

# GENETISCHE ONDERZOEK BIJ HUIDKANKER: HET ONTBREKENDE PUZZELSTUKJE?

Nascholing: DNA-diagnostiek, Precision medicine  
en Immunotherapie in de kliniek

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# Disclosures

(potentiële) belangenverstengeling	Zie hieronder
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
<ul style="list-style-type: none"><li>• Sponsoring of onderzoeksgeld</li><li>• Honorarium of andere (financiële) vergoeding</li><li>• Aandeelhouder</li><li>• Andere relatie, namelijk ...</li></ul>	<ul style="list-style-type: none"><li>• Research grant: Sanofi, MSD, BMS, Pierre Fabre, Novartis, SkinVision en SkylineDx.</li><li>• Adviesraad: Leo Pharma, Sanofi, SunPharma</li><li>• Erasmus MC: Rotterdamse bril</li></ul>



Cancer Institute

C2a.org

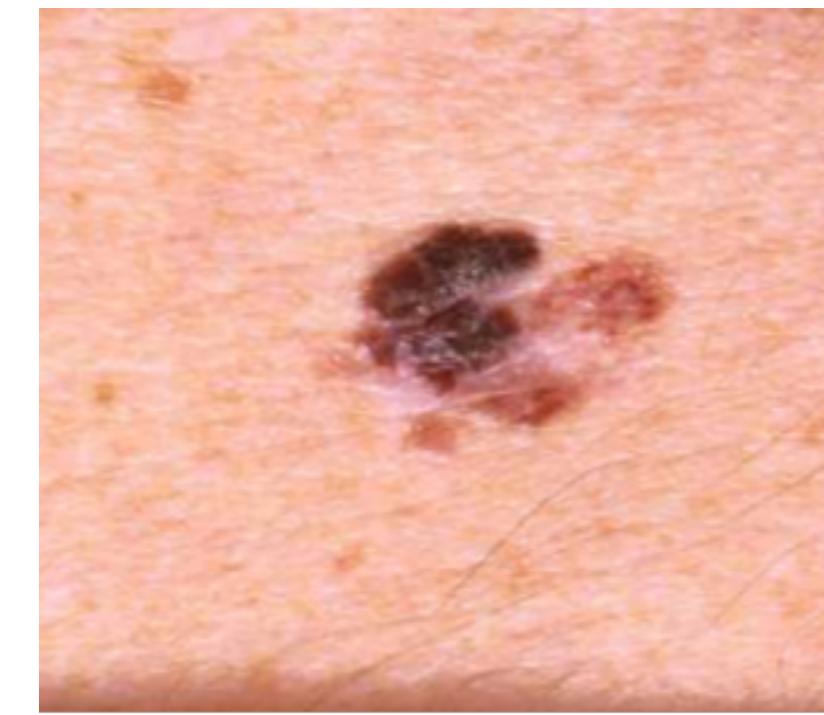
## Basal cell carcinoma



## Squamous cell carcinoma



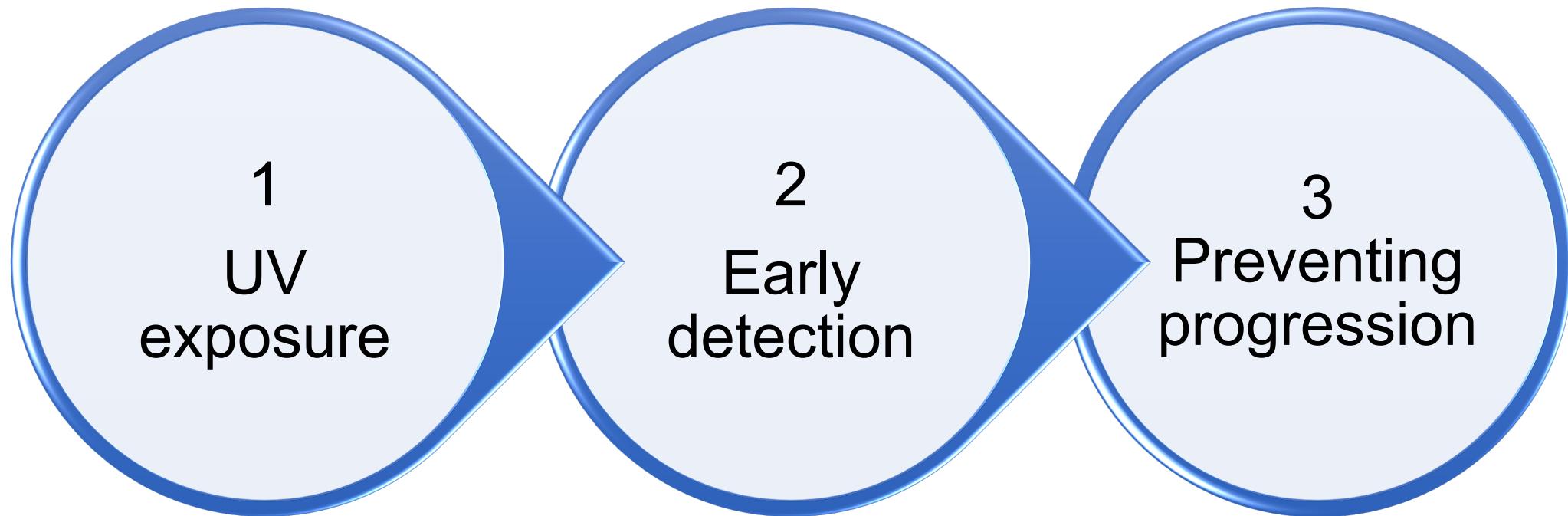
## Melanoma



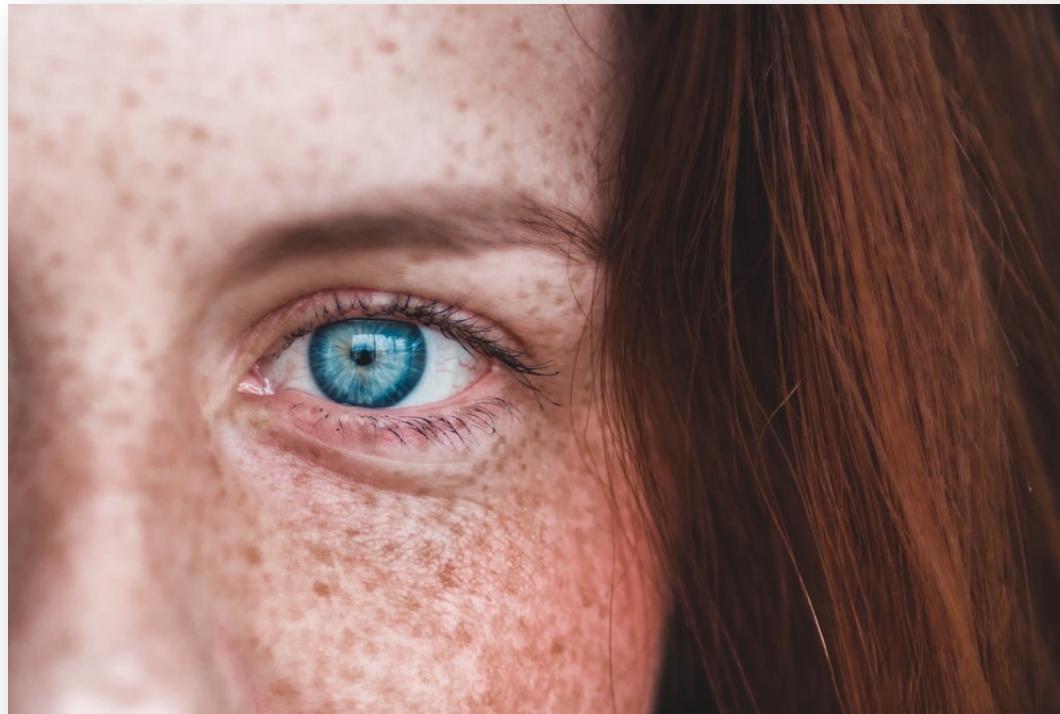
Incidence

Mortality

# Skin Cancer Prevention

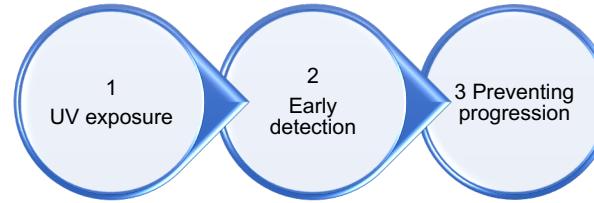


# Secondary prevention



Sarin et al, Nat Commun 2020, Hysi et al., Nat Genetics 2019, Visconti Nat Commun 2018

# Secondary prevention

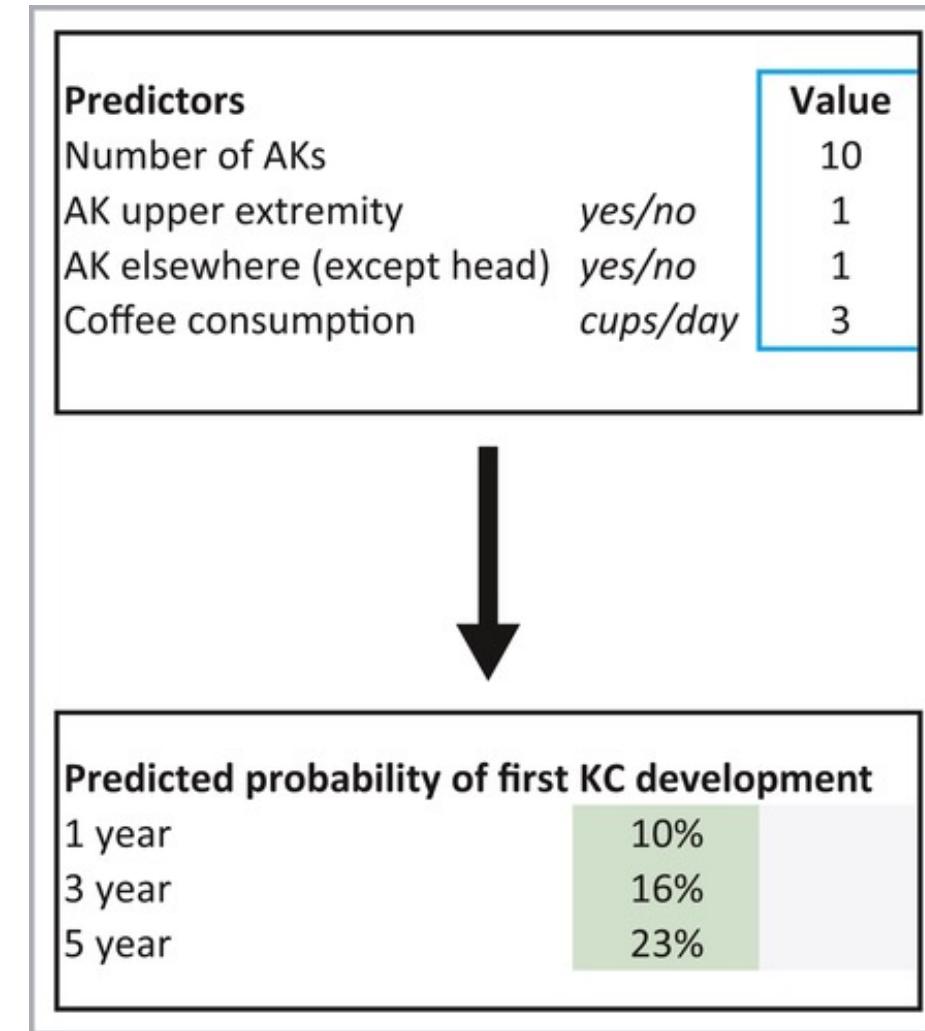
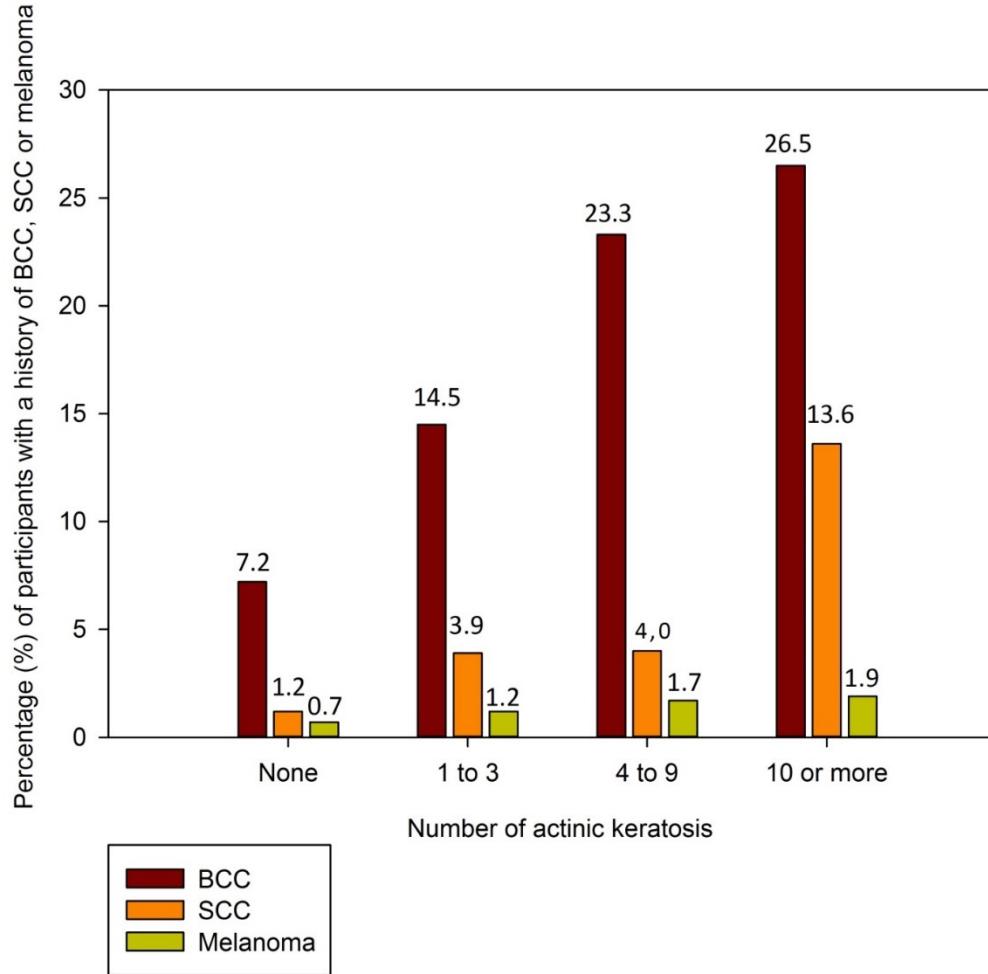


## Actinic keratoses

Prevalence: 49% men, 28% women

Flohil SC et al., JID 2013; 133: 1971-8

# Secondary prevention: Skin cancer prediction model



researchapps.github.io/cSCCsco...

