

INCONTRO DEI GIC NEOPLASIE CUTANEE

Torino, 5 dicembre 2011

Epidemiologia dei melanomi e dei tumori cutanei

Dr. Roberto Zanetti
Direttore del Registro Tumori Piemonte

CPO



INDICE della presentazione

1. Epidemiologia descrittiva: nel mondo, in Italia, a Torino
2. La lunga strada della ricerca eziologica
3. Diagnosi precoce/screening
4. Gli andamenti della sopravvivenza

INDICE della presentazione

1. Epidemiologia descrittiva: nel mondo, in Italia, a Torino

“... qualsivoglia ipotesi eziologica
deve essere in accordo con i dati
descrittivi ...”



Malcom Calum Muir
(1930 – 1995)

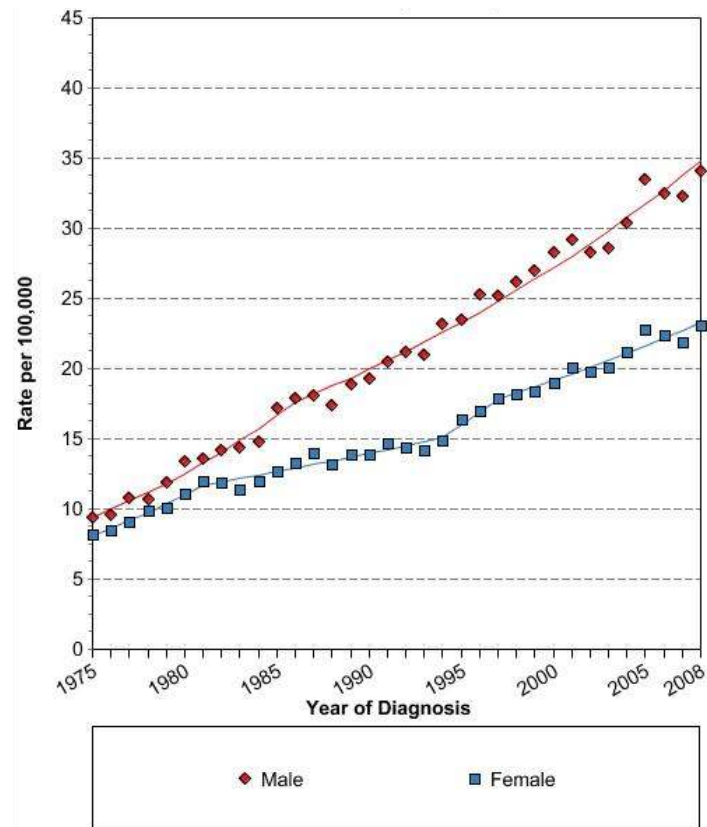
... anche qualsivoglia ipotesi valutativa...



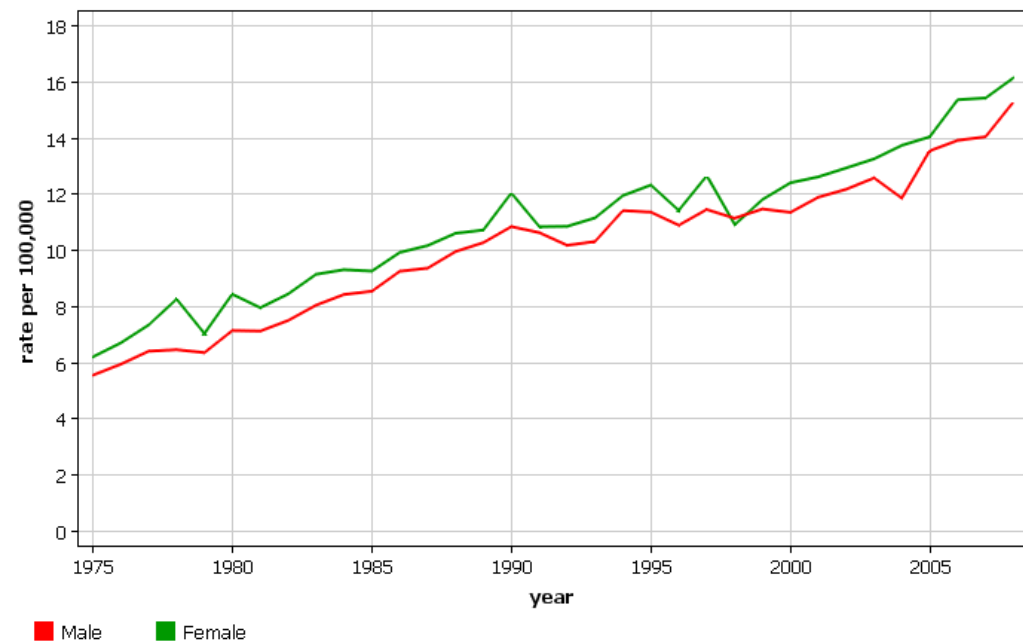
Melanoma, Incidenza

0 – 85+

USA, SEER



NORDIC COUNTRIES

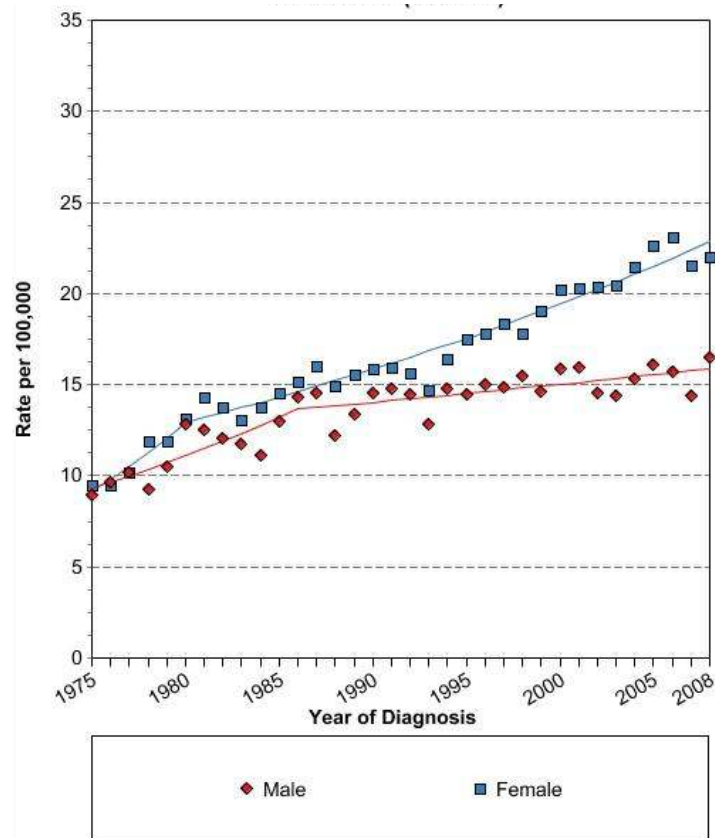


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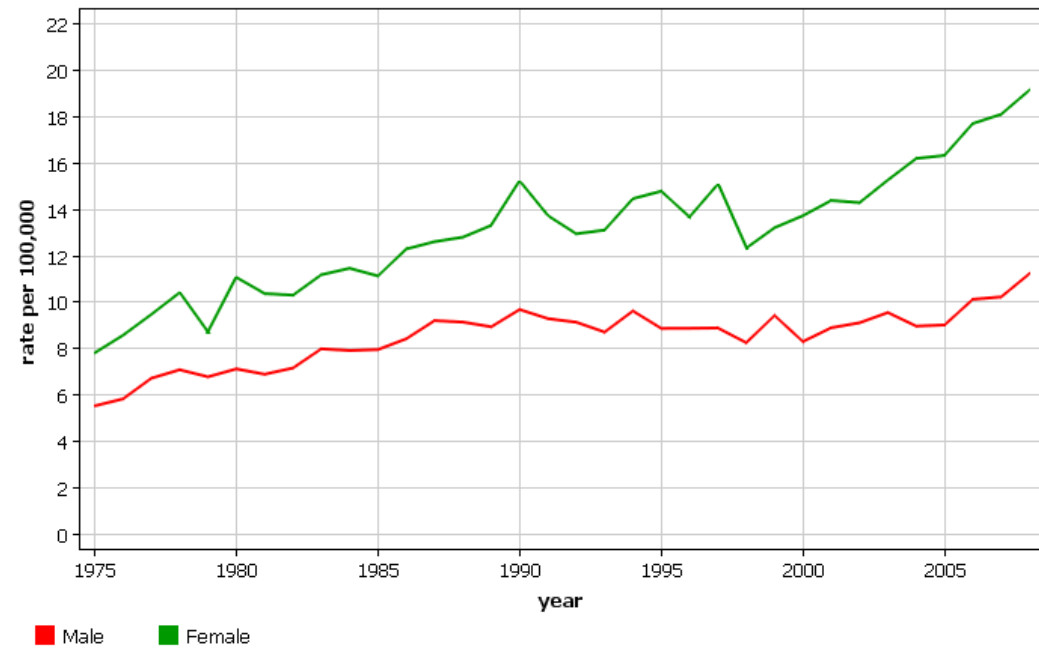


Melanoma, Incidenza 20 – 49

USA, SEER



NORDIC COUNTRIES



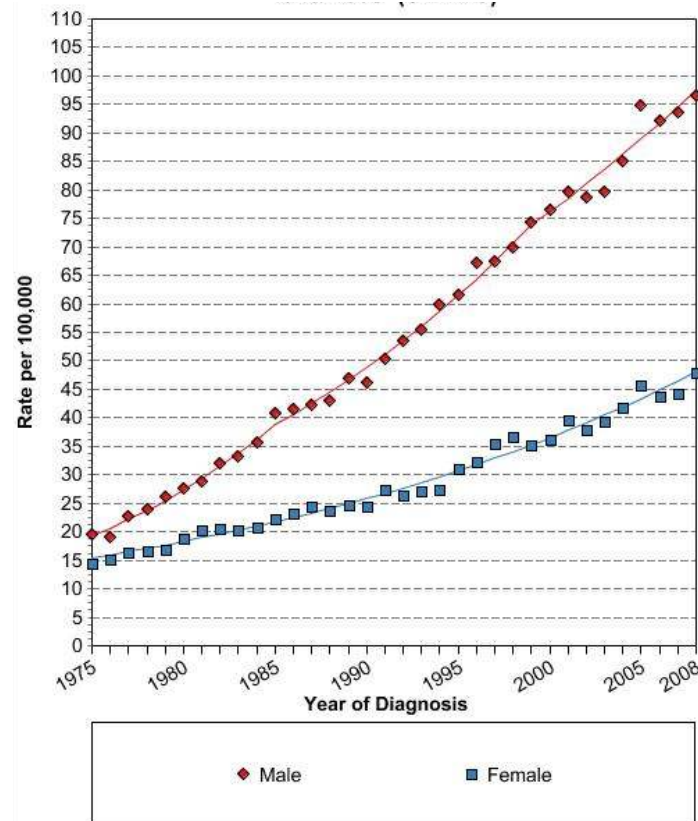
NORDCAN © Association of the Nordic Cancer Registries (2.12.2011)



