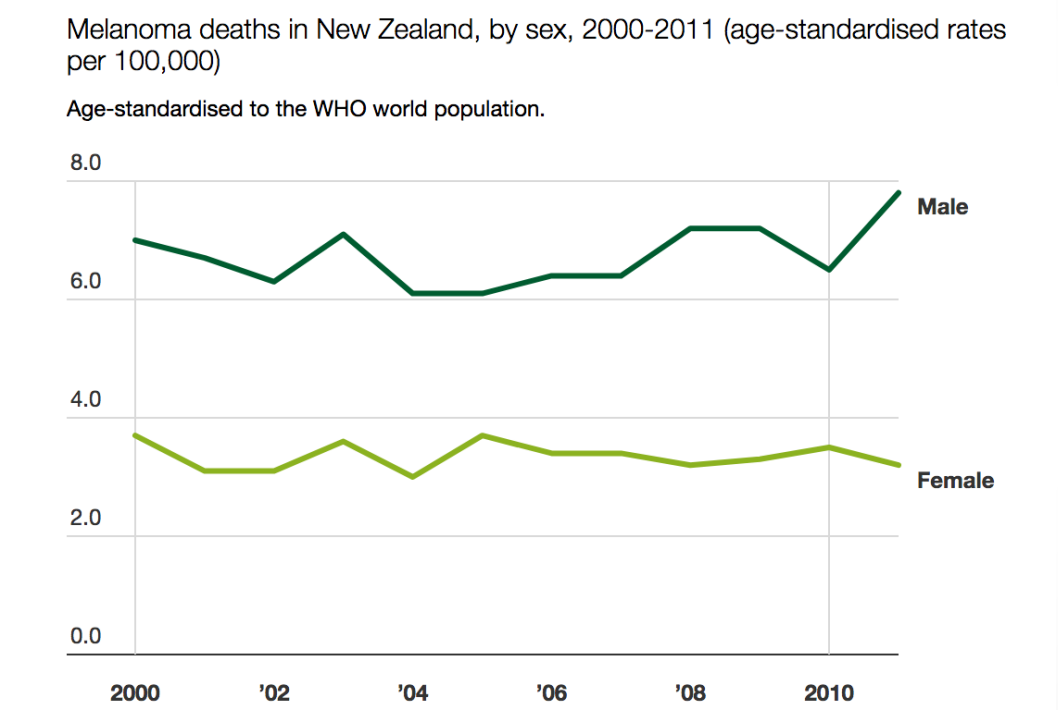
- High false positive rate (not specific)
- High false negative rate (not sensitive)

- Excisions are often in people at low risk, eg young adults

Harms due to screening

- Overdiagnosis – melanoma in situ is harmless
- No change in outcome – just an increase in time that the patient knows they have cancer (lead-time bias)
- Harm from surgery
  - Scar, discomfort, functional limitations, cost
  - Wound breakdown, infection, drug allergy, hospitalisation …
- Harm from doctors visits / referrals
- Distress to patients
- Enormous expense $$$$

Melanoma mortality



Numbers of excisions

- Who knows?
- 1.1 m. publicly funded hospital discharges in 2014
  - 14,141 were coded as nonmelanoma skin cancers
  - 2,021 were coded as melanoma
  - 1,119 melanocytic naevi
  - 605 seborrhoeic keratosis
  - 645 other benign neoplasms
- 91,000 Privately funded hospital discharges in 2014
  - 333 were coded as melanoma or other skin cancer

NNT: what is the benchmark?

• • •

Unknown. Perhaps 5.

Most lesions excised due to suspicion of melanoma are benign

- Melanocytic naevi
- Seborrhoeic keratoses
- Angiomas

Who should have a skin check?

- Population screening of asymptomatic adults is not justified
- But two-thirds of melanomas are diagnosed in "low risk" subjects

Skin checks may be justified in:

- Patients presenting with suspicious lesion
- Patients with previous melanoma, SCC, multiple BCCs, immune suppressed, familial syndromes

When not to do skin checks

- Patients at low risk of melanoma
  - Children
  - Dark skin

  Unless they present with a suspicious lesion
- Patients with low life expectancy
  - Very old
  - Very sick, eg end-stage renal disease

5. A dermatologist should triage all suspicious lesions.

- FTF review of every patient is not practical
- Whole body digital dermatoscopic surveillance
  - Effective
  - But expensive
- Teledermatoscopy referral clinics effective
  - Financial savings, fewer FSAs, fewer unnecessary procedures, faster cancer treatment

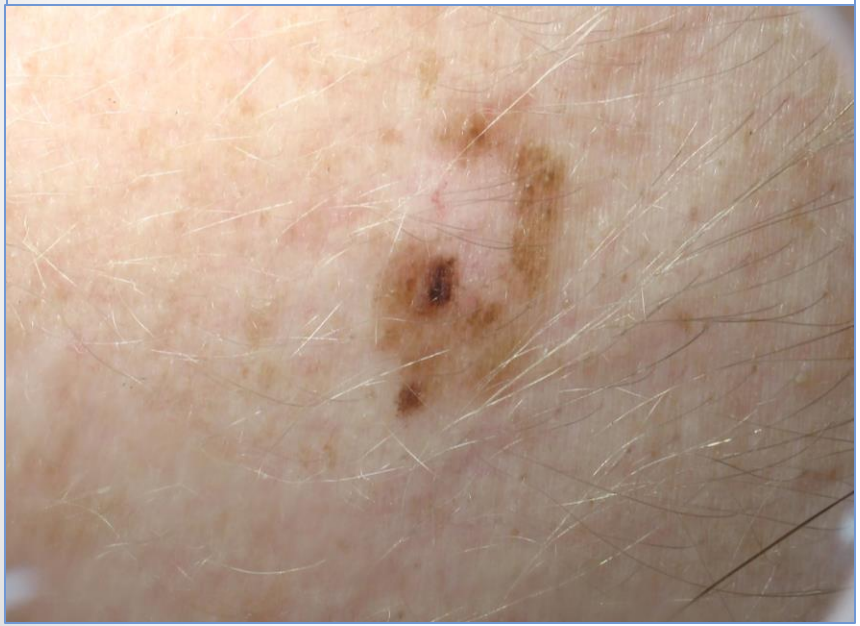
J Eur Acad Dermatol Venereol. 2015 Dec;29(12):2423-8. doi: 10.1111/jdv.13309. Epub 2015 Sep 15.