Managed bookmarks American Joint Co...

## Squamous Cell Skin Cancer (cSCC) Web Prediction Tool.

**History**

**About**

**Patient History**

I have been diagnosed in the past with an invasive squamous cell skin cancer

True  
 False

I have been diagnosed in the past with an actinic keratosis

True  
 False

**Genetic Risk**

I have been typed for the 16 genetic variants associated with increased risk of squamous cell skin cancer ([view polymorphisms](#))

True  
 False

**Family History**

Based on the squamous cell skin cancer histories of my parents, siblings and children, my genetic risk for this cancer is

Low

My current age is 60 years

My gender is

Male  
 Female

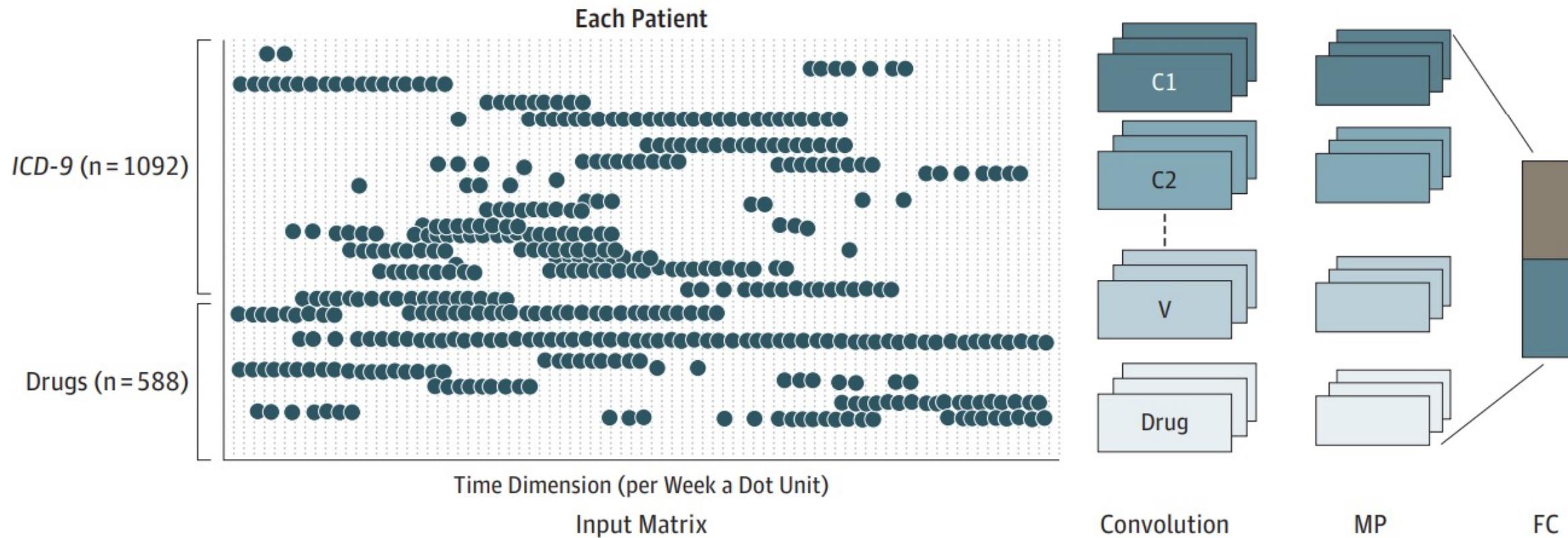
My tendency to sunburn is

Low

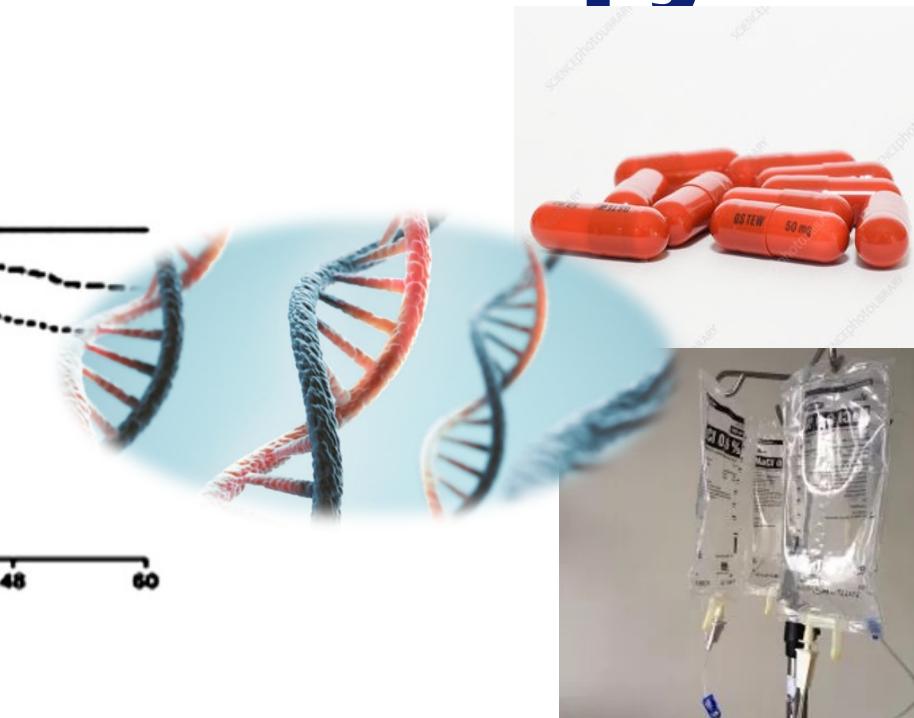
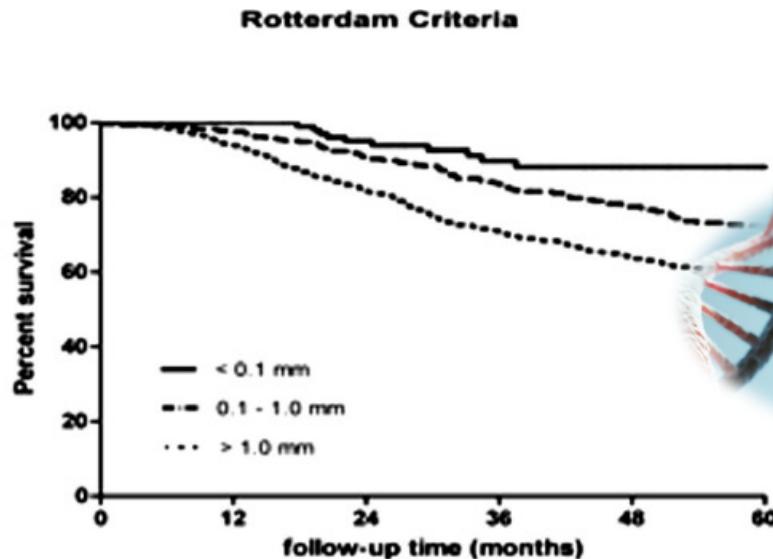
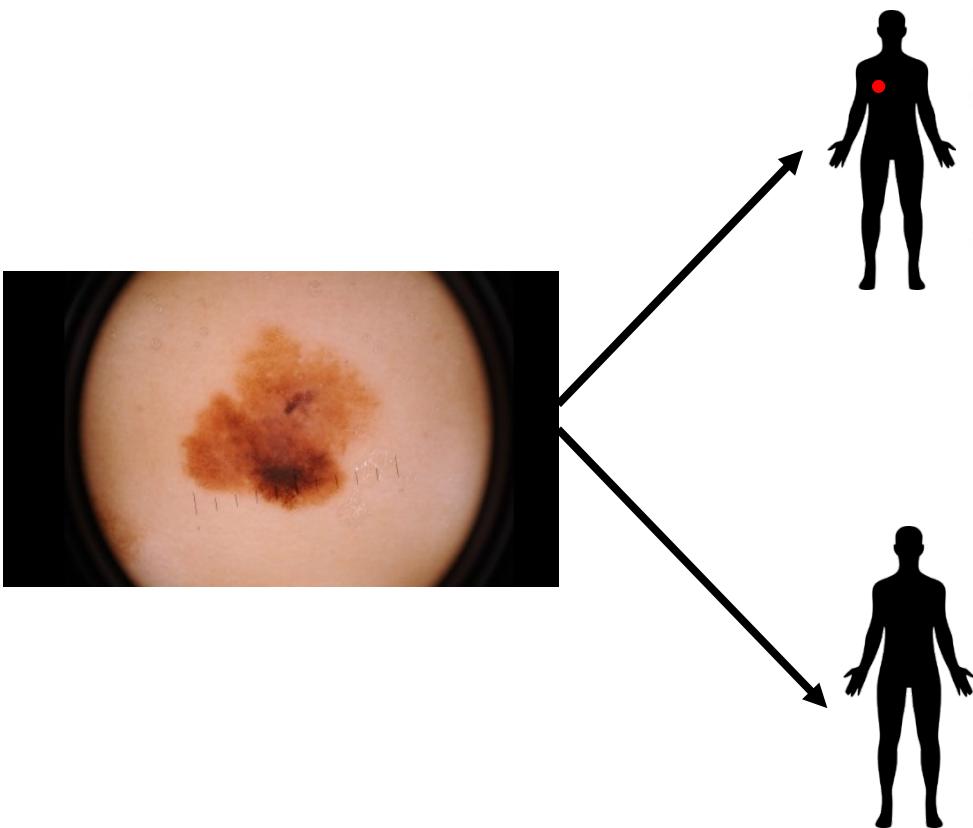
Calculate