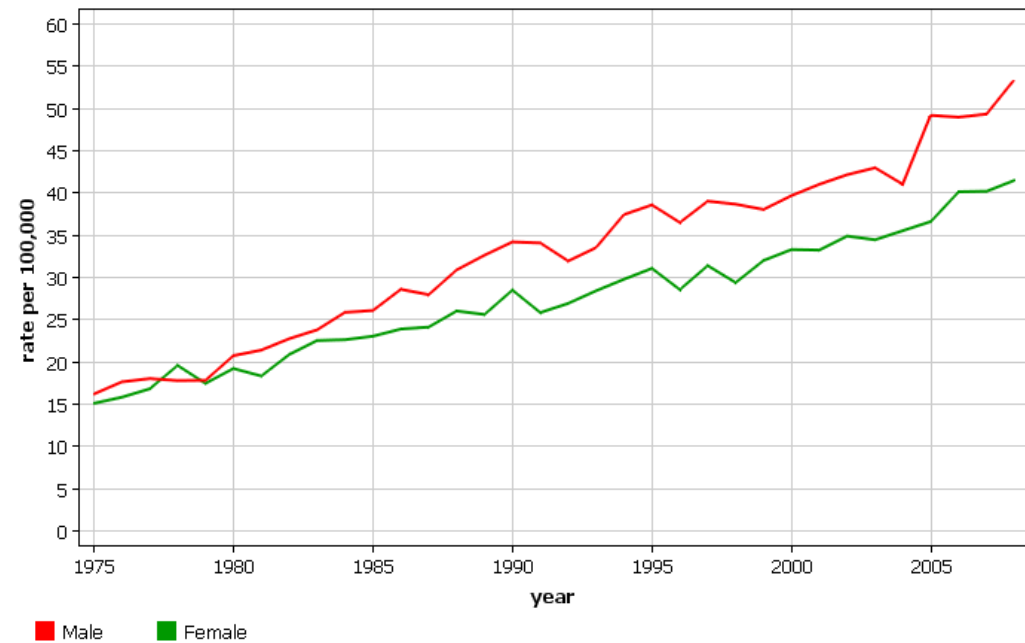
Melanoma, Incidenza

50+

USA, SEER



NORDIC COUNTRIES



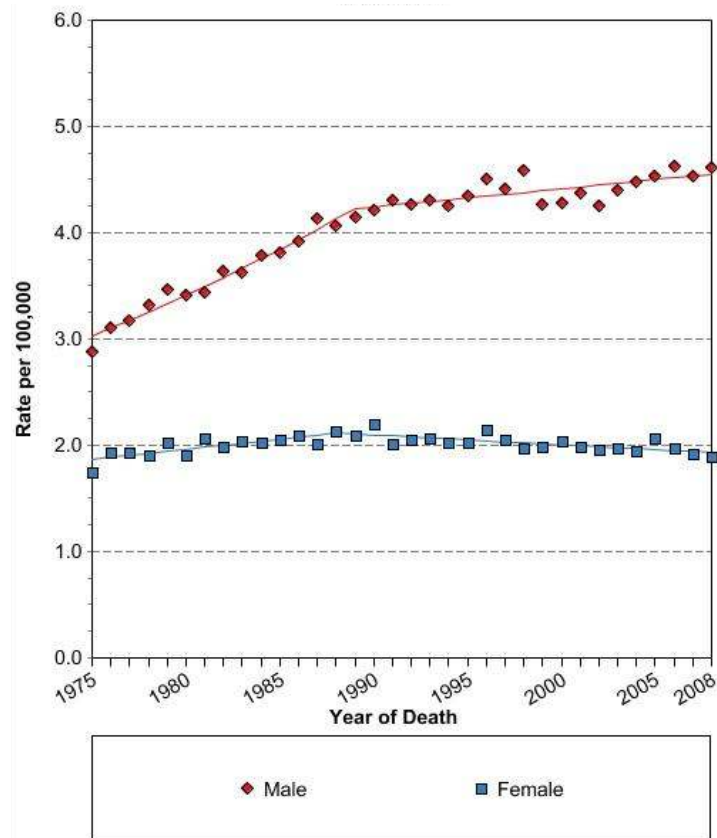
NORDCAN © Association of the Nordic Cancer Registries (2.12.2011)



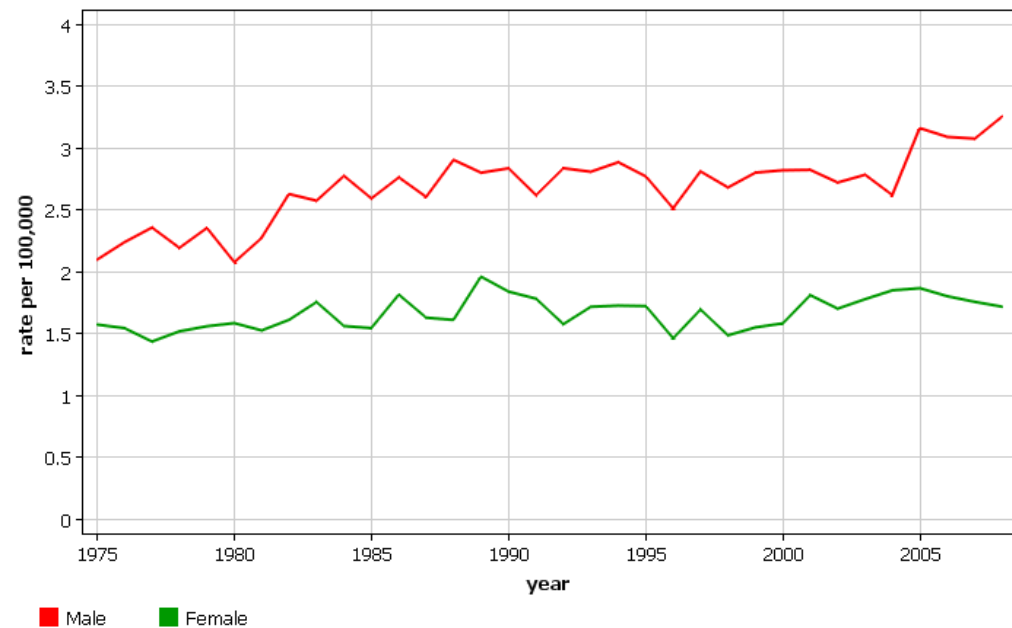
Melanoma, Mortalità

0 – 85+

USA, SEER



NORDIC COUNTRIES

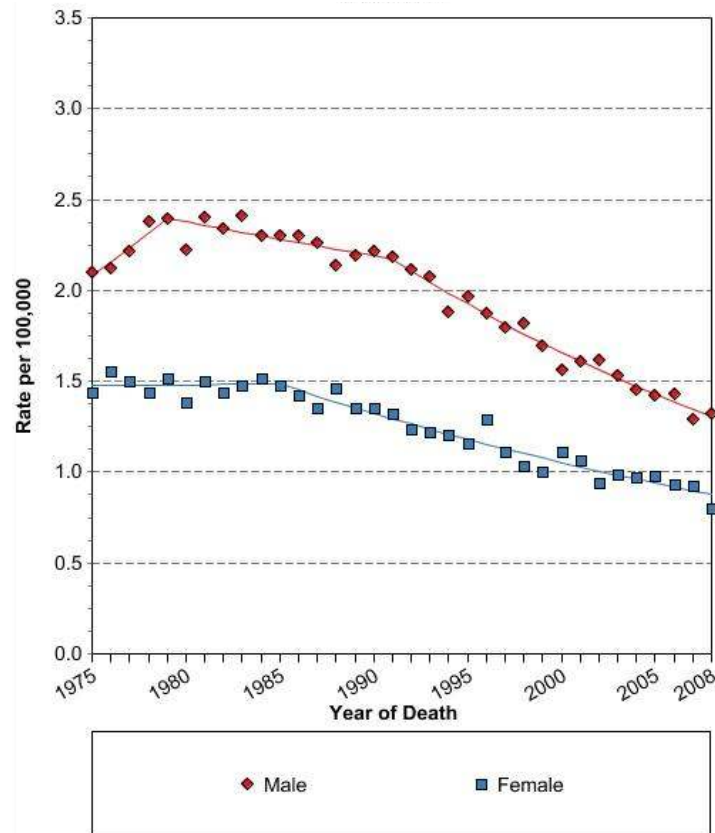


NORDCAN © Association of the Nordic Cancer Registries (2.12.2011)

