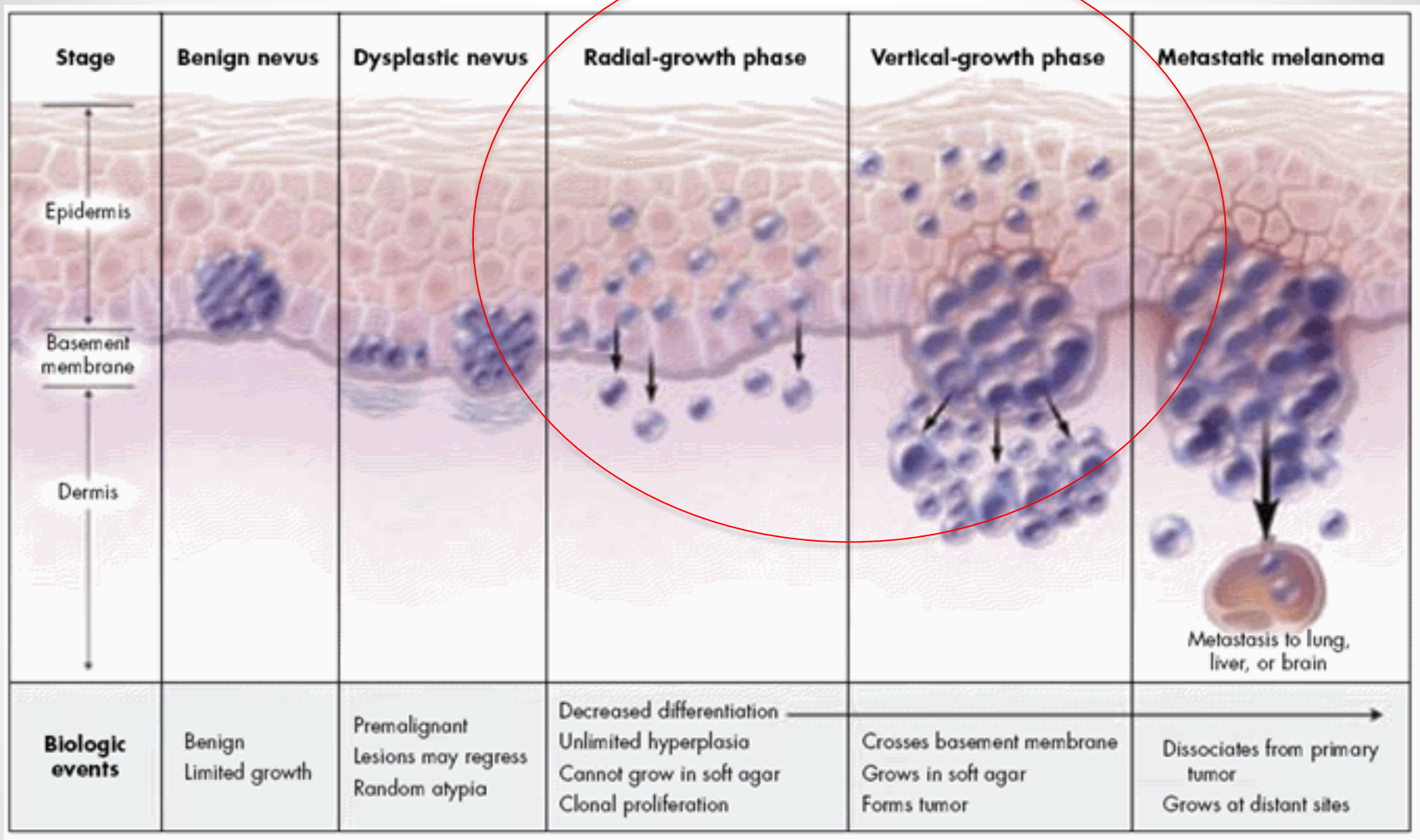
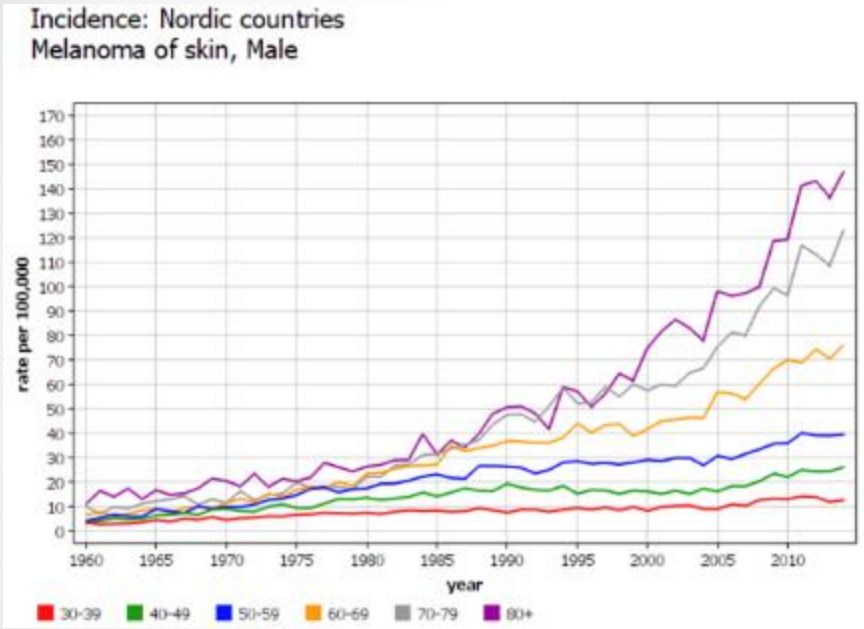
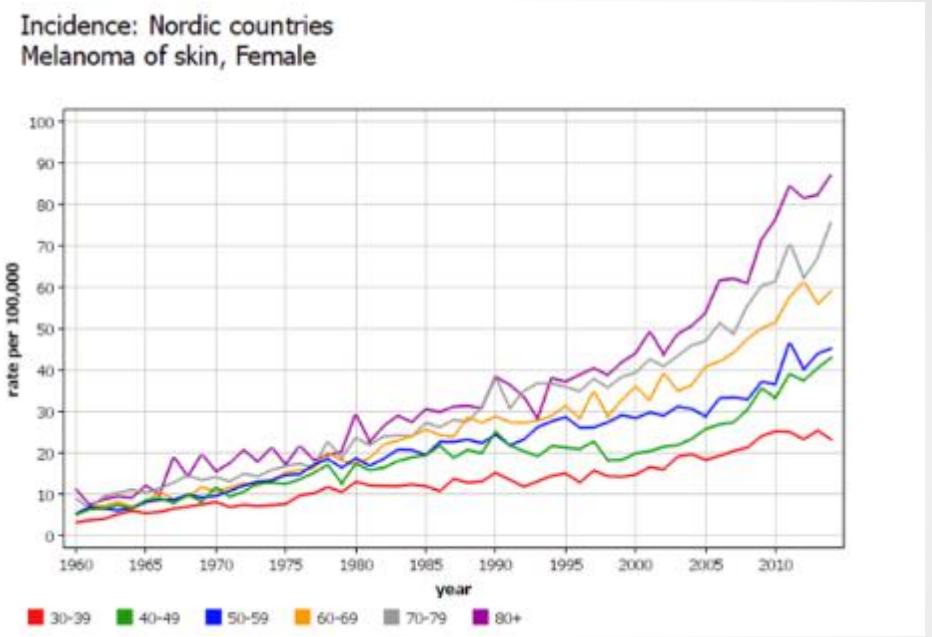
Coordinamento Wonca Italia
International Conference
Lecce, 29-30 September 2017