Successful melanoma triage by a virtual lesion clinic (teledermatoscopy).

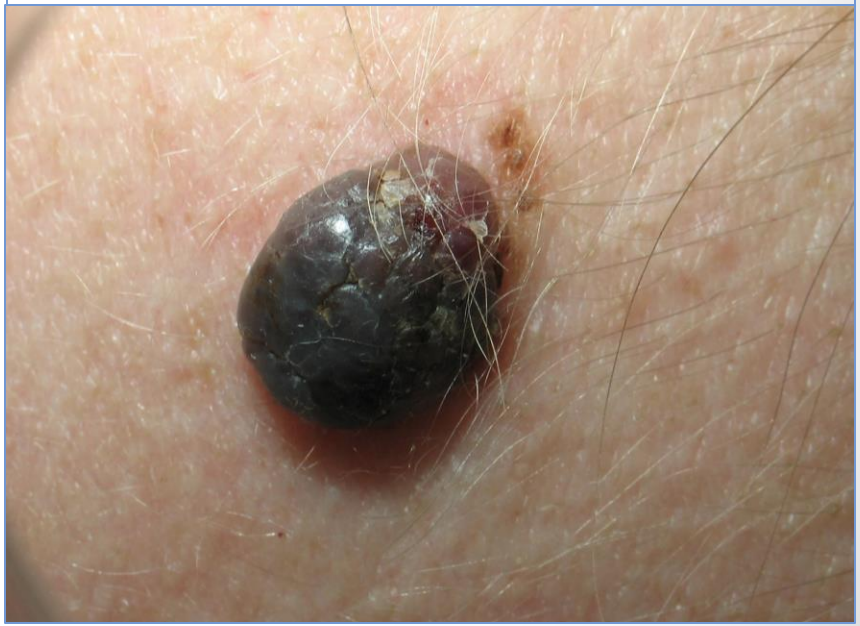
Congalton AT[1], Oakley AM[2,3], Rademaker M[2,3], Bramley D[4], Martin RC[1].

False negative by dermatologist

April 2010



November 2011: 7 mm



6. Every doctor should be trained in skin examination/dermatoscopy.

YES!

- Every *medical student* should be trained in skin examination and dermatoscopy

- Don't forget other health professionals
  - Plus beauticians, hairdressers and the general public

Train the workforce

- Training improves detection rates*
- Training reduces unnecessary referrals
- Training reduces unnecessary surgeries
- Markedly reduces costs, morbidity
  - But perhaps not mortality

*INFORMED training program

Best way to spot a melanoma?

- Ugly duckling sign

New Zealand Dermatological Society Inc. Annual Scientific Meeting
AUSTRALASIAN JOURNAL OF DERMATOLOGY
Volume 56, Issue 4, November 2015, Pages: A1–A7,

Triaging lesions suspicious for melanoma

L. Chan,[1] K. Cullingham,[2] A. Oakley[1,3]

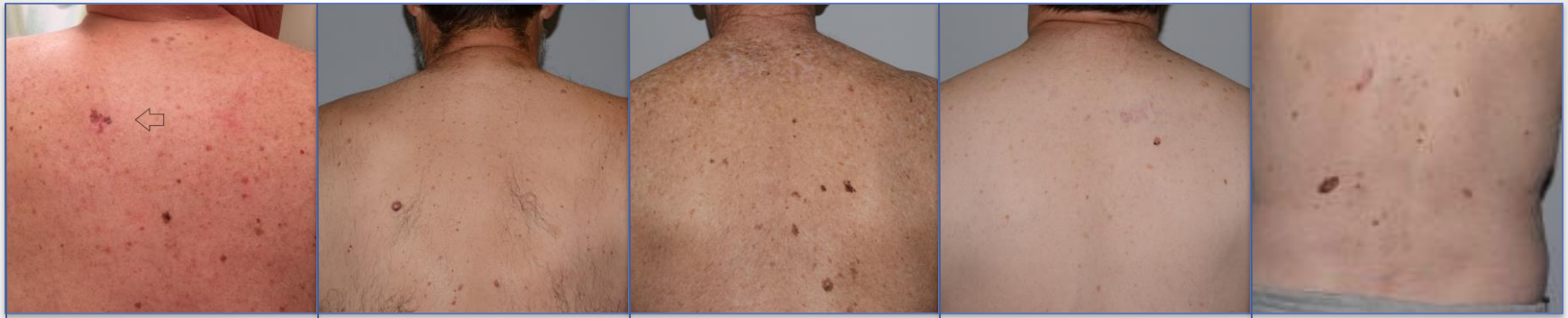
"On review of the clinical photographs, lesions were more likely to be ugly ducklings (65/70) than having a diameter greater than 6 mm (58/70)."

Arch Dermatol. 2008 Jan;144(1):58-64. doi: 10.1001/archdermatol.2007.15.

The "ugly duckling" sign: agreement between observers.

Scope A[1], Dusza SW, Halpern AC, Rabinovitz H, Braun RP, Zalaudek I, Argenziano G, Marghoob AA.