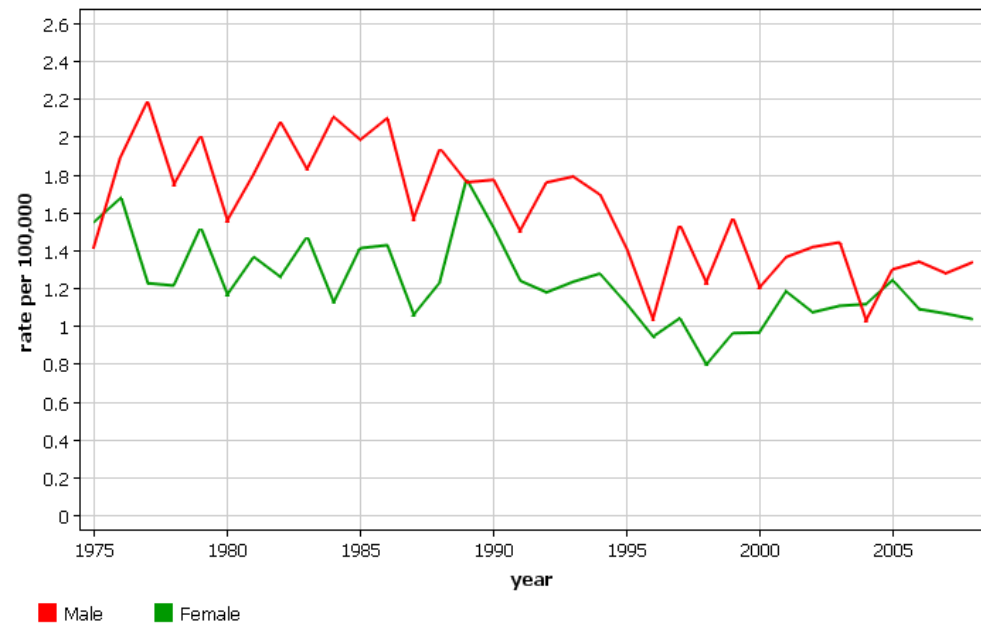


Melanoma, Mortalità 20 – 49

USA, SEER



NORDIC COUNTRIES

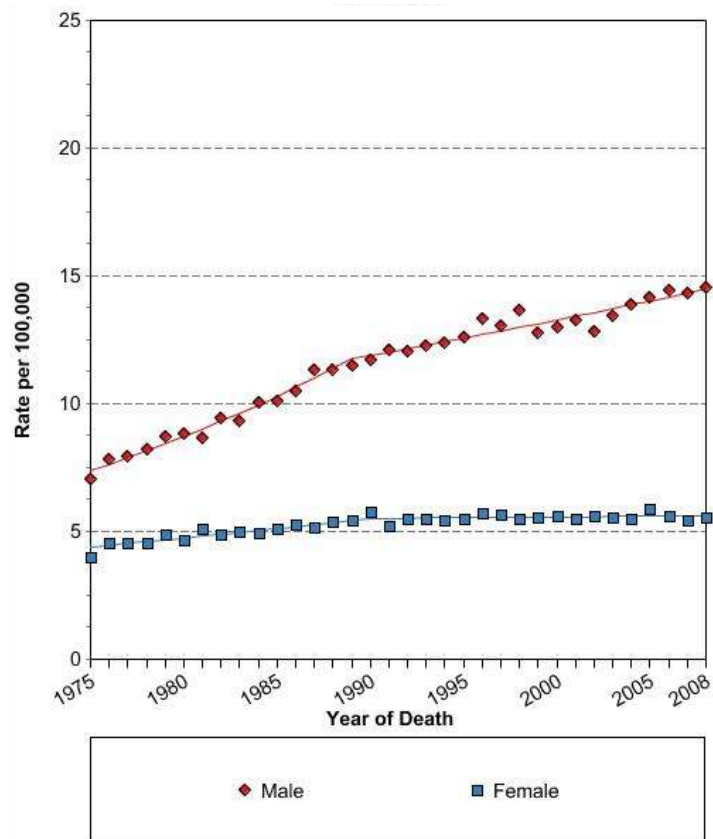


NORDCAN © Association of the Nordic Cancer Registries (2.12.2011)

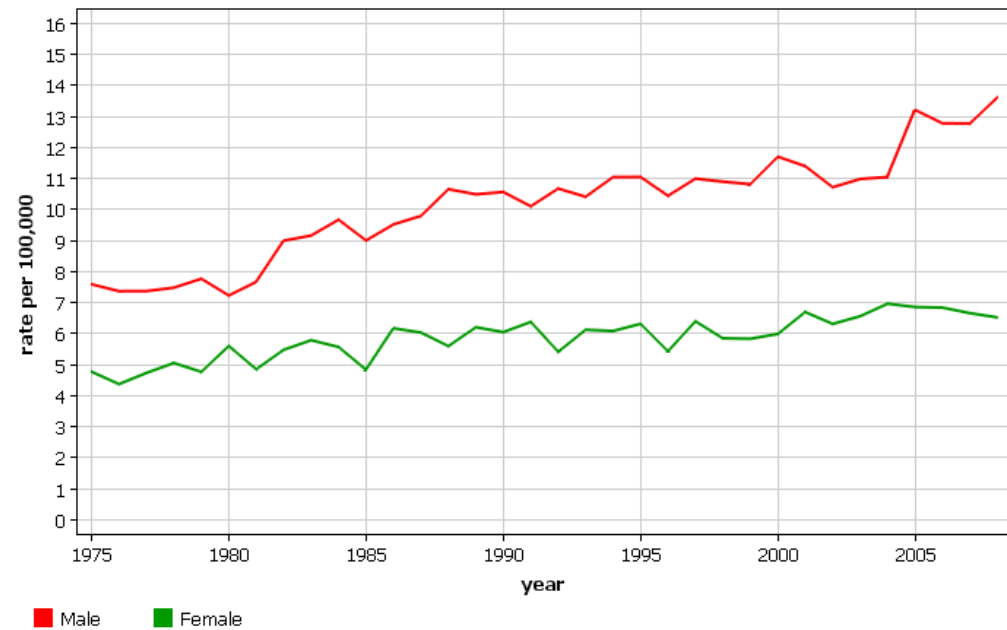


Melanoma, Mortalità 50+

USA, SEER

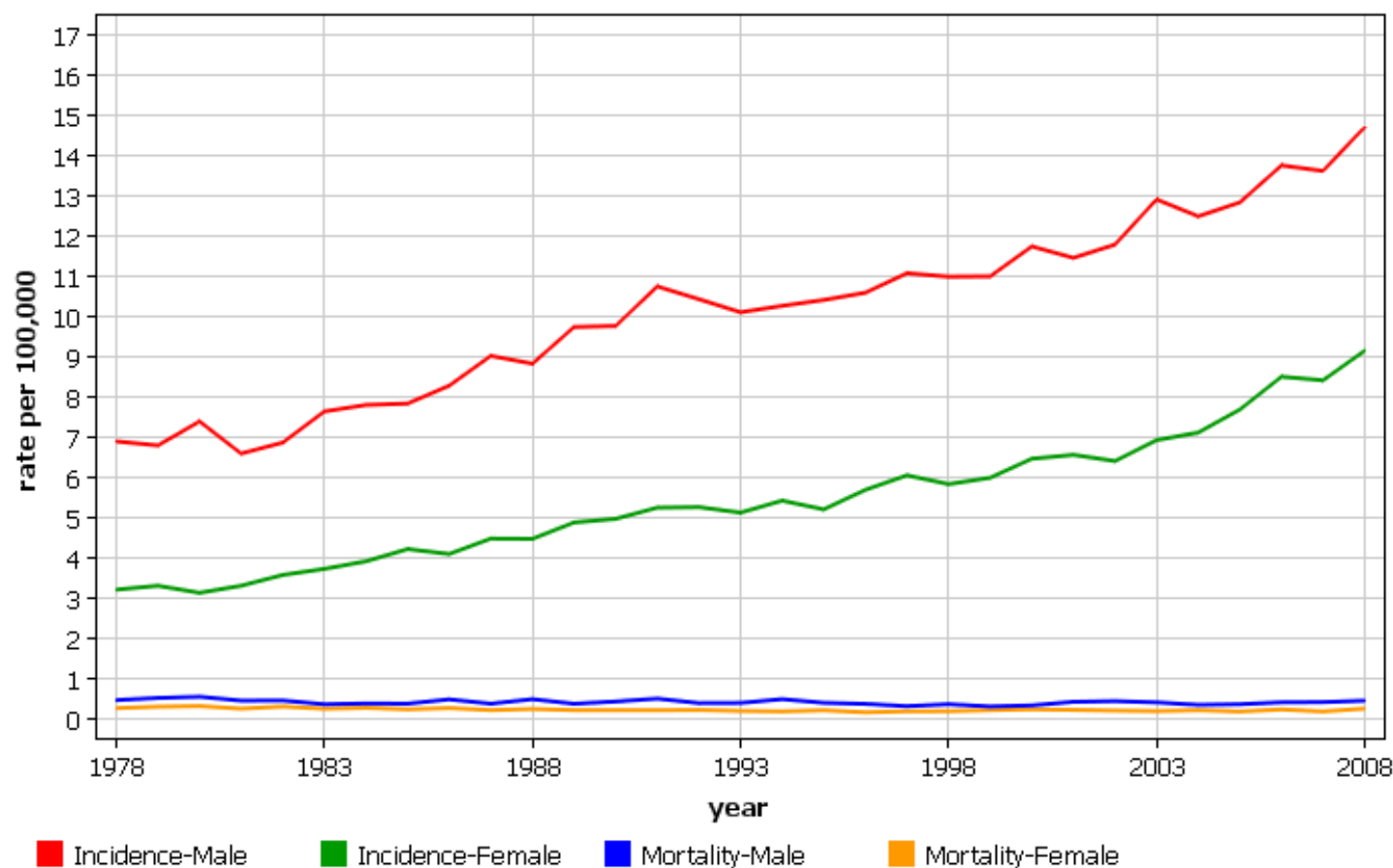


NORDIC COUNTRIES



NORDCAN © Association of the Nordic Cancer Registries (2.12.2011)

Nordic countries
Skin, non-melanoma
ASR (World) age (0-85+)



Incidence and mortality

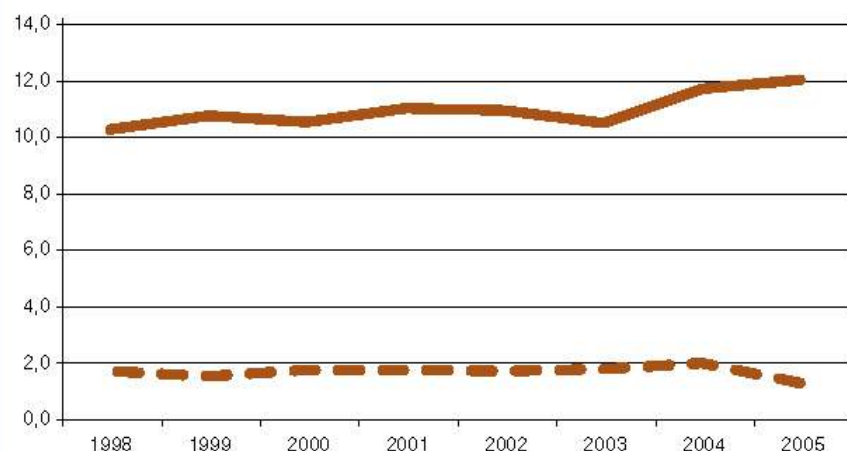


Associazione italiana registri tumori

www.registri-tumori.it

Standardized incidence and mortality rates
x 100,000

FEMALE SKIN MELANOMA



INCIDENCE 1998-2005 APC (95% CI) +1.9* (+0.5 ; +3.3)

MORTALITY 1998-2005 APC (95% CI) -0.3 (-5.8 ; +5.5)