Communications from the literature about overmedicalization evidences: Melanoma

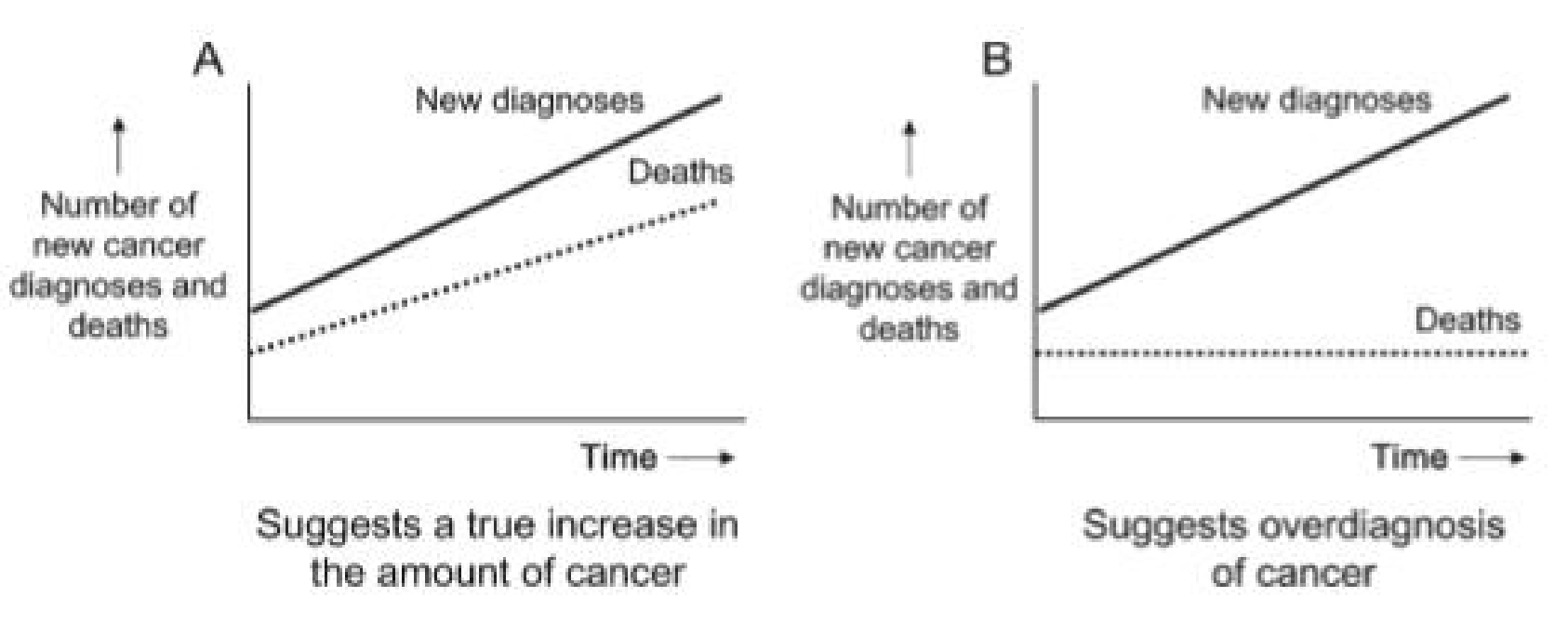
Dr. Giuseppe Febbo


Stage
Benign nevus
Dysplastic nevus
Radial-growth phase
Vertical-growth phase
Metastatic melanoma
Epidermis
Basement membrane
Dermis
Metastasis to lung, liver, or brain
Biologic events
Benign
Limited growth
Premalignant
Lesions may regress
Random atypia
Decreased differentiation
Unlimited hyperplasia