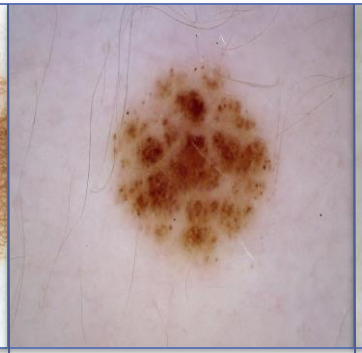
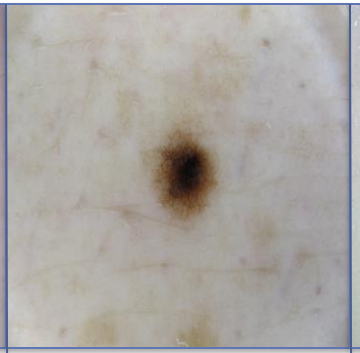
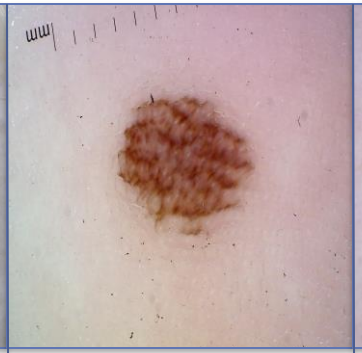
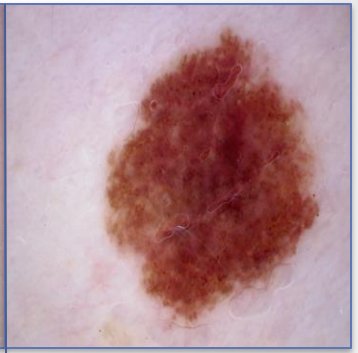
Ugly duckling



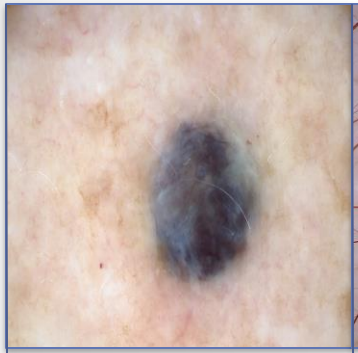
Learn dermatoscopy: to diagnose common benign lesions

- Benign melanocytic naevi
- Solar lentigines
- Seborrhoeic keratoses
- Angiomas
- Dermatofibromas

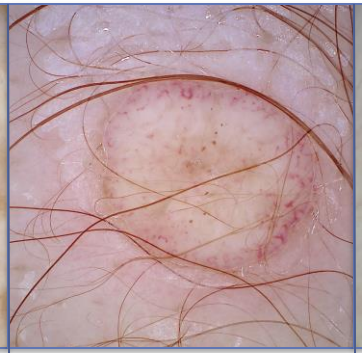
Flat naevi

				
Reticular	Repeating	Lentiginous	Parallel	Clark naevus

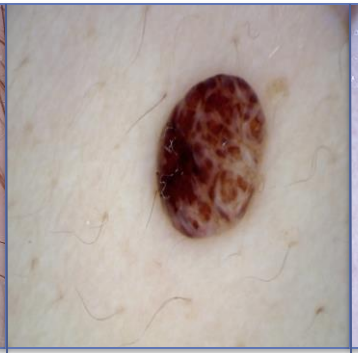
Dermal naevi



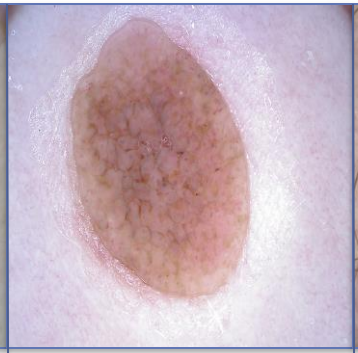
Blue



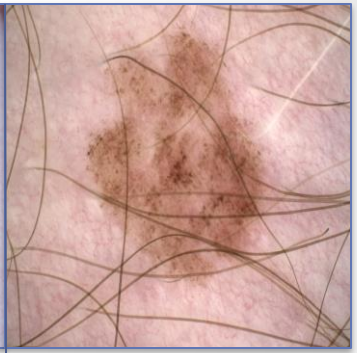
Comma vessels



Non-papillomatous

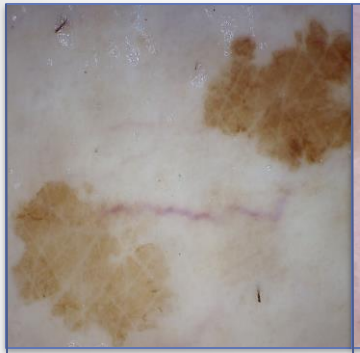
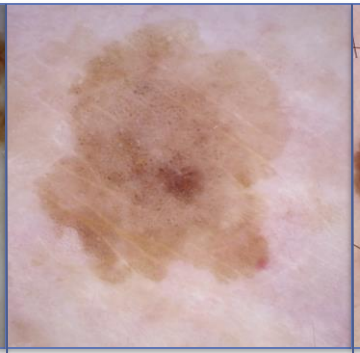
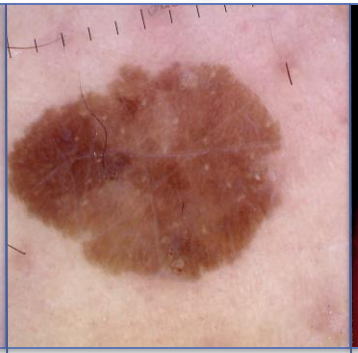
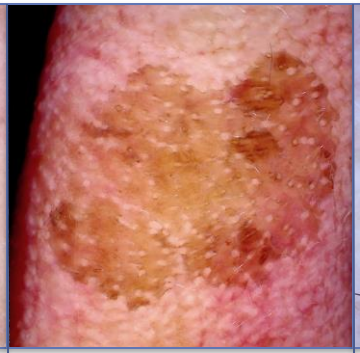
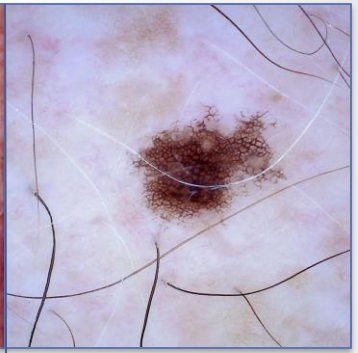