Fonte: AIRTUM 2009

Epidemiol Prev 2009; 33(4-5) Suppl 1: 1-168

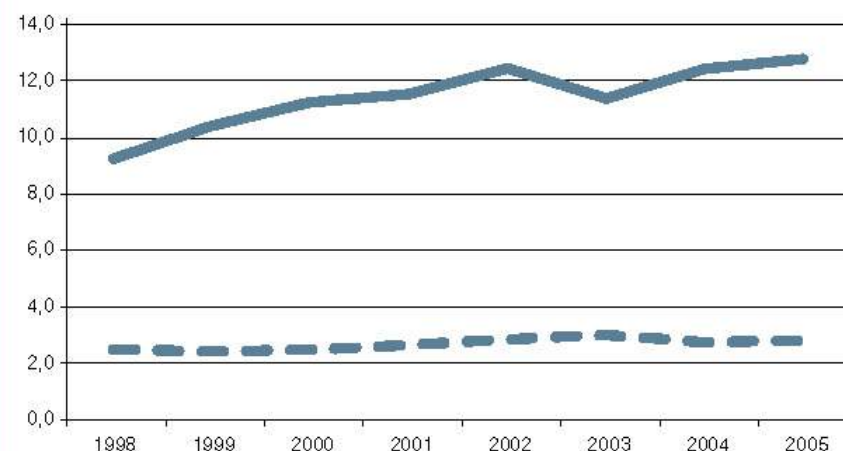


Associazione italiana registri tumori

www.registri-tumori.it

Standardized incidence and mortality rates
x 100,000

MALE SKIN MELANOMA



INCIDENCE 1998-2005 APC (95% CI) +3.8* (+1.8 ; +5.9)

MORTALITY 1998-2005 APC (95% CI) +2.6* (+0.6 ; +4.6)

Fonte: AIRTUM 2009

Epidemiol Prev 2009; 33(4-5) Suppl 1: 1-168

Piedmont Cancer Registry
City of Turin (910,504 inhabitants at 31.12.2009)

SKIN, MELANOMAS - ICD-10: C 43

COMMENTS: In both sexes incidence was importantly increasing up to 2000 when started decreasing. Mortality stabilised in women and in men. The incidence decrease of invasive cases is counterbalanced by the concurrent rise of in situ cases. Survival is quite good and improving during the considered period.

INCIDENCE Last Update: 2006-2008				
	MEN		WOMEN	
	Invasive	In situ	Invasive	In situ
N° (average/annual)	84	27	75	30
RATES				
Crude	19.4	6.1	16.0	6.4
Age adj (ITA81)	13.5	4.4	12.0	5.0
Age adj (WORLD)	10.6	3.5	9.1	3.8
Age specific rates	► MEN		► WOMEN	

MORTALITY Last Update: 2006-2008				
	MEN		WOMEN	
N° (average/annual)	16	14		
RATES				
Crude	3.6	3.0		
Age adj (ITA81)	2.1	1.8		
Age adj (WORLD)	1.5	1.1		
Age specific rates	► MEN		► WOMEN	

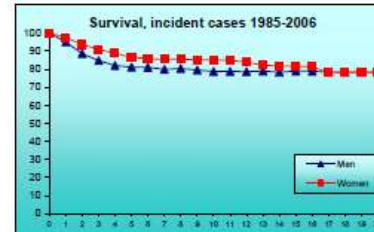
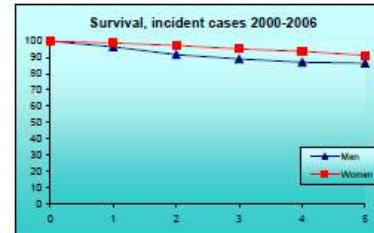
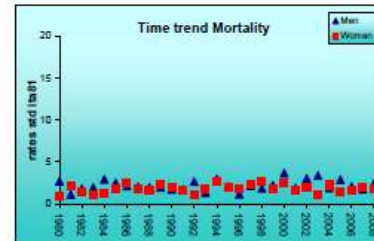
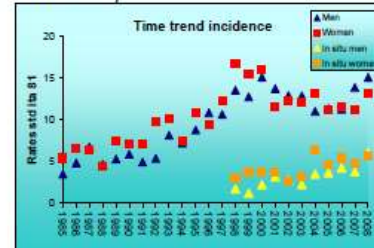
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5 year standardized	76.3	81.4

SURVIVAL Complete data: 1985-2006 (f.u. 2008)		
	MEN	WOMEN
N° of cases	1070	1270
5 year relative	81.1	86.5
10 year relative	78.8	85.1
15 year relative	79.9	81.6
20 year relative	80.3	80.1

5 year Relative Survival TRENDS (f.u. 2008)		
	MEN	WOMEN
1985-1987	56.5	-
1988-1990	57.8	69.3
1991-1993	77.4	83.8
1994-1996	84.5	87.8
1997-1999	85.2	91.3
2000-2003	84.5	91.9

PREVALENCE 31/12/2008		
N° of cases x 100.000		
	MEN	WOMEN
observed (since 1985)	190.2	204.4

INDICATORS / METHODS	
INCIDENCE - MORTALITY - NUMBER OF CASES	
AGE SPECIFIC RATES - CRUDE RATES - STANDARDIZED RATES - SURVIVAL - OBSERVED SURVIVAL	
RELATIVE SURVIVAL AND AGE-STANDARDIZED RELATIVE SURVIVAL - PREVALENCE - NOTES	



[PREVIOUS](#)

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Piedmont Cancer Registry
City of Turin (910,504 inhabitants at 31.12.2009)

SKIN, MELANOMAS - ICD-10: C 43

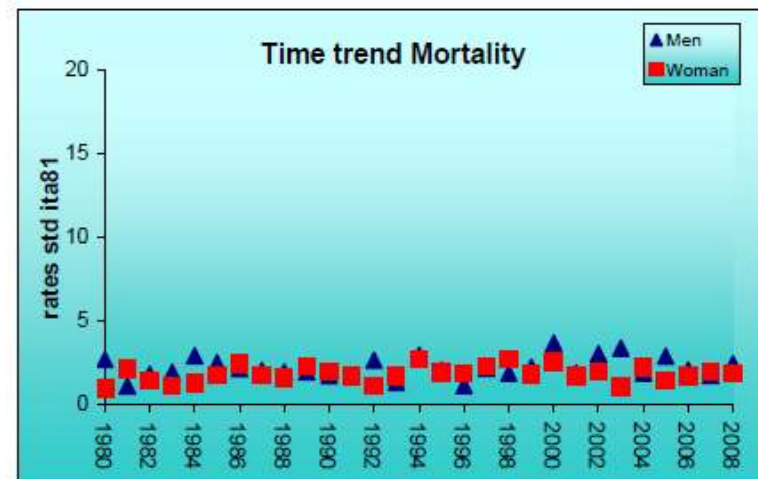
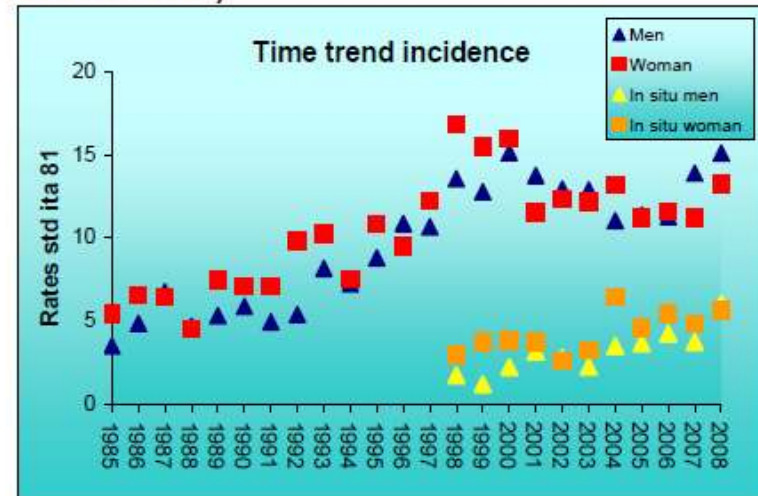
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Age specific rates		► MEN	► WOMEN

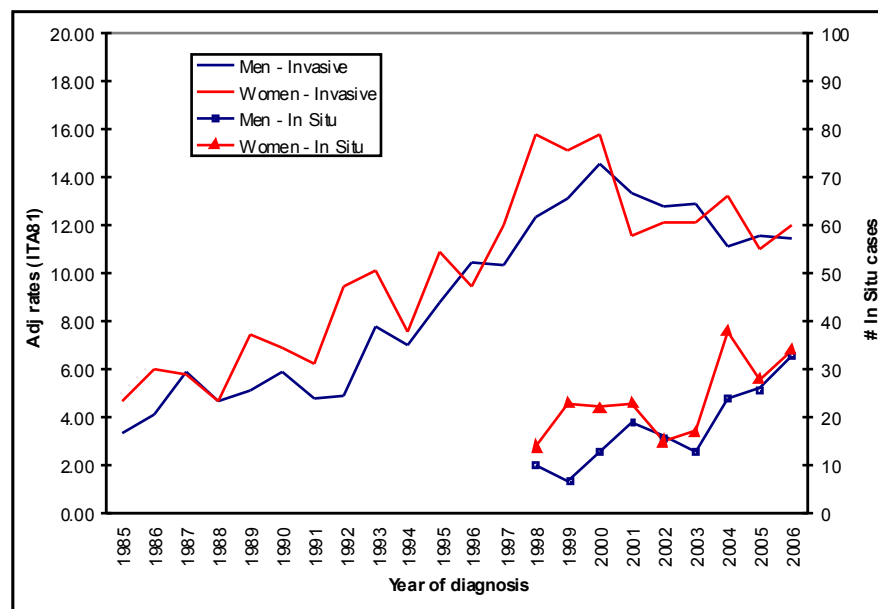


Andamenti dell'incidenza dal 1985 al 2008 in Torino

Il picco negli anni 1997-2000 sembra essersi stabilizzato. Fu probabilmente causato dalle iniziative di diagnosi precoce proposte alla popolazione in quegli anni. La conseguente flessione può essere dovuta all'esaurirsi dell'onda di prevalenza, così come avviene per gli screening organizzati. L'incidenza negli anni successivi, benché diminuita, non è tuttavia ritornata ai valori precedenti registrati all'inizio degli anni '90.

L'effetto dell'anticipazione diagnostica è anche visibile nell'andamento dei casi di melanoma in situ che il RTP raccoglie a partire dalla fine degli anni '90 (diapositiva successiva).