Cannot grow in soft agar
Clonal proliferation
Crosses basement membrane
Grows in soft agar
Forms tumor
Dissociates from primary tumor
Grows at distant sites

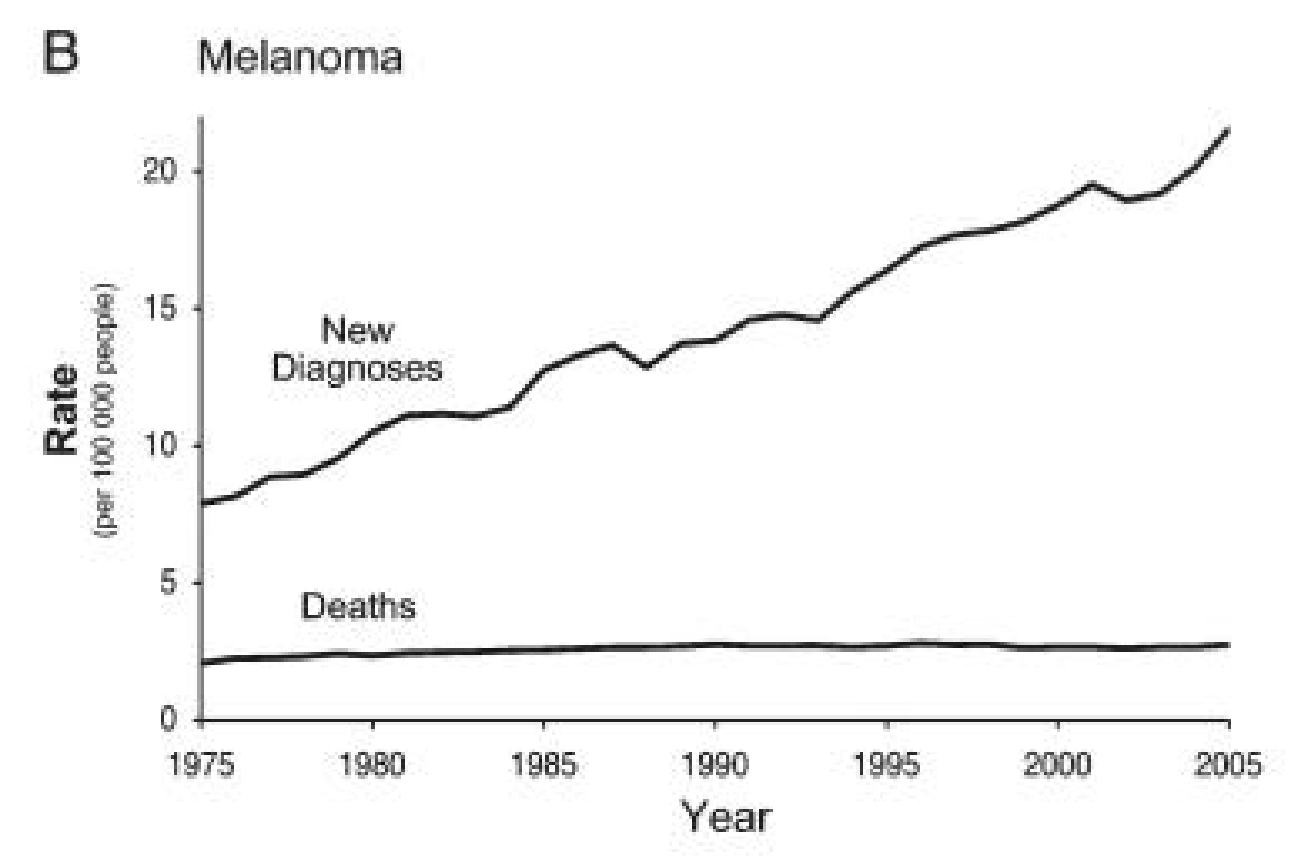




NORDCAN© Association of the Nordic Cancer Registries (6.12.2016)



Welch HG, Black WC. Overdiagnosis in cancer. J Natl Cancer Inst 2010; 102: 605–613



Welch HG, Black WC. Overdiagnosis in cancer. J Natl Cancer Inst 2010; 102: 605–613