Wang et al, JID 2018

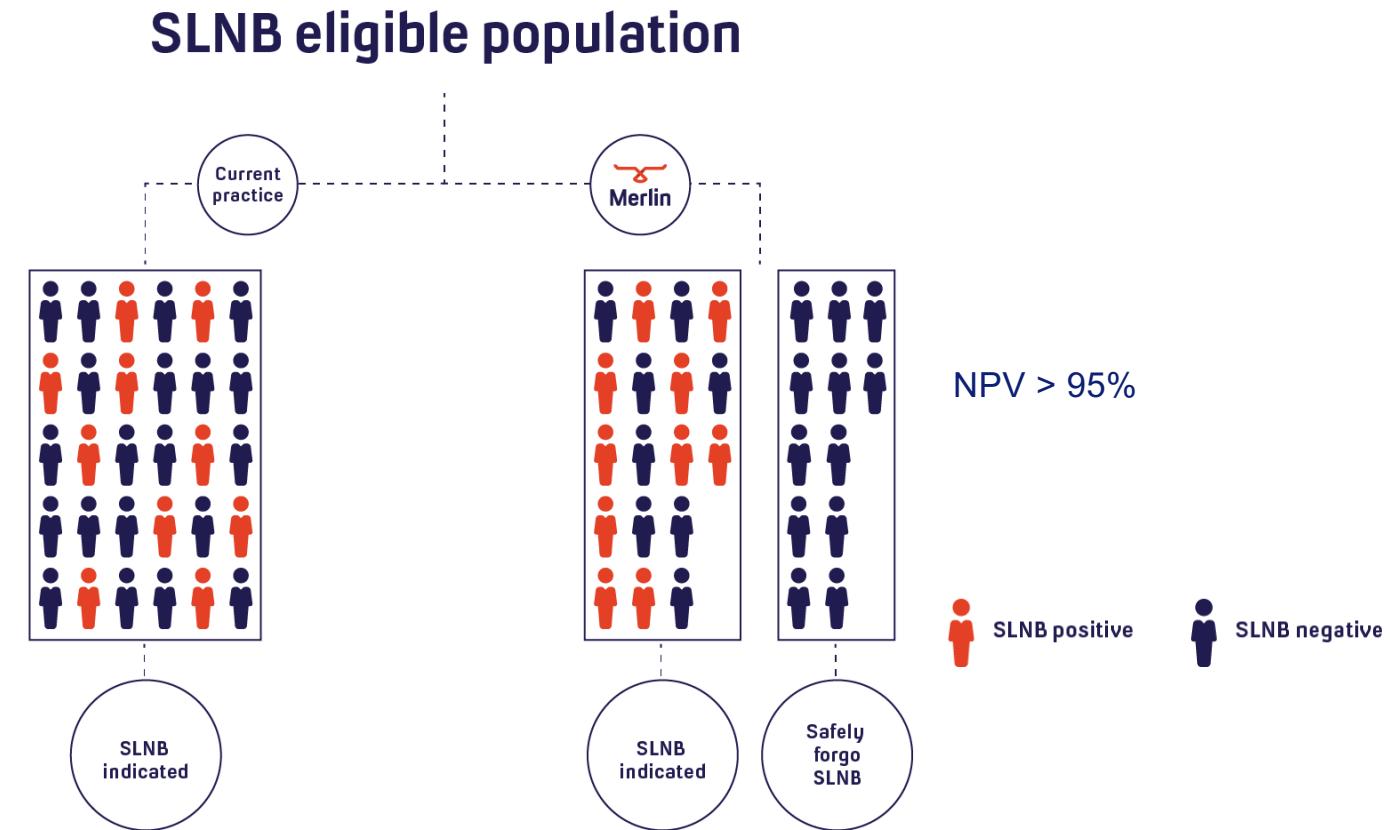
# Assessment of Deep Learning Using Nonimaging Information and Sequential Medical Records to Develop a Prediction Model for Nonmelanoma Skin Cancer