Andamento dell'incidenza dei melanomi in situ ed invasivi



Se consideriamo la somma dei casi incidenti in situ ed invasivi si vede come complessivamente il numero di casi di melanoma continui ad aumentare, ed il rischio non sia perciò ancora da considerarsi in via di stabilizzazione o diminuzione. Tuttavia, le conseguenze sulla miglior prognosi dei casi sono evidenti

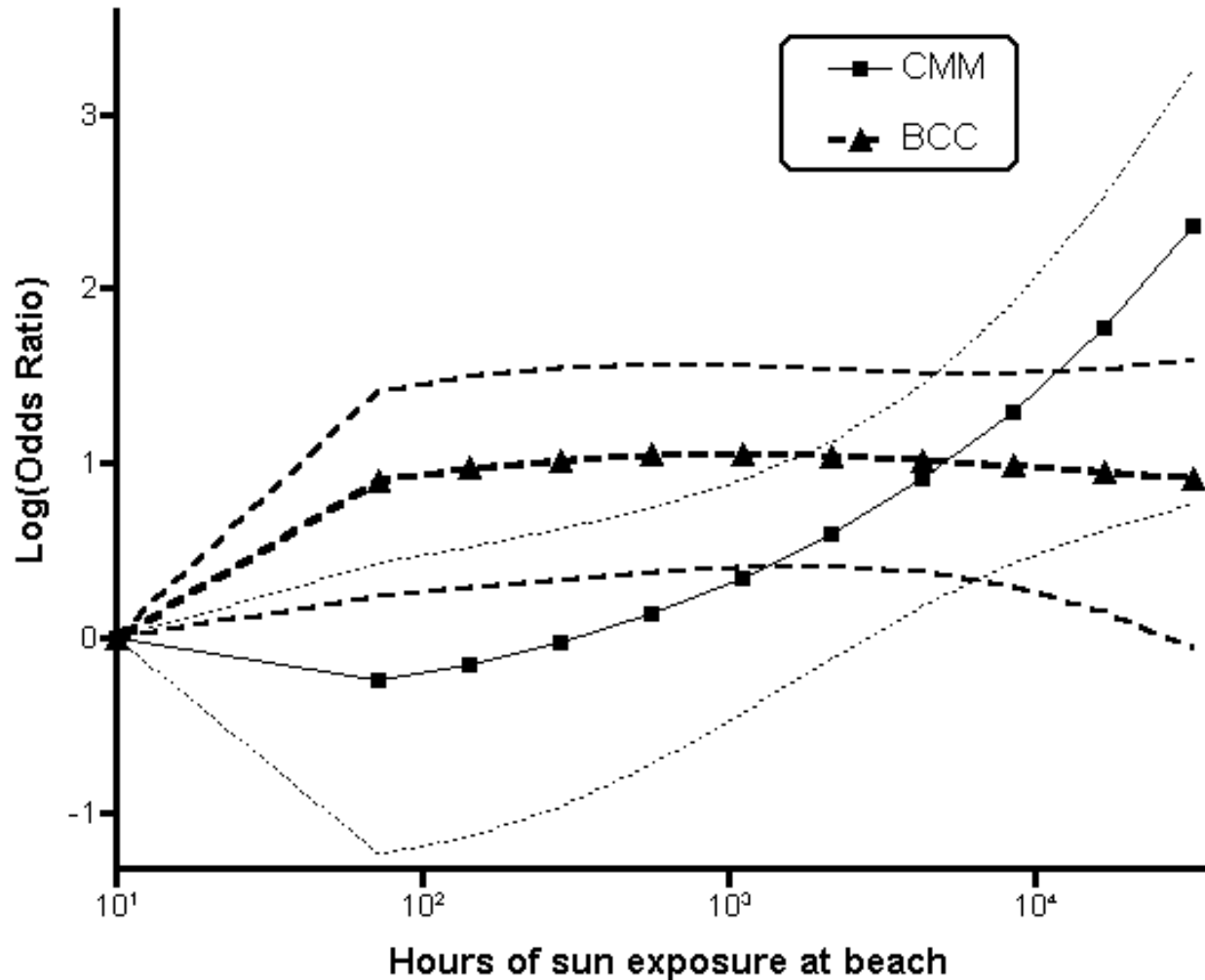
INDICE della presentazione

2. La lunga strada della ricerca eziologica

2 fasi negli studi epidemiologici eziologici

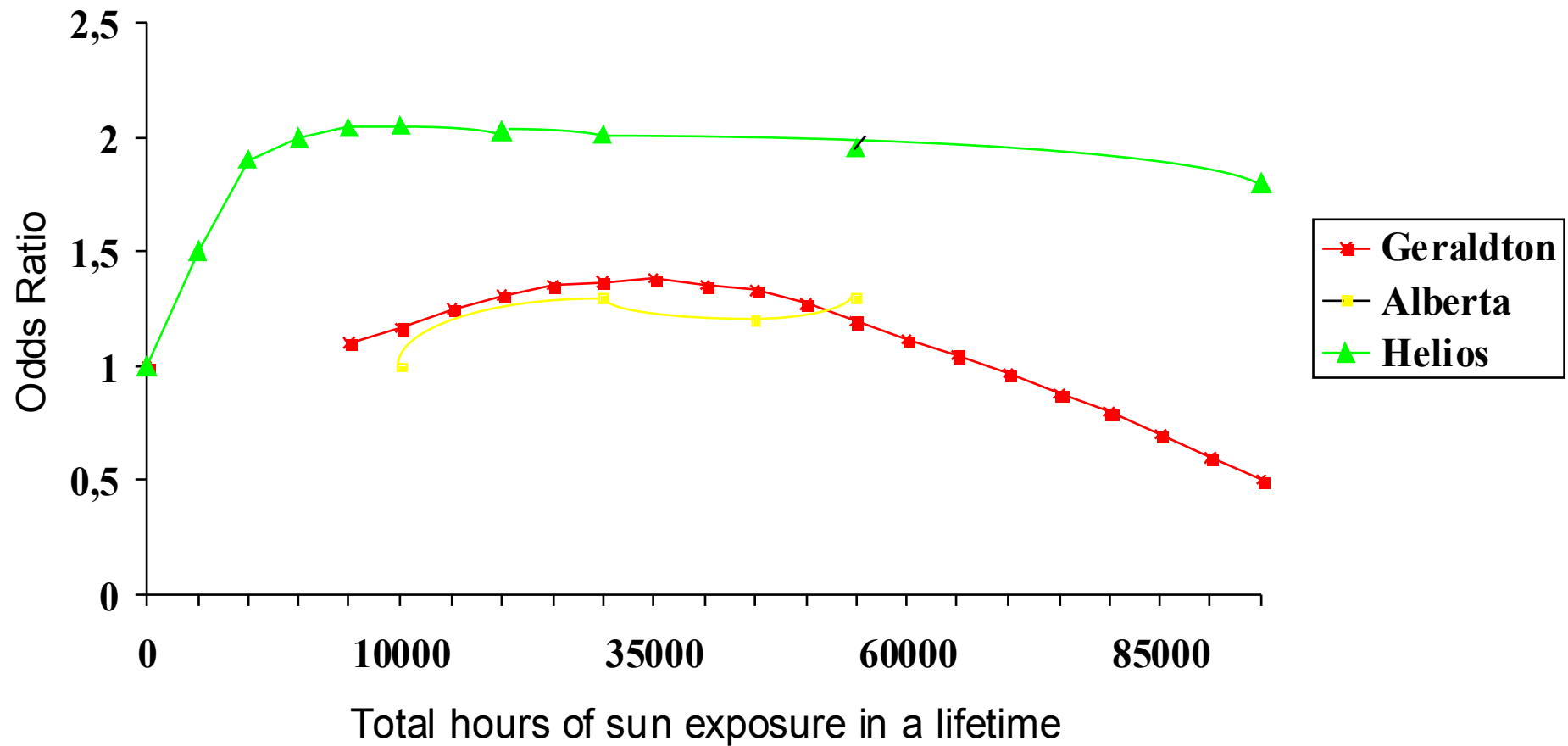
- - 1970-2000: studi tradizionali con interviste e metodi semi-oggettivi per la determinazione del fenotipo; principali risultati:
 - - esposizione solare
 - - conta dei nevi Rischi Relativi: 1,5 – 3.0
 - - altri fattori fenotipici
 - - UV artificiale e uso di protettivi