Papillomatous

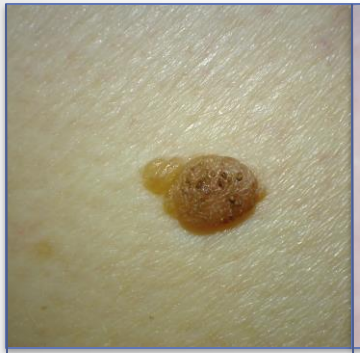
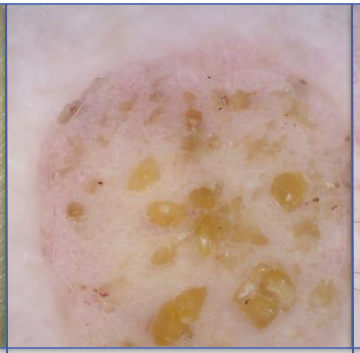
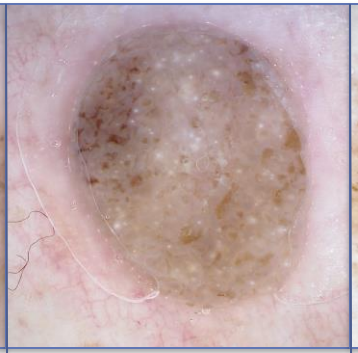
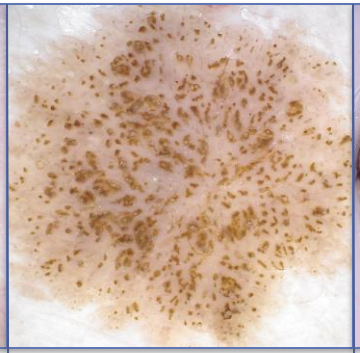
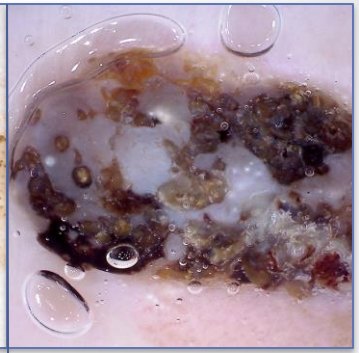