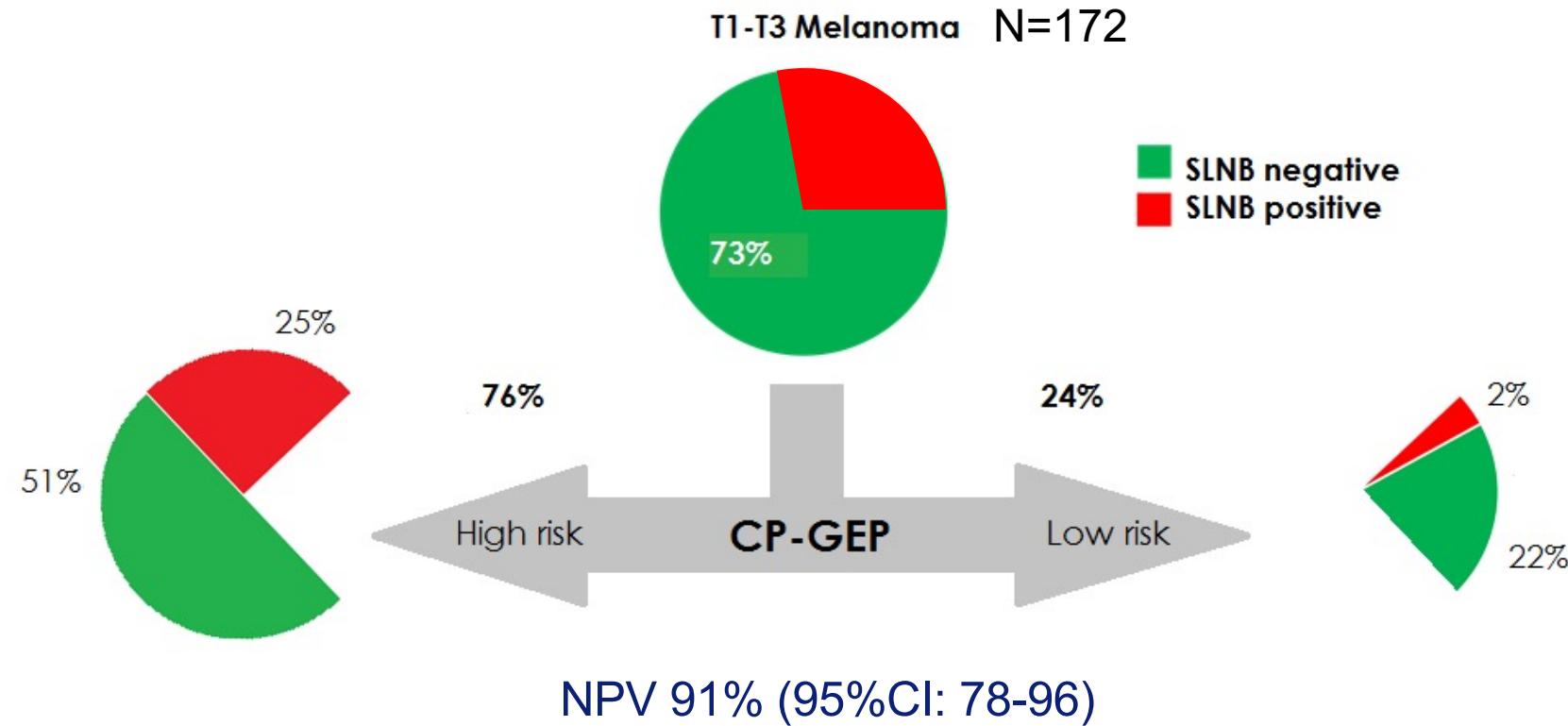
# Tertiary prevention: adjuvant therapy



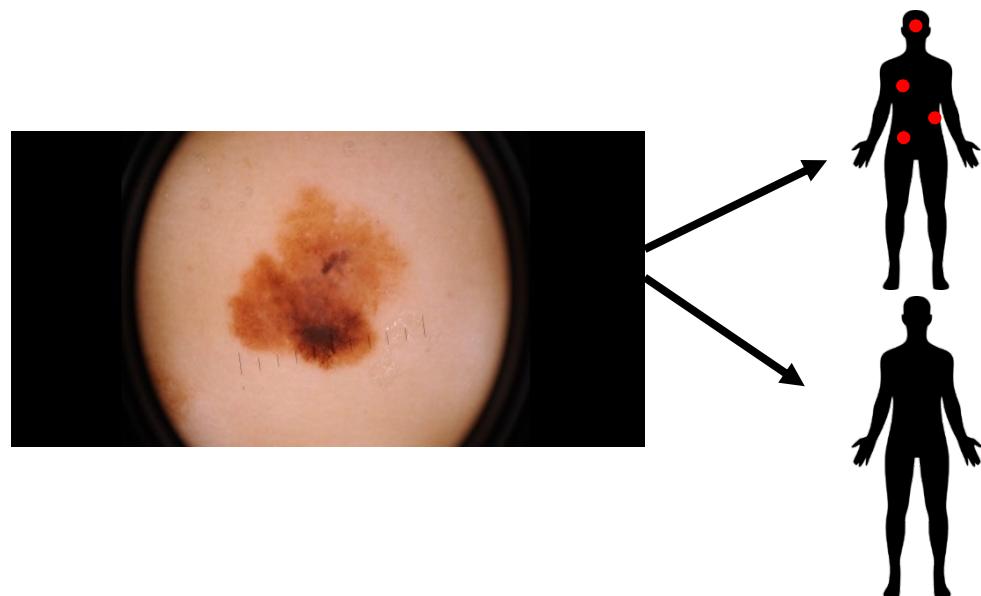
# Tertiary prevention: Predicting sentinel lymph node metastasis in melanoma