LA curva dose-risposta

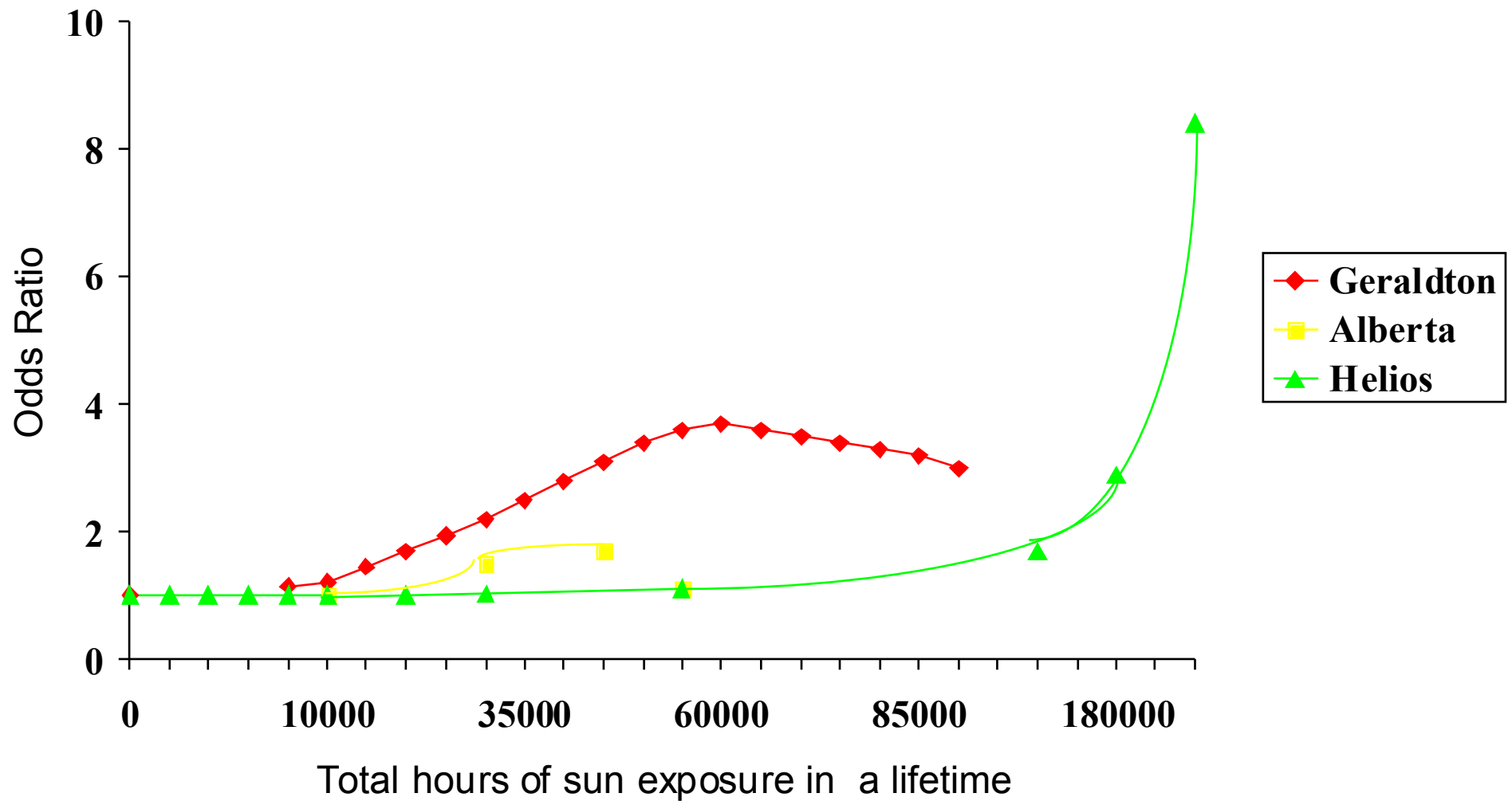


*Rosso, Zanetti, Pippione, Sancho-Garnier,
Melanoma Res 1998; 8: 573-583*

Dose-response curves for sun exposure and BCC

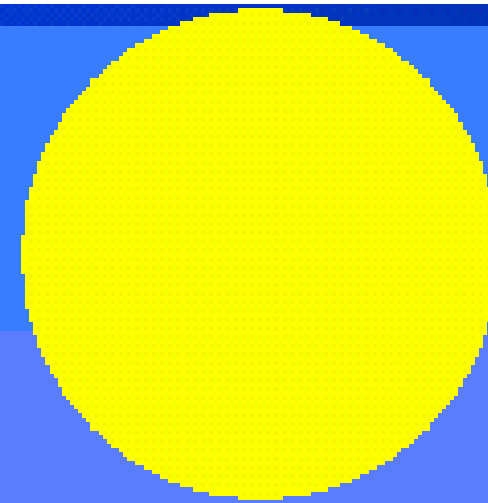


Dose-response curves for sun exposure and SCC



Occupational risks for skin carcinoma

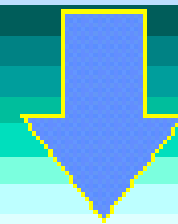
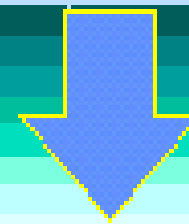
	cases	cas-n	contr	con-n	Oradj	li3	ls3
Secondary Education Teachers	46	1539	25	1482	1.75	1.05	2.891
Factory Manager	9	1576	2	1505	3.46	0.73	16.33
Specialized Farmer	55	1530	36	1471	1.49	0.96	2.324
Miners and Quarrymen	29	1556	4	1503	7.04	2.44	20.31
Mason	69	1516	47	1460	1.54	1.04	2.273
Railway Engine Driver and Firemen	10	1575	2	1505	4.14	0.89	19.29
Laborers n.e.c	122	1463	90	1417	1.37	1.02	1.847



U.V. EXPOSURE

Susceptible
Skins

Not susceptible
Skins



BCC-SCC-CMM

SCC



All'inizio del millennio nuovi studi su markers biologici

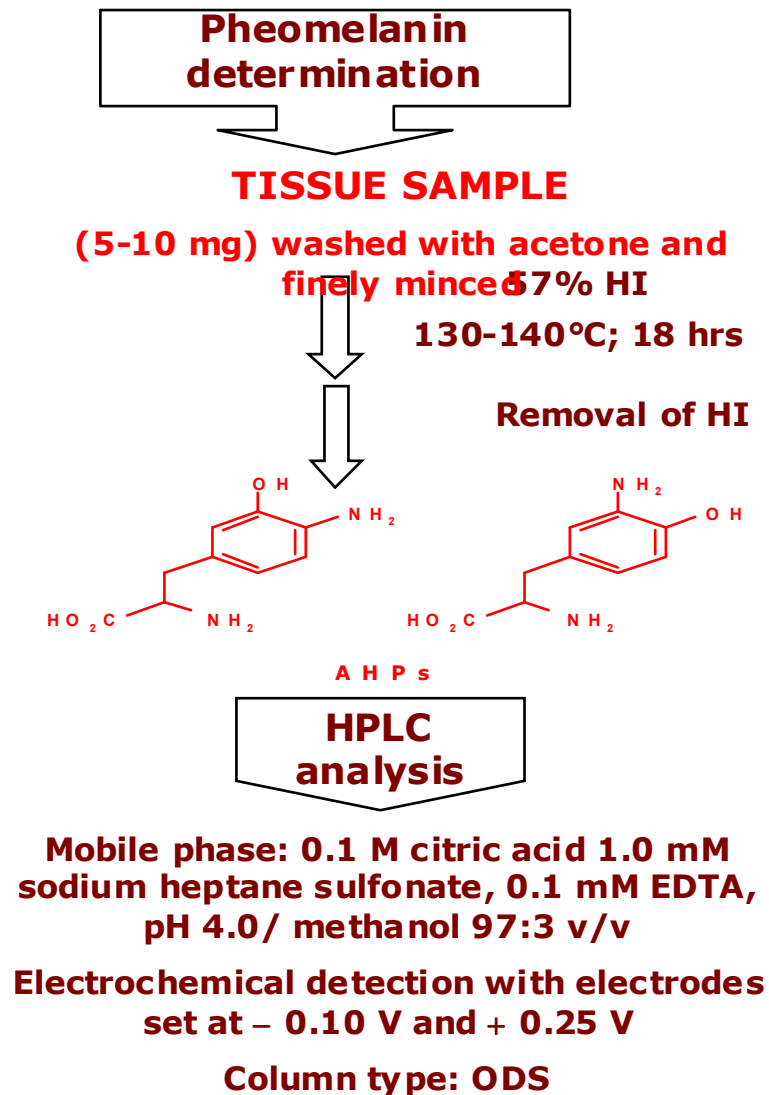
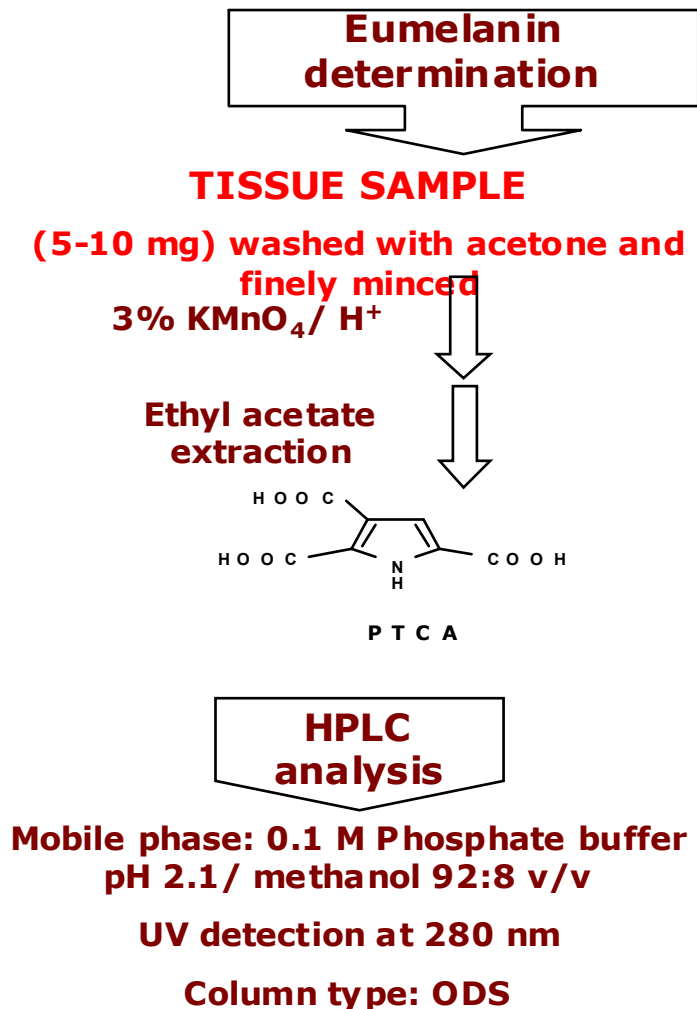
- Studi su markers somatici del melanoma (es. BRAF), proto-oncogeni (es CDKN2C) o polimorfismi (MC1R)
- Studi su marker biochimici: melanine

Human pigmentation-related genes

Locus	Protein	Function
Melanosome proteins		
TYR	Tyrosinase	Oxidation of tyrosine, dopa
TYRP1	gp75, TRYP1	DHICA-oxidase, TYR stabilisation
DCT	DCT, TRYP2	Dopachrome tautomerase
SILV	gp100, pMel17, Silver	DHICA-polymerisation and melanosome striations
OCA2	P-protein	pH of melanosome and melanosome maturation
MATP	MATP, AIM-1	Melanosome maturation
Signal proteins		
ASIP	Agouti signal protein	MC1R antagonist
MC1R	MSH receptor	G-protein coupled receptor
POMC	POMC, MSH, ACTH	MC1R agonist
OA1	OA1 protein	G-protein coupled receptor
MITF	MITF	Transcription factor
Proteins involved in melanosome transport or uptake by keratinocytes		
MYO5A	MyosinVa	Motor protein
RAB27A	Rab27a	RAS family protein
HPS1	HPS1	Organelle biogenesis and size
HPS6	HPS6	Organelle biogenesis