Cockade

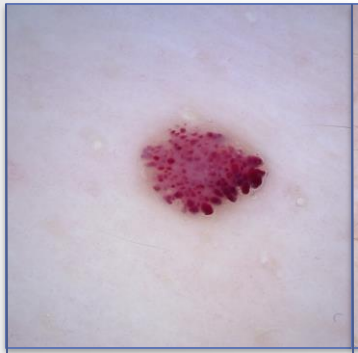
Lentigines

				
Ephilides	Moth-eaten	Fingerprinting	Psuedoreticular pattern	Ink spot lentigo

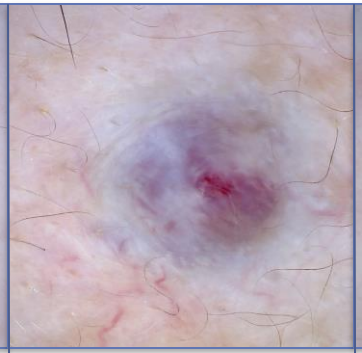
Seborrhoeic keratoses

				
Stuck on	Orange clods	White clods	Brain-like	Chaotic but harmless

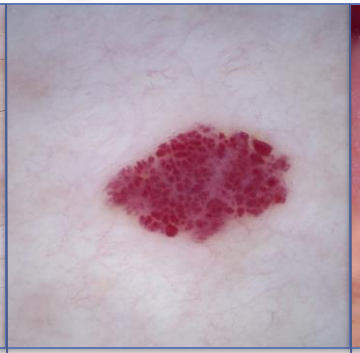
Angiomas



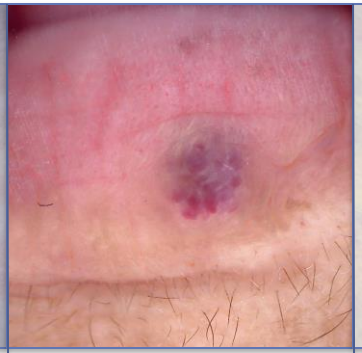
Red



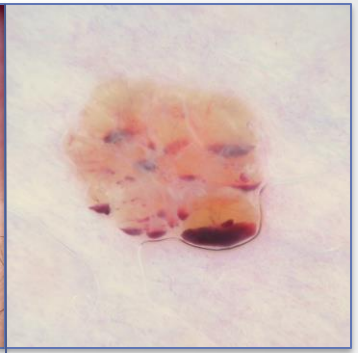
Blue



Clods

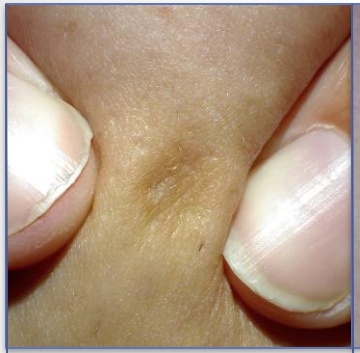


Lip

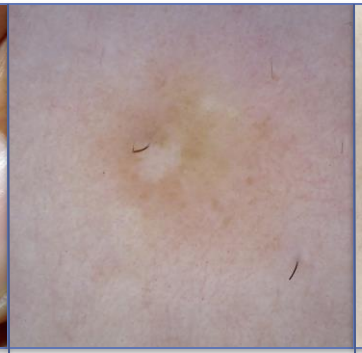


Lymphangioma

Dermatofibromas

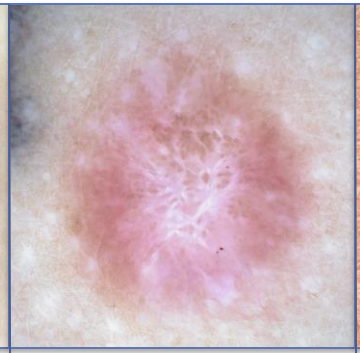


Pinch sign

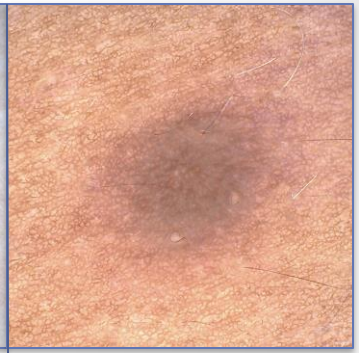


White centre

Fine pigment network



Radial lines

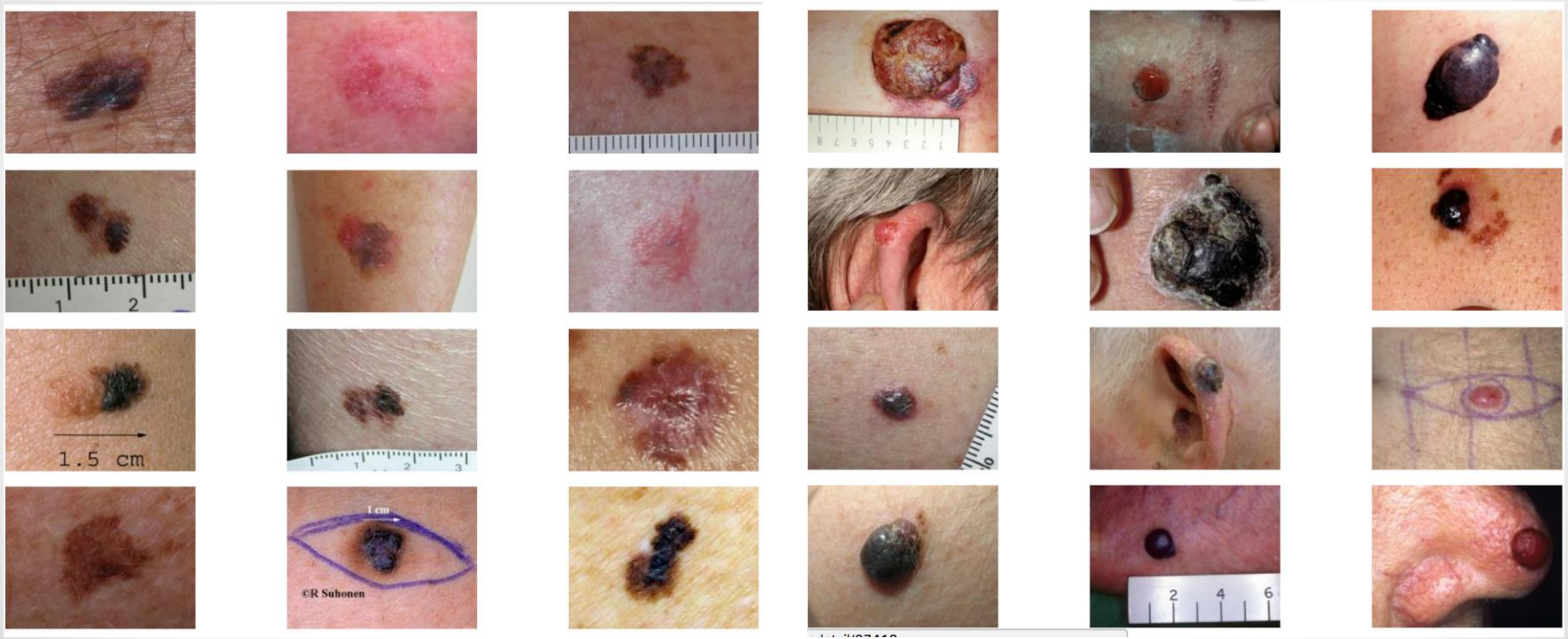


Absent white centre

Perceptual learning

- We learn by repetition
- We see lots of benign lesions
- We don't see many melanomas
- Training should include lots of images of benign and malignant skin lesions

Lots of melanoma pix



Perceptual adaptive learning module: PALM

- Computer based system for teaching pattern recognition
- Radiology, ECGs, dermatology, histopathology
- Coming soon, dermatoscopy!