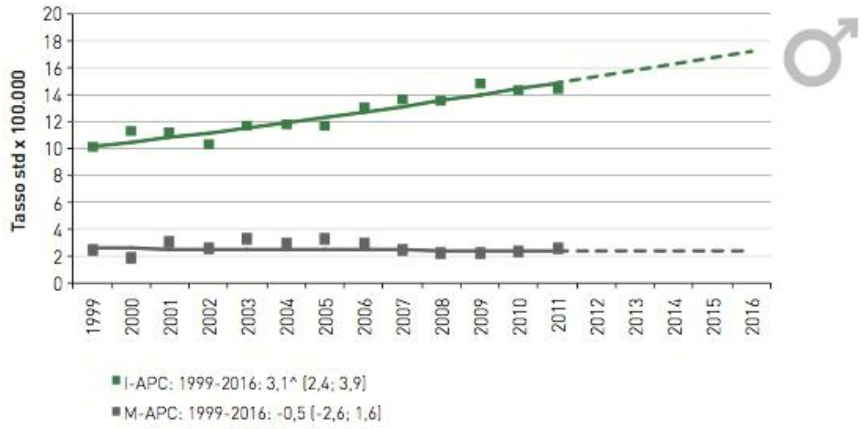


FIGURA 17A. Cute (melanomi), maschi. AIRTUM: stima dei trend tumorali di incidenza e mortalità 1999-2016. Tassi standardizzati popolazione europea. APC = Annual Percent Change (variazione percentuale media annua), I = incidenza, M = mortalità.

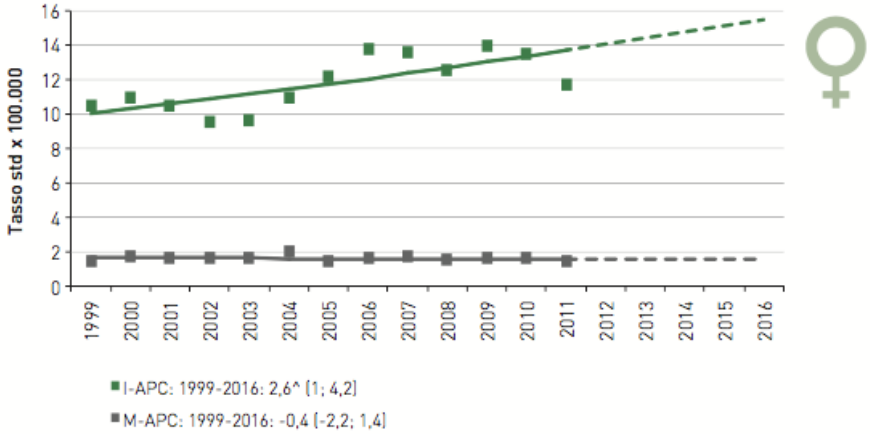
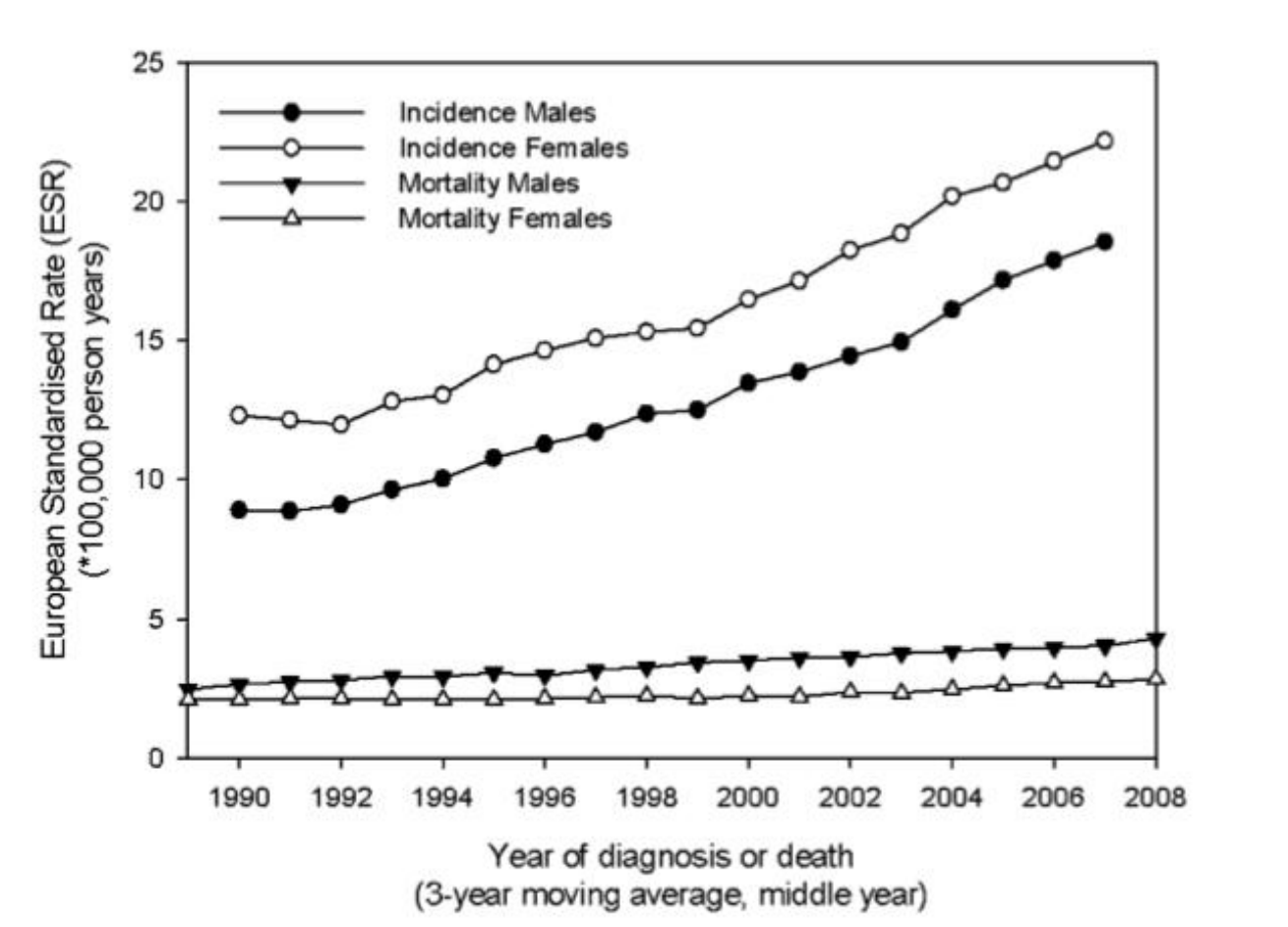