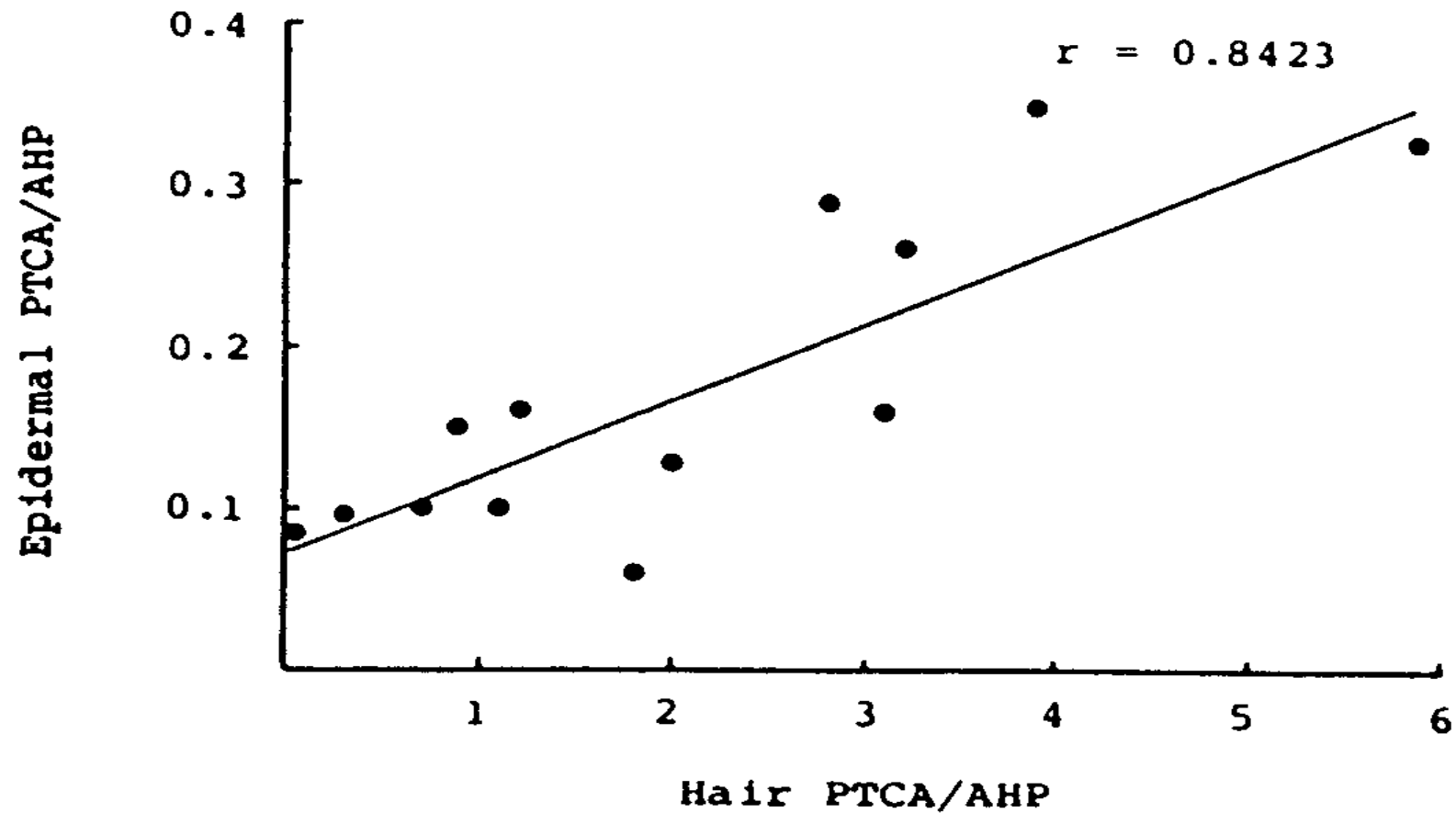
CHEMICAL DEGRADATION AND HPLC QUANTITATION OF EUMELANIN AND PHEOMELANIN STRUCTURAL MARKERS

CURRENT PROCEDURES*



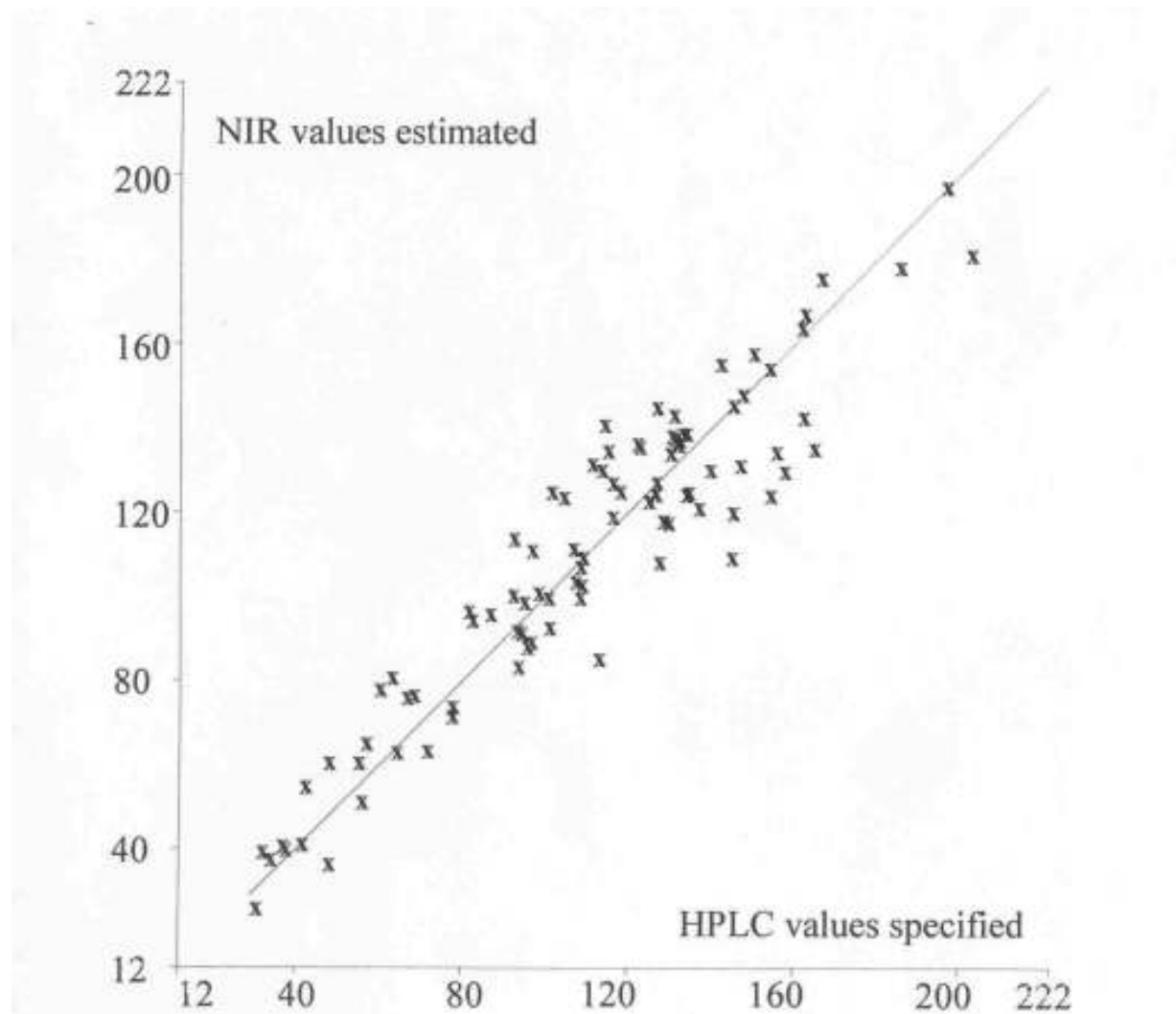
* Ito, S.;Fujita, K. *Anal. Biochem.* 1985, 144, 527-536.

Relationship between hair and epidermal Eumelanin and Phaeomelanin



Thody AJ. et al. *Invest. Dermatol.* 1991, 97, 340-344.

NIR spectrophotometry PTCA values in ng/mg of hair



Zoccola M, Mossoti R, Innocenti R, Loria DI, Rosso S, Zanetti R. *Pigment Cell Res.* 2004; 17: 379-385.

Conclusions

- Good reliability of Eumelanin measurement
- Reliability of Pheomelanin measurement to be improved
- Eumelanin and Pheomelanin are not only structurally different but also are associated to epidemiological measures of skin characteristics in a different way
- They likely convey a different information on risk patterns of skin

The GEM Study

- Memorial Sloan-Kettering Cancer Centre - coordinating centre- (M. Berwick)
- Recruiting centres: New Jersey, North Carolina, Michigan, British Columbia, Ontario (Toronto), Australia (NSW), Tasmania, Italy (Turin)
- Laboratories: MSKCC, Rebbeck (PA), Millikan (NC), UCI

Summary of results from the GEM study

- Nucleotide excision repair genes
 - XPD 312 (OR 1.5) XPD 751 (OR 1.4) *Millikan et al 2006*
- CDKN2A *Berwick et al 2006* (**OR 4.3 p<0.05**)
- MC1R *Dwyer et al 2003* (OR 1.4 ns)
- MC1R *Kanetsky et al 2006* (**OR 1.6 p<0.05**)
- EGF G/G vs A/A (OR 1.09 ns) *Amend et al 2004*
- INK4A (OR 7.2 ns) *Berwick et al 2004*

... un nuovo filone di studi su
melanoma, Parkinson e
LevoDopa

- Zanetti R, Loria DI, Rosso S. Melanoma, Parkinson's disease and levodopa: causal or spurious link? A review of the literature. *Melanoma Res.* 2006; **16**: 201-6.
- Zanetti R, Rosso S Levodopa and risk of melanoma. *Lancet.* 2007; **369**: 257-8.
- Zanetti R, Rosso S, Loria DI. Parkinson's disease and cancer. *Cancer Epidemiol Biomarkers Prev* 2007; **16**: 1081.

INDICE della presentazione

3. Diagnosi precoce/screening

Nel caso dei tumori cutanei...

- Intensità di diagnosi precoce
- Assenza di evidenza formale
- Assenza di programmi che rispettino i requisiti dello screening formale di popolazione
- Virtuale (effettiva?) impossibilità di svolgere un trial (dimensione, incontaminazione del gruppo di controllo)

Conseguenze della intensità di diagnosi precoce

- Aumento dell'incidenza di forme sottili
- Diminuzione (o stabilità?) dell'incidenza di forme avanzate
- Aumento della consapevolezza personale (prevenzione primaria)
- Miglioramento dell'accesso ai trattamenti
- Miglioramento della qualità dei trattamenti
- Maggiore intensità di Follow-up (allorché i Registri contano i casi, non le persone)
- Riduzione della mortalità per SCC, e per CMM nei giovani