# Tertiary prevention: Predicting sentinel lymph node metastasis in melanoma

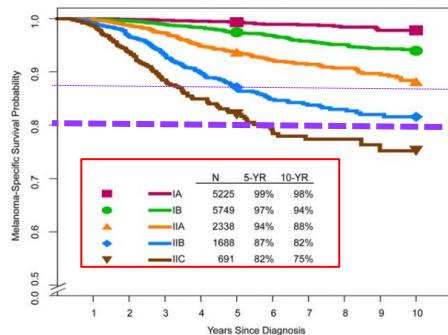


# Next steps in tertiary prevention: signatures for distant metastasis/survival

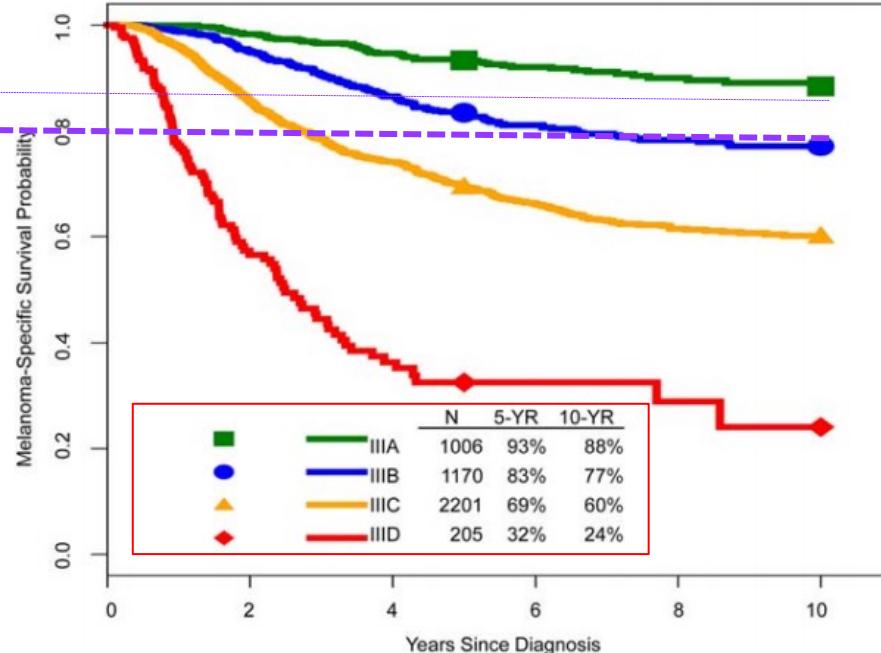


# Next steps in tertiary prevention: Also relevant for thin melanomas

Stage II



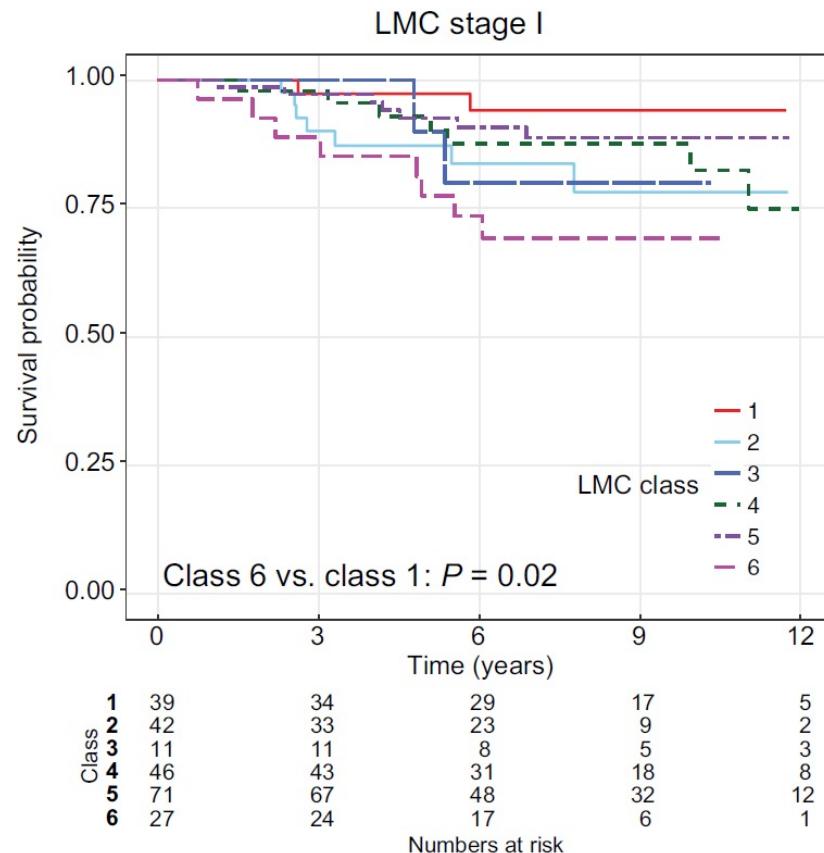
Stage III



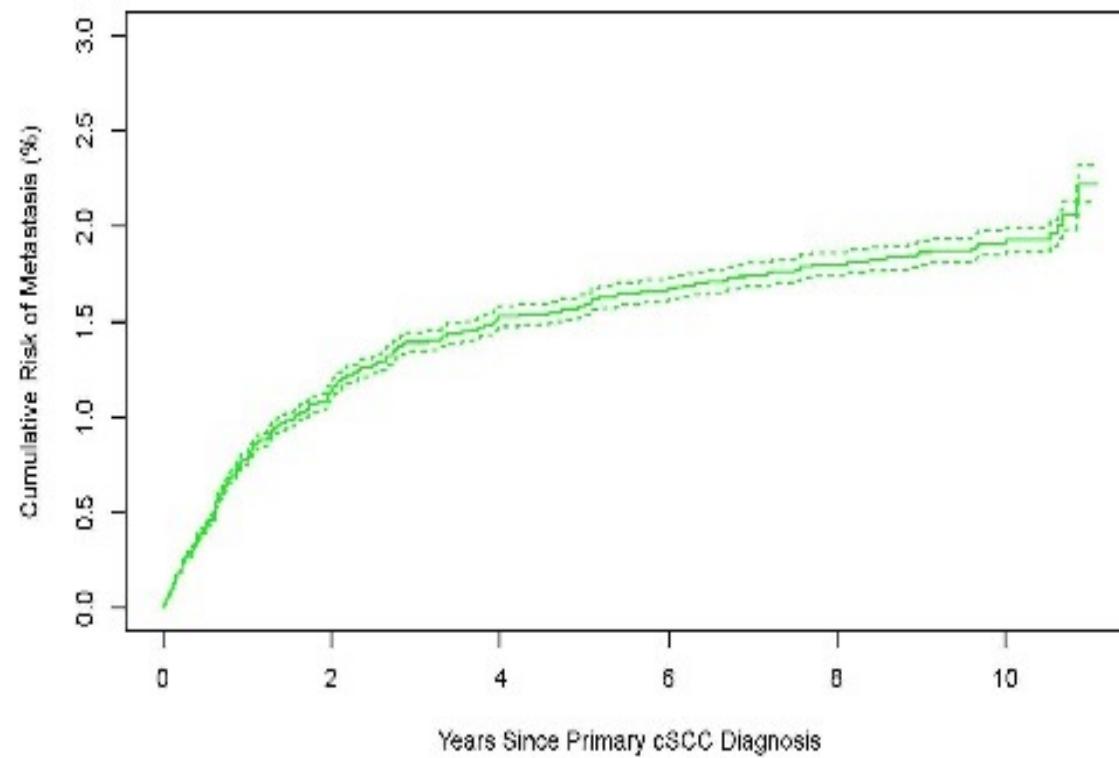
	N	5-YR	10-YR
■ IA	5225	99%	98%
● IB	5749	97%	94%
▲ IIA	2338	94%	88%
◆ IIB	1688	87%	82%
▼ IIC	691	82%	75%

\*Melanoma specific survival US cohort

# Stage I Gene Expression Profile from Leeds Melanoma Cohort



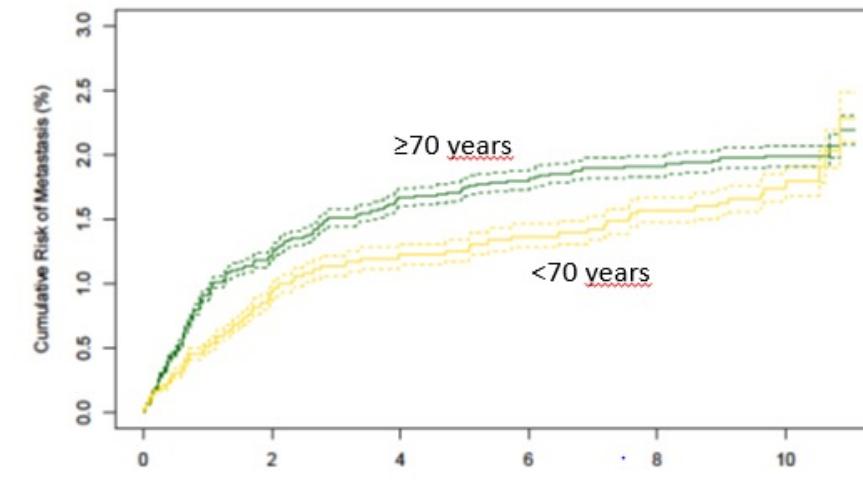
# Tertiary prevention in squamous cell carcinoma