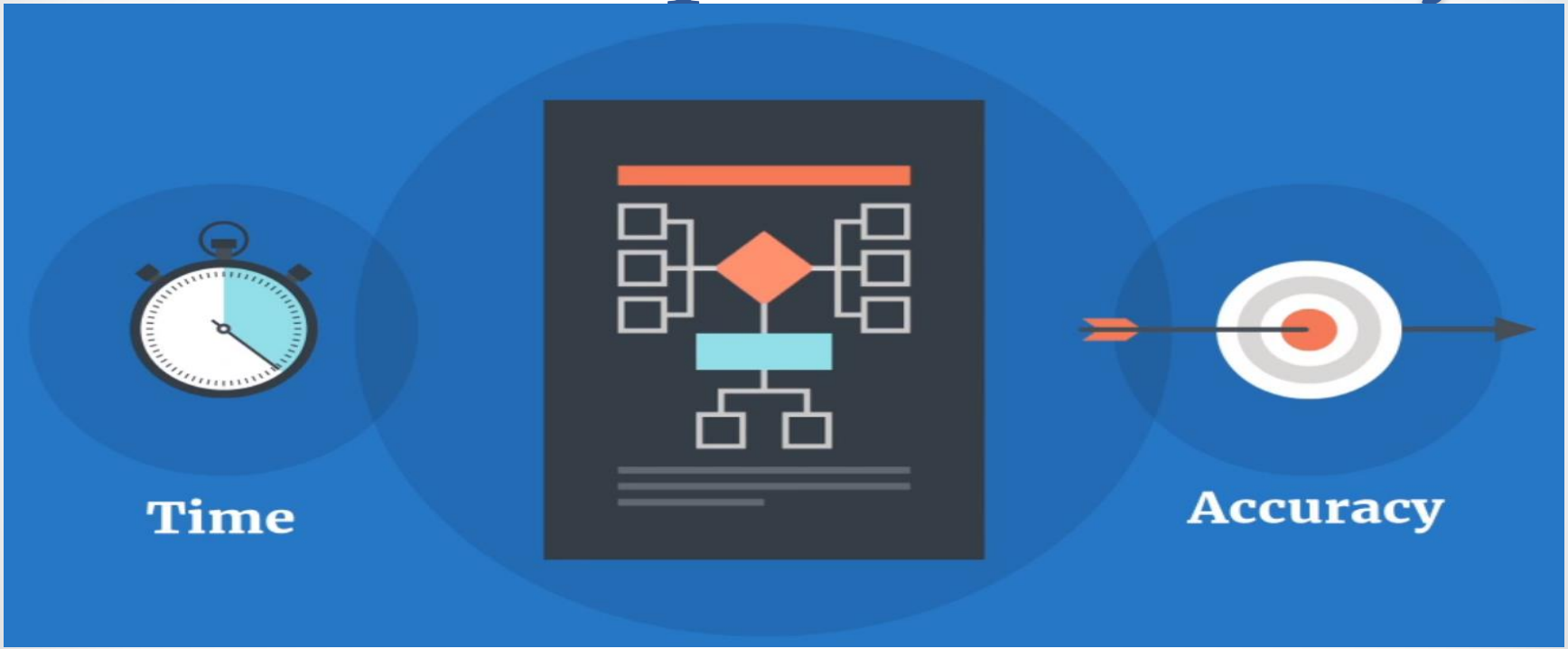
http://med.insightlt.com/site/

Adaptive responsive time based sequencing system

- ARTS
- Algorithms space and sequence different diagnoses according to the learner's accuracy and response time
- Accuracy of diagnosis improves
- Speed of response improves

http://med.insightlt.com/site/

Measure speed/accuracy



http://med.insightlt.com/site/

7. Can machines diagnose melanoma?

- Machines have been used to image the lesion
- Priority has been sensitivity (eg, 100%*)
  → low specificity (eg, 5.5%*)
- Small datasets used for training/testing

* Fink et al, J Dtsch Dermatol Ges 2017;15:414

NZ Melanoma Standards 2013

Standards of Service Provision for Melanoma Patients in New Zealand – *Provisional*

National Melanoma Tumour Standards Working Group

Clinicians do not rely on the use of automated instruments alone to diagnose primary melanoma.

Aus Melanoma guidelines 2017

View

What is the role of automated instruments in melanoma diagnosis?

(Redirected from Guidelines:Melanoma/Automated instruments)

Clinical practice guidelines for the Diagnosis and Management of Melanoma > **Clinical question**

There is insufficient evidence to recommend the routine use of automated instruments for the clinical diagnosis of primary melanoma. However, particularly when a benign measurement is found using the cited protocols of Nevisense™ and MelaFind™, this information may aid the clinician.