FIGURA 17B. Cute (melanomi), femmine. AIRTUM: stima dei trend tumorali di incidenza e mortalità 1999-2016. Tassi standardizzati popolazione europea. APC = Annual Percent Change (variazione percentuale media annua), I = incidenza, M = mortalità.

I numeri del cancro in Italia. Documento AIOM-AIRTUM 2016, pg. 47



Hollestein LM et al. Trends of cutaneous melanoma in The Netherlands: increasing incidence rates among all Breslow thickness categories and rising mortality rates since 1989. Annals of Oncology 2012; 23: 524–530

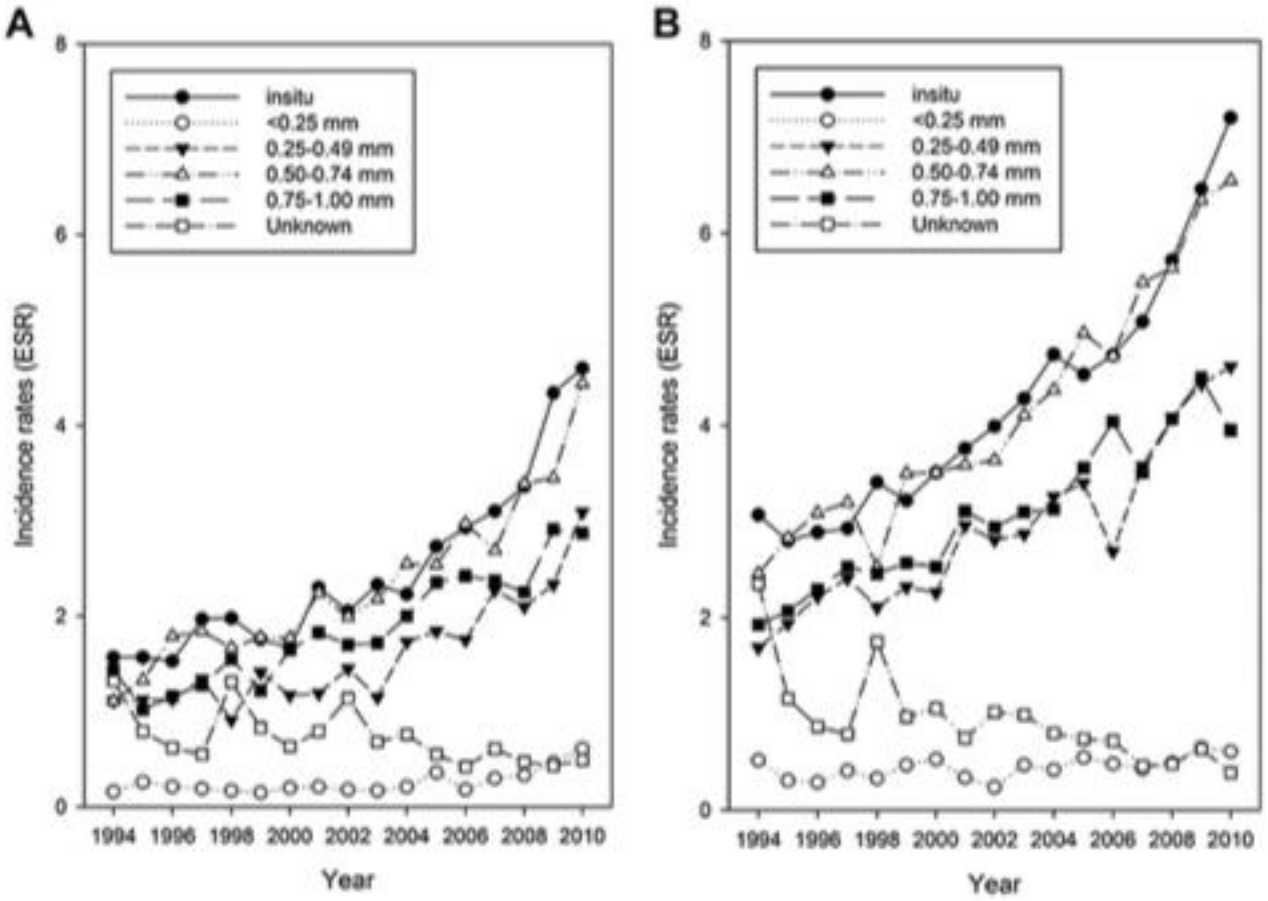


Fig. 1. **A,B** European standardised incidence rates (ESR, per 100,000 person-years) of *in situ* and thin melanomas between 1994 and 2010 in Dutch males (1A) and females (1B). Source: Netherlands Cancer Registry period 1994 until 2010, excluding region Rotterdam. ESR: European standardised rate.