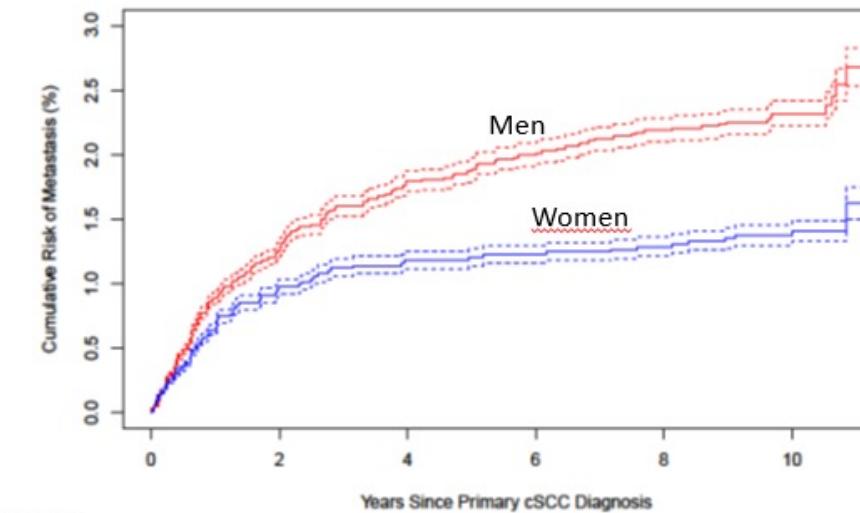
A



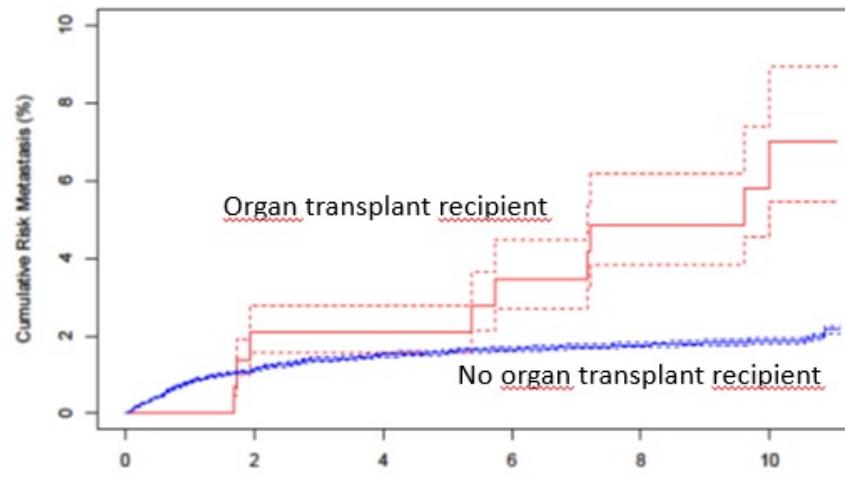
# Tertiary prevention: patient characteristics



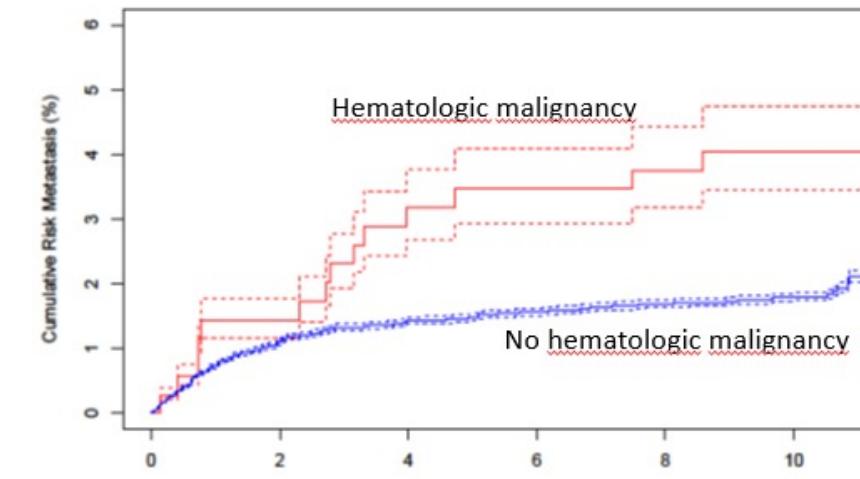
No. at risk	Years Since Primary cSCC Diagnosis					
≥70 years	7621	6215	5066	4060	3206	1259
<70 years	3514	3340	3211	3069	2910	1478



No. at risk	Years Since Primary cSCC Diagnosis					
Males	6315	5374	4584	3891	3293	1499
Females	4817	4176	3690	3235	2819	1235



No. at risk	Years Since Primary cSCC Diagnosis					
OTR	144	123	113	97	76	36
No OTR	10979	9418	8152	7022	6030	2695



No. at risk	Years Since Primary cSCC Diagnosis					
HM	346	227	171	124	93	34
No HM	10538	9103	7919	6859	5919	2670

# Validating 4 Staging Systems for Cutaneous Squamous Cell Carcinoma Using Population-Based Data

Table 3. External

Staging System

AJCC, Seventh Ed

Breuninger et al<sup>8</sup>

BWH<sup>9</sup>

AJCC, Eighth Edit

statistics

$R^2$

0.04

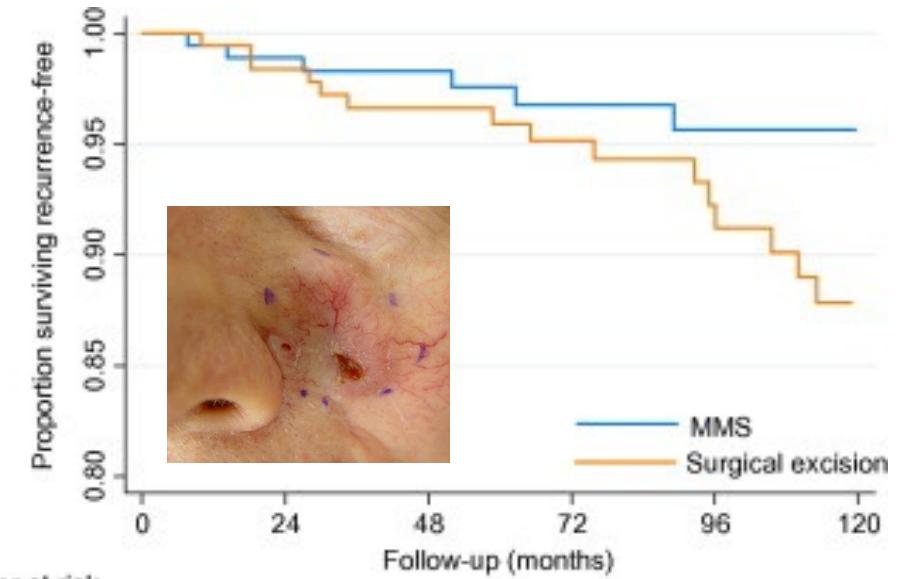
0.23

0.18

0.12

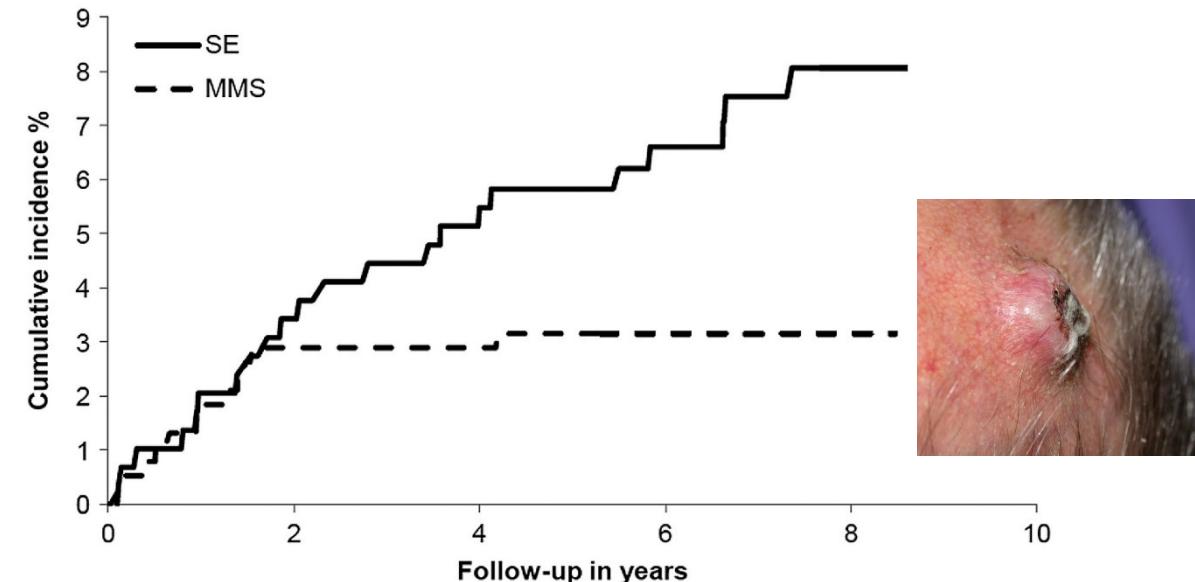


# Surgical treatment: Mohs surgery



Number at risk					
MMS	198	171	140	106	79
Surgical excision	199	176	139	117	89

	MMS				
	N at risk	N of recurrences	N at risk	N of recurrences	N at risk
	380	0	291	11	246
			12	12	96
SE	SE				
	N at risk	N of recurrences	N at risk	N of recurrences	N at risk
	292	0	246	10	206
			16	16	134
				19	71
					22