INDICE della presentazione

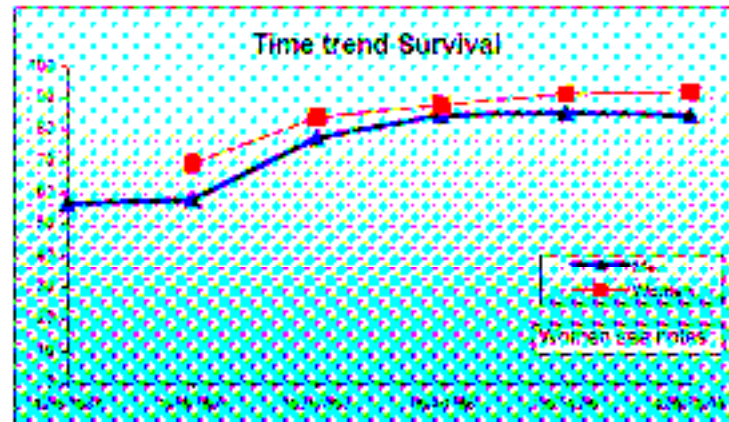
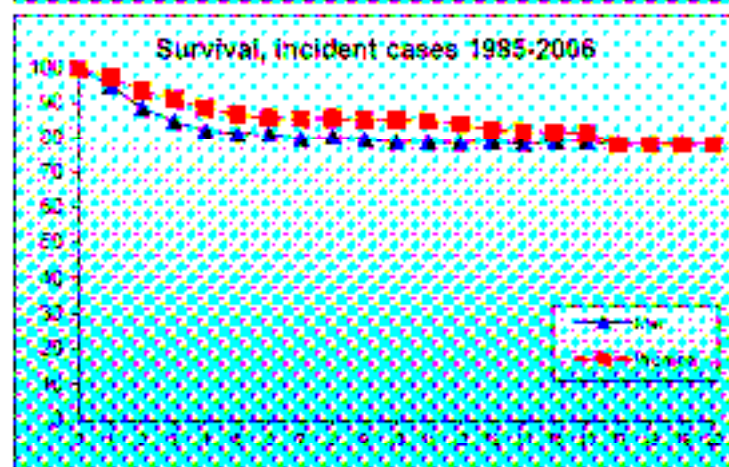
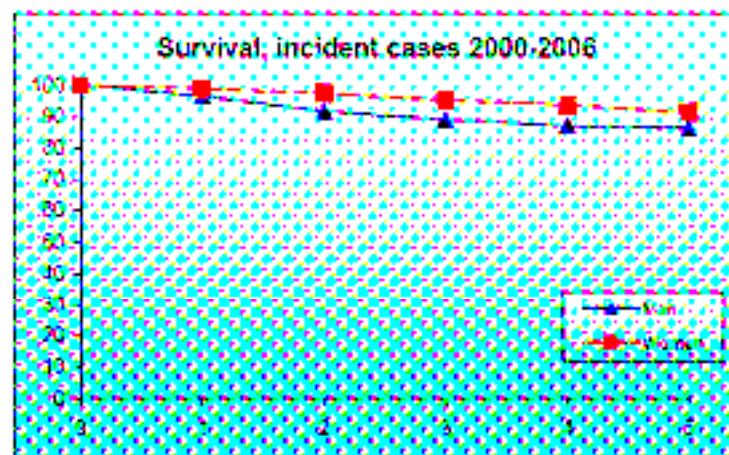
4. Gli andamenti della sopravvivenza

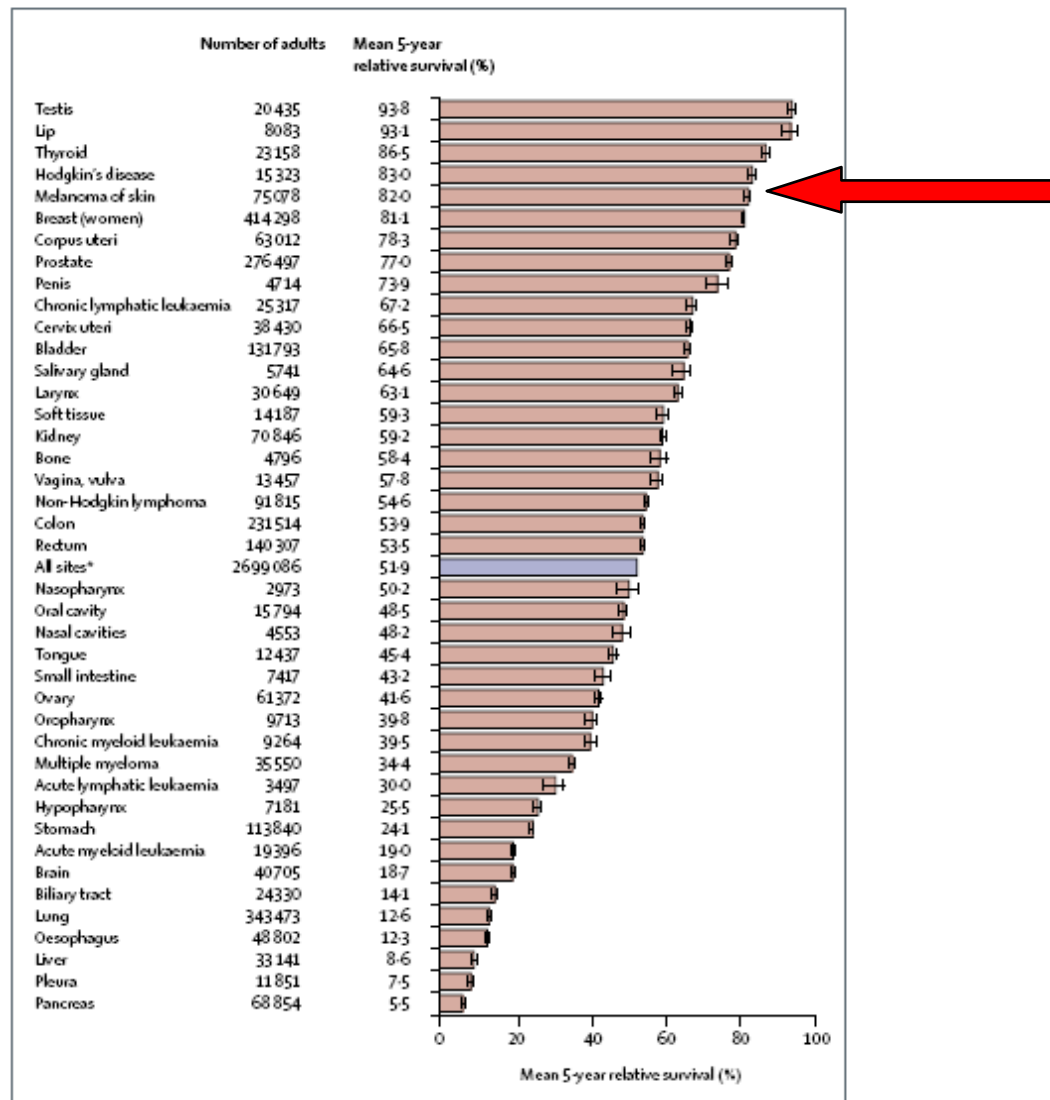
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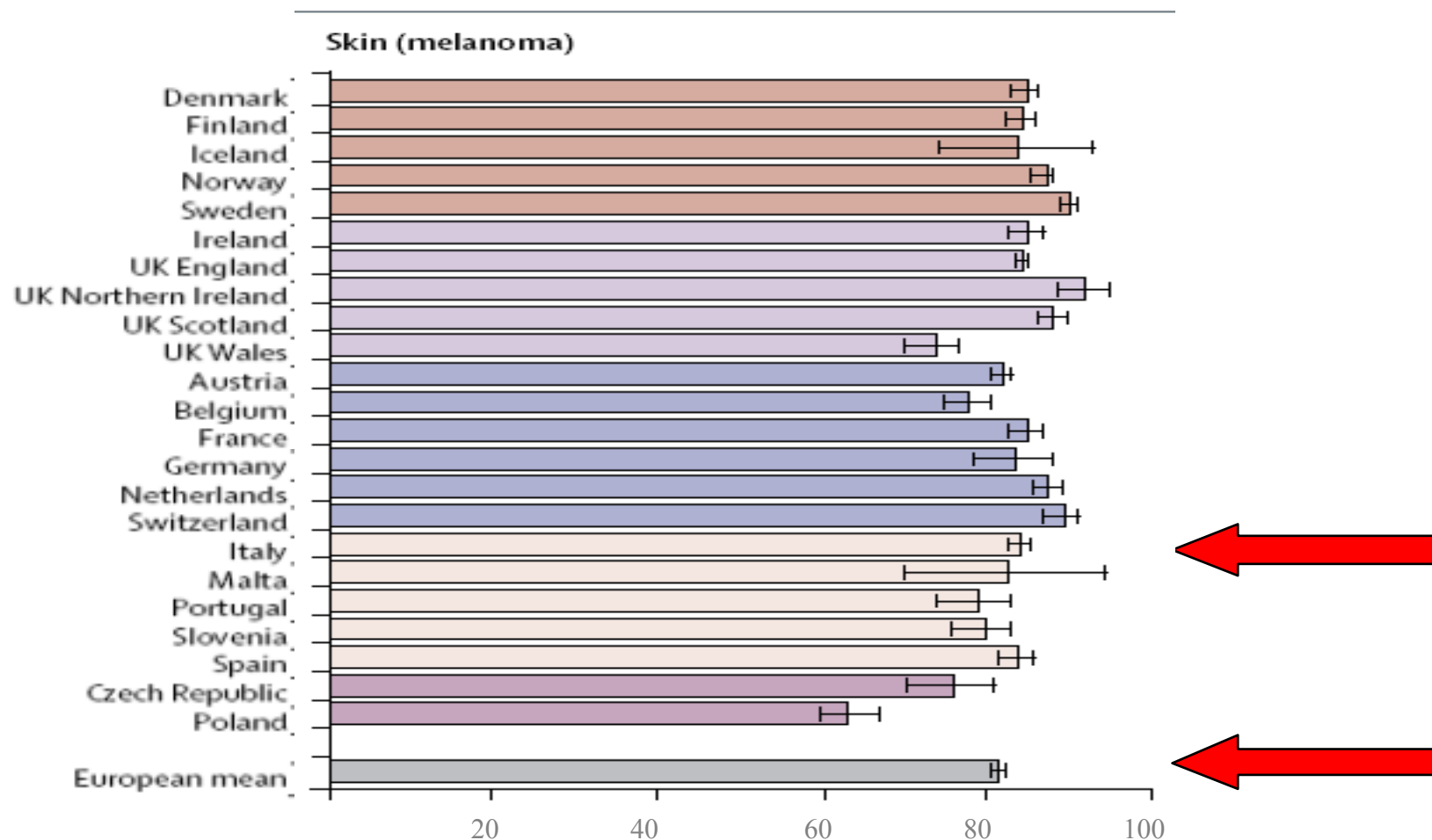
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PREVALENCE 31/12/2008		
N° of cases x 100.000		
	MEN	WOMEN
observed (since 1985)	190.2	204.4





Eurocare 4. Sopravvivenza a 5 anni dei casi diagnosticati nel periodo 1995 – 1999. Confronto fra le sopravvivenze di diversi tumori



Studio Eurocare 4. Sopravvivenza a 5 anni dei casi diagnosticati nel periodo 1995 – 1999, in diversi paesi Europei, e media Europea

**GRAZIE
PER
L'ATTENZIONE**