Van der Leest et al. Increasing time trends of thin melanomas in The Netherlands: what are the explanations of recent accelerations? European Journal of Cancer 2015; 51: 2833-2841

Table. Change in Incidence and Mortality of Cancers Over Time From 1975 to 2010 as Reported in Surveillance, Epidemiology and End Results[1]

	Incidence			Mortality		
	Per 100 000		%	Per 100 000		%
Change[a]	1975	2010[b]	Change	1975	2010[b]	Change
Example 1						
Breast[c]	105.07	126.02	20	31.45	21.92	−30
Prostate	94	145.12	54	30.97	21.81	−30
Lung and bronchus[d]	52.26	56.68	8	42.56	47.42	11
Example 2						
Colon	41.35	28.72	−31	28.09	15.51	−45
Cervical	14.79	6.71	−55	5.55	2.26	−59
Example 3						
Thyroid	4.85	13.83	185	0.55	0.51	−7
Melanoma	7.89	23.57	199	2.07	2.74	32

[a] Example 1: Indolent and consequential tumors are identified with screening, leading to an overall increase in incidence rates. Example 2: Prescreened tumor population is more homogeneous, slower-growing but consequential. Screening substantially decreases incidence (through detection and removal of precursor lesions) and mortality. Example 3: Screening expands the population of indolent tumors, with little or no effect on the small population of more aggressive tumors.

[b] Represents period in which screening (except for lung cancer) is prevalent.

[c] At least two-thirds of the mortality reduction is believed attributable to adjuvant therapy.[2,3]

[d] The National Lung Screening Trial conducted among individuals at risk for lung cancers shows that the proportion of stage I detected tumors is more than 2-fold higher than the decrease in the higher-stage tumors, accounting for its inclusion in example 1.[5]

↑incidence ↓ mortality

↓incidence ↓ mortality

↑incidence = mortality

Esserman LJ et al. Overdiagnosis and overtreatment in cancer: an opportunity for improvement. JAMA 2013; 310(8): 797-798

Table 5. Staging, Survival, and Follow-Up of Cutaneous Malignant Melanoma

Stage	Description	Survival (%) 5-year	Survival (%) 10-year	Specific melanoma follow-up*	Additional testing
0 (in situ)	Disease confined to epidermis (top layer of skin)	99 to 100	99 to 100	Every six months for first year, then every year up to year 5, then yearly for life	None
I	Confined to skin, but thicker (up to 1.0 mm) and has not spread Stage IA: skin covering melanoma remains intact Stage IB: skin covering melanoma may have broken open (ulcerated)	IA: 97 IB: 92	IA: 95 IB: 86	Every three to four months for first year, then every six months for second year, then yearly up to year 5, then yearly for life	None
II	Melanoma has grown thicker, ranging from 1.01 to 4.0 mm, but has not spread May or may not have ulcerated	IIA: 81 IIB: 70 IIC: 53	IIA: 67 IIB: 57 IIC: 40	Every three to four months for years 1 through 3, then every six months for years 4 and 5, then yearly for life	CBC, chemistry panel, and LDH level
III	Melanoma has spread to one or more nearby lymph nodes or nearby skin	IIIA: 78 IIIB: 59 IIIC: 40	IIIA: 68 IIIB: 43 IIIC: 24	Every three to four months for years 1 through 3, then every six months for years 4 and 5, then yearly for life	CBC, chemistry panel, and LDH level PET and/or CT as determined by treating physician
IV	Melanoma has spread to an internal organ or lymph nodes further from the original melanoma, or is found on the skin far from the original melanoma	15 to 20	10 to 15	Every three to four months for patients at high risk of relapse Follow-up in patients receiving adjuvant or palliative therapy should be based on the specific treatment prescribed	CBC, chemistry panel, and LDH level PET and/or CT every two to four months for first five years and then yearly thereafter Additional testing in patients receiving adjuvant or palliative therapy should be based on the specific treatment prescribed

CBC = complete blood count; CT = computed tomography; LDH = lactate dehydrogenase; PET = positron emission tomography.