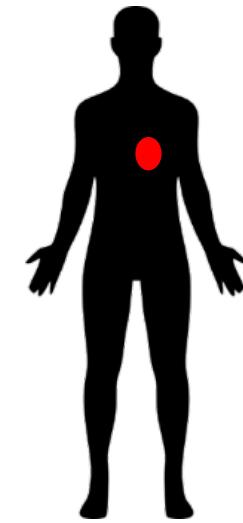
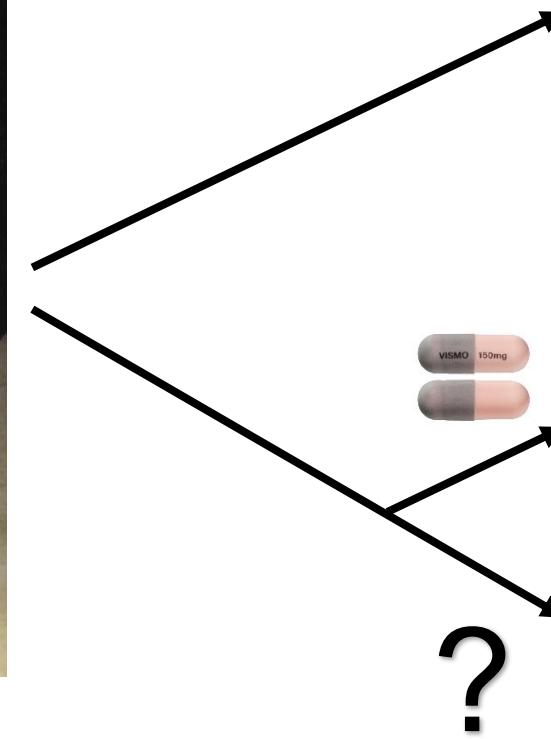
# From prevention to treatment



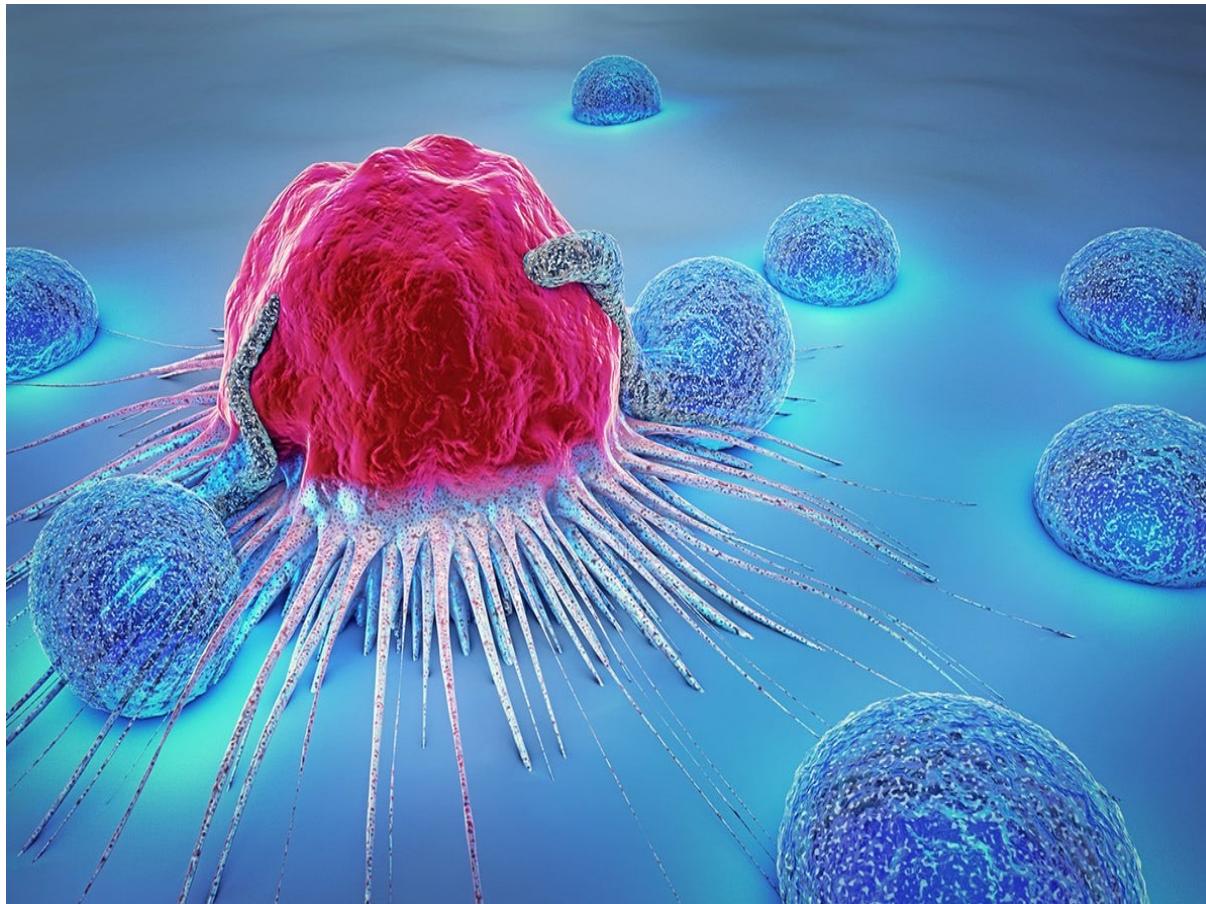
# Targeted therapy



# Targeted therapy in basal cell carcinoma

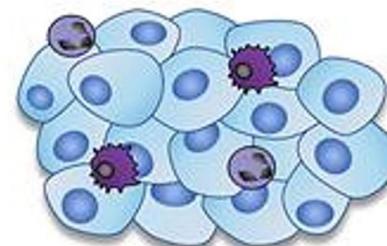


# Immunotherapy



A

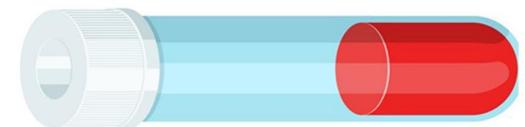
## Tissue based tests



- PDL-1 Immunohistochemistry
- Mismatch repair (MSI/MMR) status
- Tumor mutational burden (TMB)
- Immunoscore®
- PanCancer IO 360™
- Tumor neoantigen testing (e.g. MANAFEST)
- Tumor infiltrating lymphocyte score
- Tumor immune signature (TIS)
- IMPRES and TIDE gene signatures

B

## Blood based tests



- Soluble PDL-1 ELISA test
- Exosomal PDL-1 expression
- PDL-1 expression on circulating tumor cells
- Circulating tumor DNA testing
- Serum proteins and cellular markers

# Conclusion