Cancer Council Australia

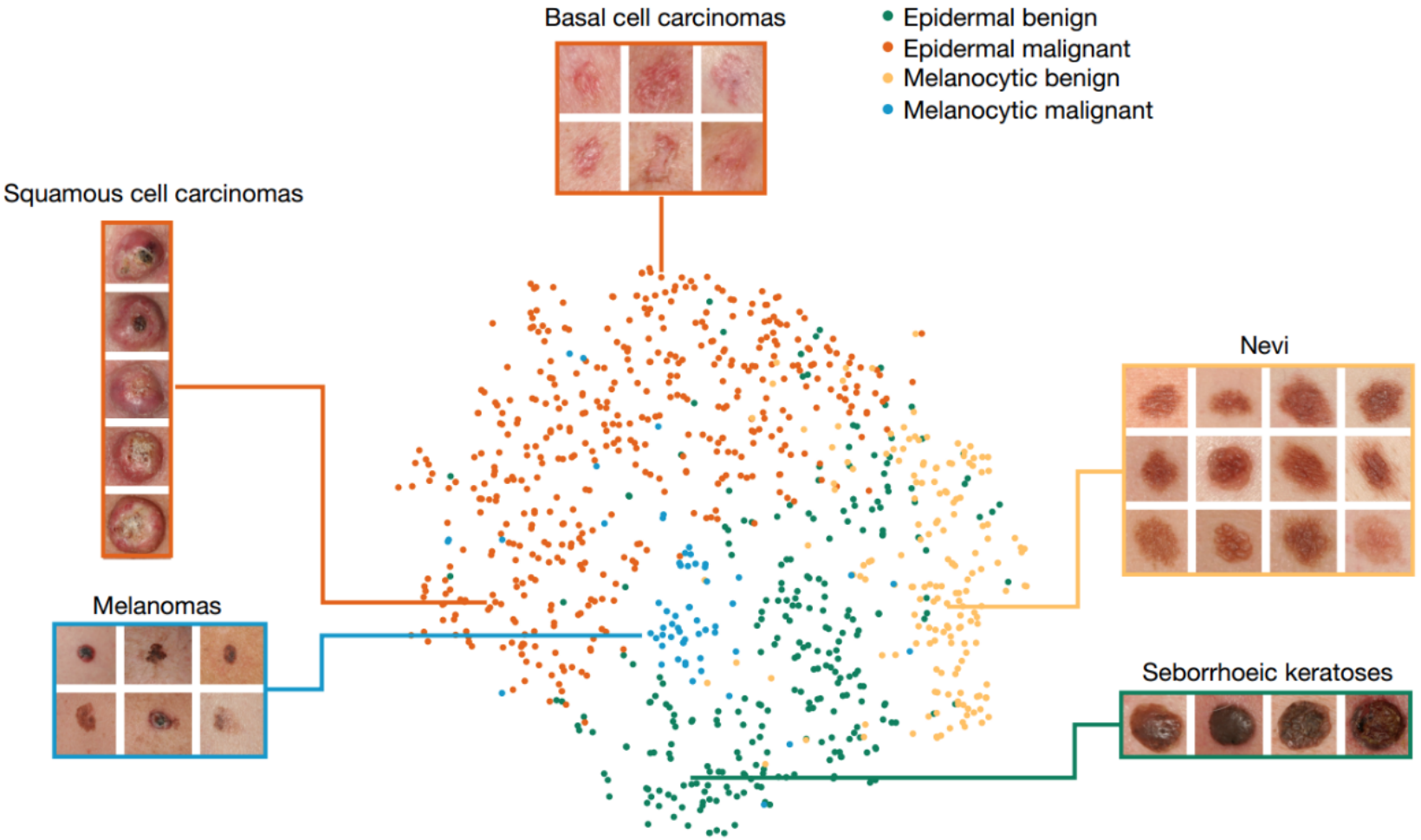
Artificial intelligence wins

- In 2017, a machine equalled or bettered the experts
- 129,450 images in its dataset
  - 2,032 different diseases
- Tested:
  - Keratinocyte carcinomas vs. seborrheic keratoses
  - Melanomas vs. benign nevi

Nature. 2017 Feb 2;542(7639):115-118. doi: 10.1038/nature21056. Epub 2017 Jan 25.

Dermatologist-level classification of skin cancer with deep neural networks.

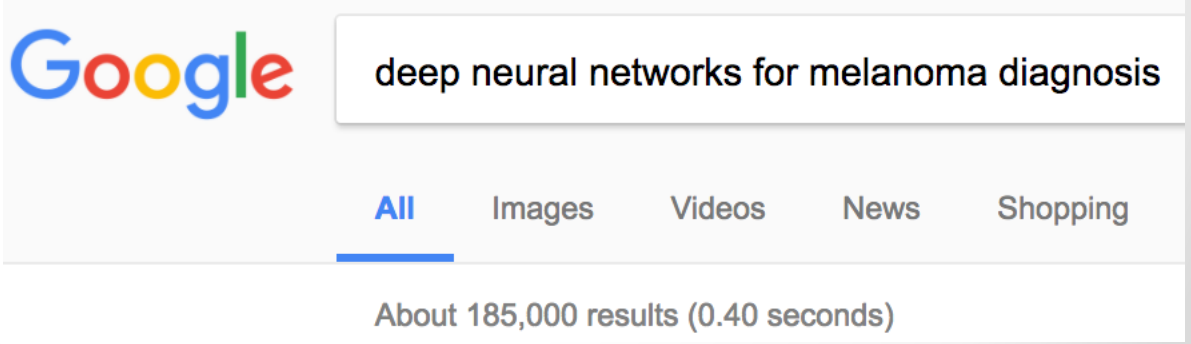
Esteva A[1], Kuprel B[1], Novoa RA[2,3], Ko J[2], Swetter SM[2,4], Blau HM[5], Thrun S[6].



This is how the AI split up what it saw into different categories. Fig. 1b, Esteva, Kuprel et al., 2017

Intelligent assistance

- Deep neural networks will assist health practitioners to diagnose melanomas from their own photos
- Timeframe: 2–5 years. Maybe less …
- Availability will linclude mobile personal devices
- Accurate
- Inexpensive



Computer assisted diagnosis

Some conclusions

...

Prevention better than cure

- USPSTF recommends that children and adults with fair skin be counselled about **minimising their exposure to ultraviolet radiation** to reduce their risk of developing skin cancer

Self-skin examination

- Teach our **high-risk patients** to conduct thorough and regular SSE
- Use apps to support these
- Supplement SSE by occasional skin checks in primary care

Support primary care

1. Encourage DHBs and PHOs to provide **teledermatoscopy services** to GPs
2. Encourage training of all GPs and other HPs in skin examination
3. Encourage interested GPs to undertake accredited courses and training programmes
   - University of Queensland
   - HealthCert
   - Skin Cancer College of Australasia

Bring on AI!