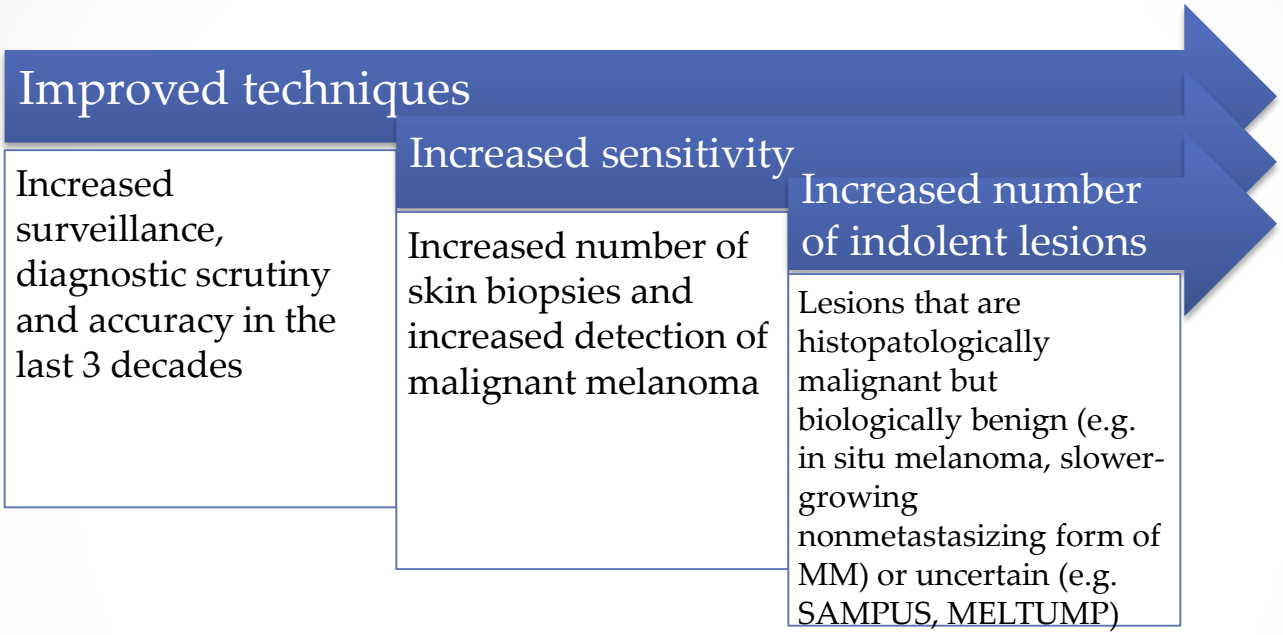
**—Follow-up for the first five years is specifically for the diagnosis of melanoma. Annual follow-up for life is recommended to be performed by a dermatologist for routine skin cancer screening.*

Information from references 33 through 35.

Stage	T	N	M
0	Tis	N0	M0
IA	T1a	N0	M0
IB	T1b	N0	M0
	T2a	N0	M0
IIA	T2b	N0	M0
	T3a	N0	M0
IIB	T3b	N0	M0
	T4a	N0	M0
IIC	T4b	N0	M0
IIIA	T(1-4)a	N1a	M0
	T(1-4)a	N2a	M0
IIIB	T(1-4)b	N1a	M0
	T(1-4)b	N2a	M0
	T(1-4)a	N1b	M0
	T(1-4)a	N2b	M0
	T(1-4)a	N2c	M0
IIIC	T(1-4)b	N1b	M0
	T(1-4)b	N2b	M0
	T(1-4)b	N2c	M0
	Any T	N3	M0
IV	Any T	Any N	M1

Shenenberger DW. Cutaneous malignant melanoma: a primary care perspective. Am Fam Physician 2012; 85(2):161-168.

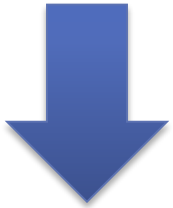
Melanoma overdiagnosis



- Overestimation of suspicious and uncertain lesions by the dermatologist and the pathologist: defensive medicine? *(Piepkorn MW et al. Reply: Surgical margins for possibly malignant melanocytic lesions and the overdiagnosis of melanoma. J Am Acad Dermatol 2014; 71(3): 590)*

Melanoma overtreatment

- Skin biopsies and wide local excisions (WLE)➔ 1 melanoma vs 29 benign lesions excised!
- Sentinel lymph node biopsies (SLNB)➔ 96% unnecessarily!



- Cosmetic, or more rarely, functional adverse effects
- Psychological consequences of becoming aware to "have a cancer"

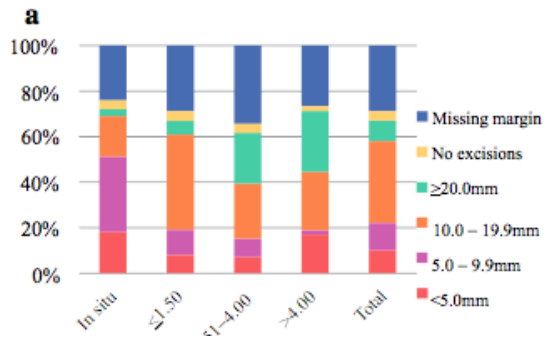
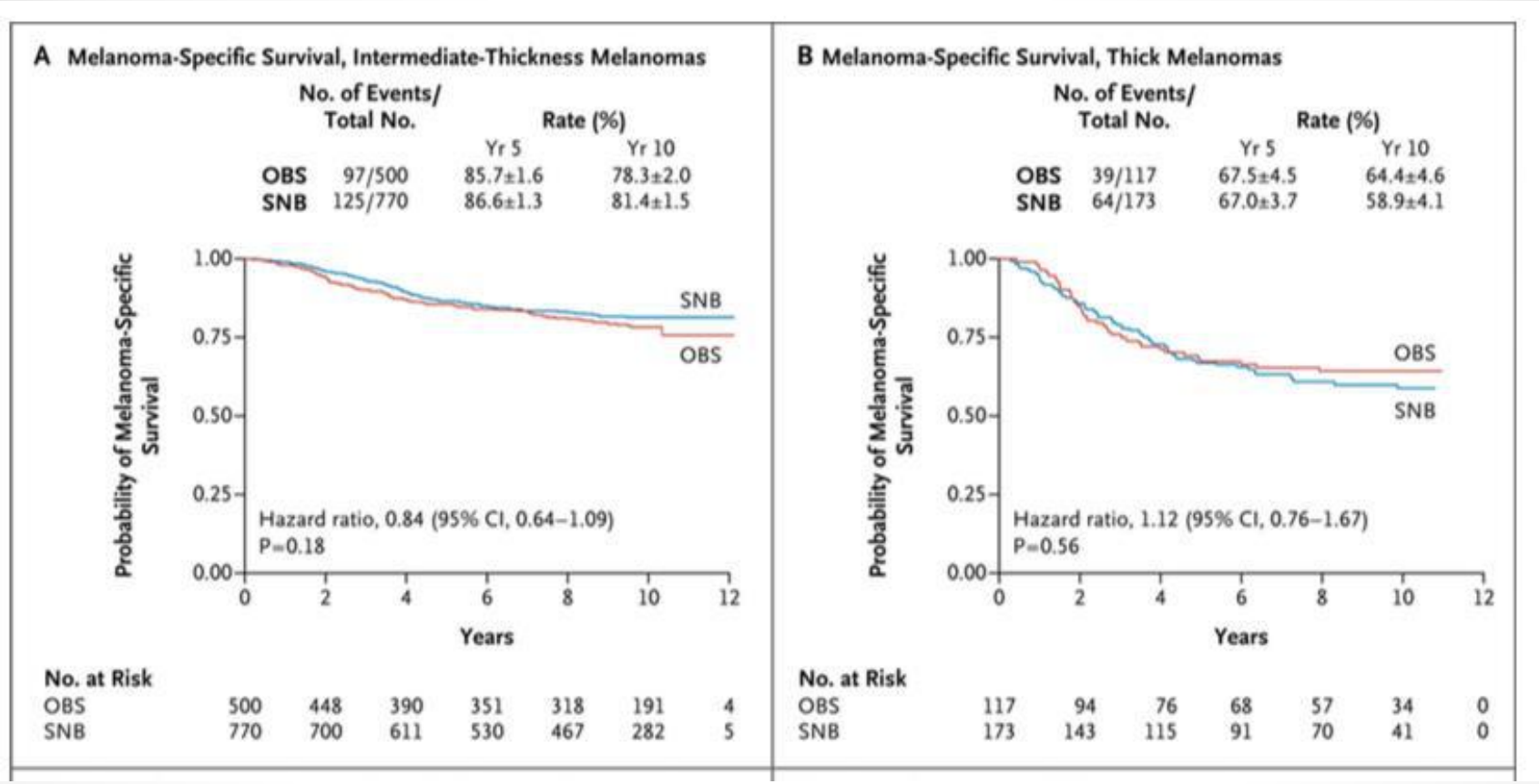


FIG. 1 **a** Total Excision Margin by Breslow Thickness. Distribution of total excision margins according to tumour thickness, where recorded (missing in around 30% of each category). **b** Total Excision Margin Concordance. Differences in the rates of excision margin concordance with the 1999 Australian and New Zealand guidelines according to tumour thickness. Margins were calculated as the sum of both biopsy and wide local excision (*narrowest*) margins, with allowance for shrinkage on pathological assessment. Notably, only 35% overall compliance was achieved, with the best being 63%, which was for intermediate thickness (>1.5–4.0 mm) tumours. **c** Wide Local Excision Performed by Excision Biopsy Physician. Differences by specialty in whether or not the doctor who performed the initial diagnostic excision biopsy also performed the wide local excision. **d** Reconstruction method post resection of melanoma. Differences by specialty in the method of reconstruction utilized following wide local excision. *GP* general practitioner

Varey AHR et al. Poor adherence to National Clinical Management Guidelines: a population-based, cross-sectional study of the surgical management of melanoma in New South Wales, Australia. Ann Surg Oncol 2017; 24: 2080–2088



Morton DL et al. Final trial Report of sentinel-node biopsy versus nodal observation in Melanoma. N Engl J Med 2014; 370(7): 599–609

How to prevent melanoma overmedicalization?

- Change cancer terminology
- Focus on diagnosis rather than prognosis
- Make a clinicopathologic correlation
- Prevention of factors known to impede a correct histopathologic diagnosis
- Large registries for potentially indolent conditions

Take home messages

- Until we have new methods for determining the malignant potential of pigmented neoplasms, or a time machine, we must keep in mind the grim yet real possibility that the incidence of aggressive metastatic melanoma would be much worse if we left all of these thin indolent melanomas enough time to grow up.

- To prevent is better than cure, when prevention is less harmful than healing.


overdiagnosis
Improved techniques
Increased sensitivity
Increased number of indolent lesions
Increased surveillance,
Increased number of skin biopsies and increased detection of malignant melanoma
Lesions that are histopatologically malignant but biologically benign (e.g. in situ melanoma, slower-growing
GRAND HOTEL TIZIANO