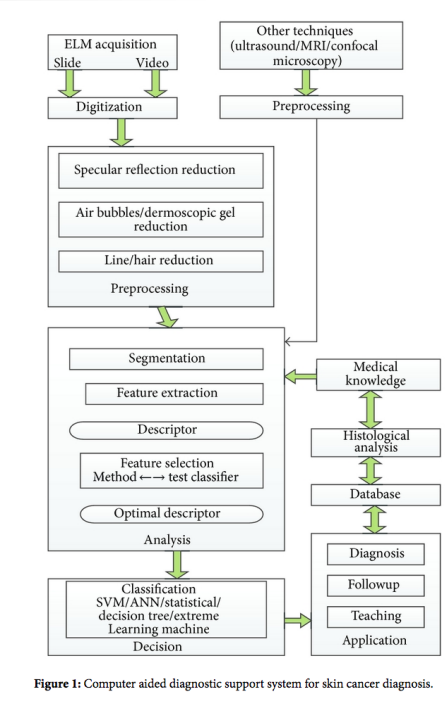
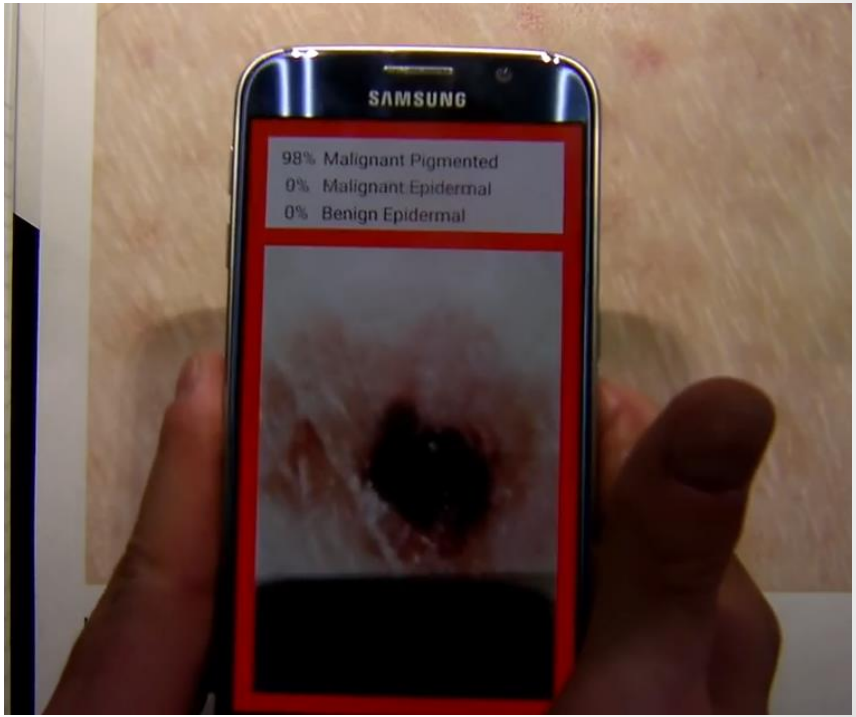


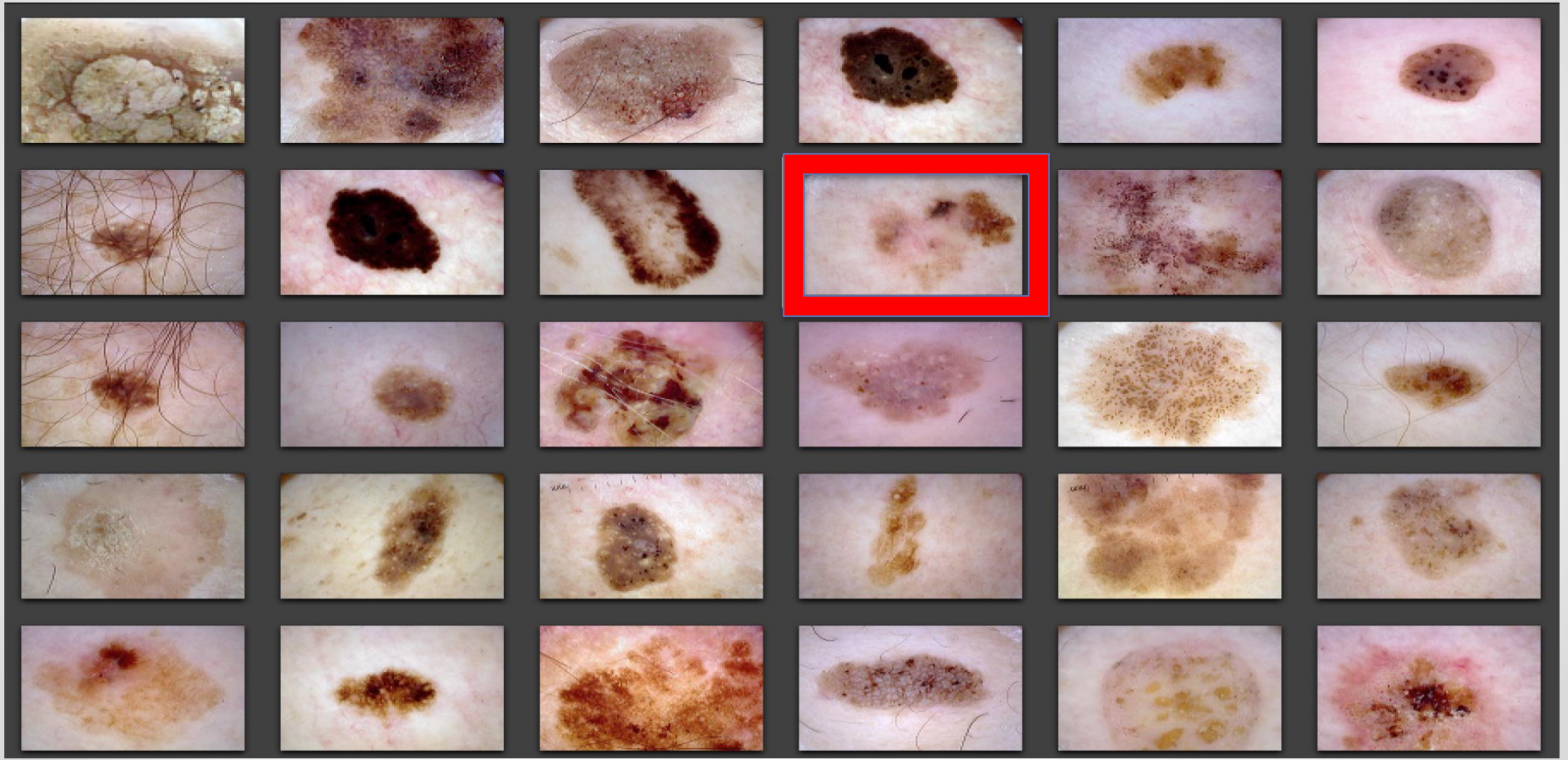
Figure 1: Computer aided diagnostic support system for skin cancer diagnosis.

https://www.hindawi.com/journals/ijbi/2013/323268/fig1/



https://medium.com/towards-data-science/what-happened-at-the-tensorflow-dev-summit-2017-part-1-3-community-applications-77fb5ce03c52

If deep learning can spot the melanoma,



I will be able to retire!

Amanda@DermNetNZ.org