

Decreasing Breslow tumour thickness and enhanced treatment have both contributed to improve survival from cutaneous malignant melanoma in Italy over the last two decades

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INTRODUCTION [1/2]

BACKGROUND

- **Increasing incidence** of cutaneous malignant melanoma (CMM) in most Western countries after World War II:
 - UV radiation exposure and change in sunbathing habits
- Incidence increase primarily driven by **early-stage CMM** cases, i.e. cases with low Breslow tumour thickness (with short distance between the most superficial layer of the skin to the deepest level of invasion).
The incidence of **thick CMM** has also increased, but to a lesser extent
- **Increase in survival**
- A low Breslow thickness is the most favourable prognostic factor
 - The survival increase has *generally* been attributed to the rise in thin CMM incidence rates
- However, a positive temporal correlation not necessarily implies a *causal* link
- **Advances in treatment** should be taken into account

INTRODUCTION [2/2]

OBJECTIVE

In view of the implications in policies for secondary prevention and treatment of CMM, this study explores the role of decreasing tumour-thickness in the upward trend in survival from CMM observed in **ITALY** in the last decades.

METHODS _[1/2]

DATA

- Source: Italian Association of Cancer Registries (AIRTUM)
- Breslow Thickness (mm) collected: *not a standard registration item*
- Breslow Thickness (mm) classified as per American Joint Committee on Cancer (AJCC) staging criteria 7th edition:
 - 0.00–1.00
 - 1.01–2.00
 - 2.01–4.00
 - >4.00 mm
- 15-year study period (**2003-2017**)
 - 11** Registries included
 - 17,674** eligible cases (aged ≥15 years)
- Covered population: 8,056,608 (on 1st January 2010) → 13.5% of the Italian population

METHODS [2/2]

STATISTICAL METHODS

- ❖ **Net survival (NS):** to estimate 5 years survival from CMM controlling for the risks of death from other causes, a *complete approach* was also used: patients followed for less than 5 years contributed with their own follow-up time;
- ❖ **Average Annual Percent Changes (AAPC):** estimated by fitting a GLM for the natural logarithm of the age-standardised incidence rates and year as a linear trend, with a Gaussian distribution and identity link function;
- ❖ **Multivariate analysis of 5-year NS:** performed by estimating the relative excess risk of death (RER) by fitting a GLM with a Poisson error structure based on aggregated data using exact survival time (person-years);
 - ❖ **Excess risk of death:** risk above what would have been observed if the reference population death rates had been the same of the study population.

RESULTS [1/4]

PROGNOSTIC FACTORS

- ✓ Strong inverse prognostic significance of tumour thickness and age confirmed by multivariate analysis
- ✓ Higher average 5-year NS for women than men:
 - 93.7 (95% CI, 92.8-94.7) versus 91.6 (95% CI, 90.6-92.6), $p < 0.001$

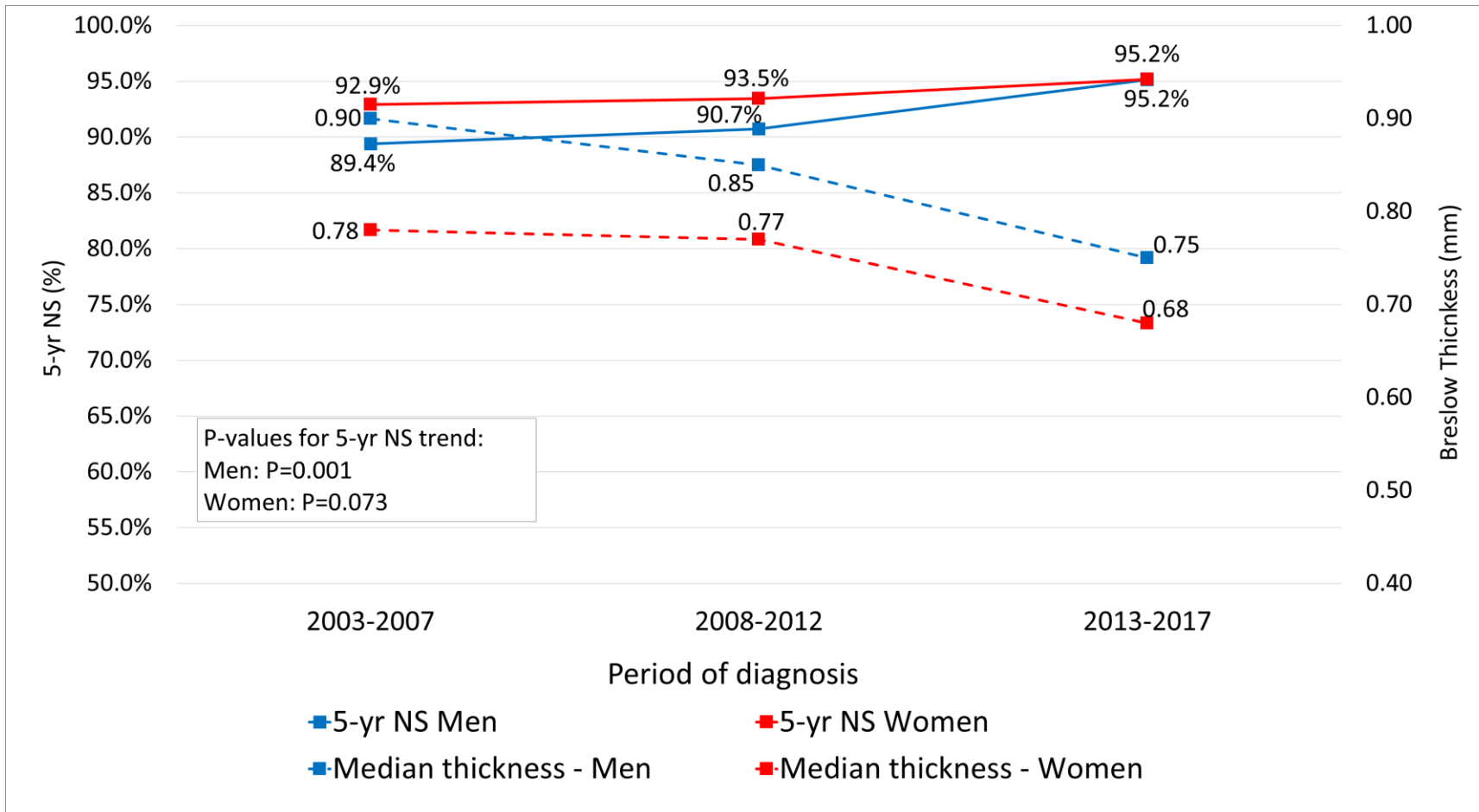
TIME TRENDS IN INCIDENCE BY THICKNESS

- ✓ More rapid **incidence increase** for thin CMM than for the two intermediate thickness categories:

	Men	Women
Thickness (mm)	EAAPC (95% CI)	EAAPC (95% CI)
0-1	6.7* (5.7-7.8)	4.7* (3.4-6.0)
1.01-2	3.1* (1.6-4.5)	1.6* (0.4-2.9)
2.01-4	3.2* (1.9-4.4)	3.1* (1.3-4.8)
>4	4.9* (3.4-6.4)	5.0* (2.7-7.2)

RESULTS [2/4]

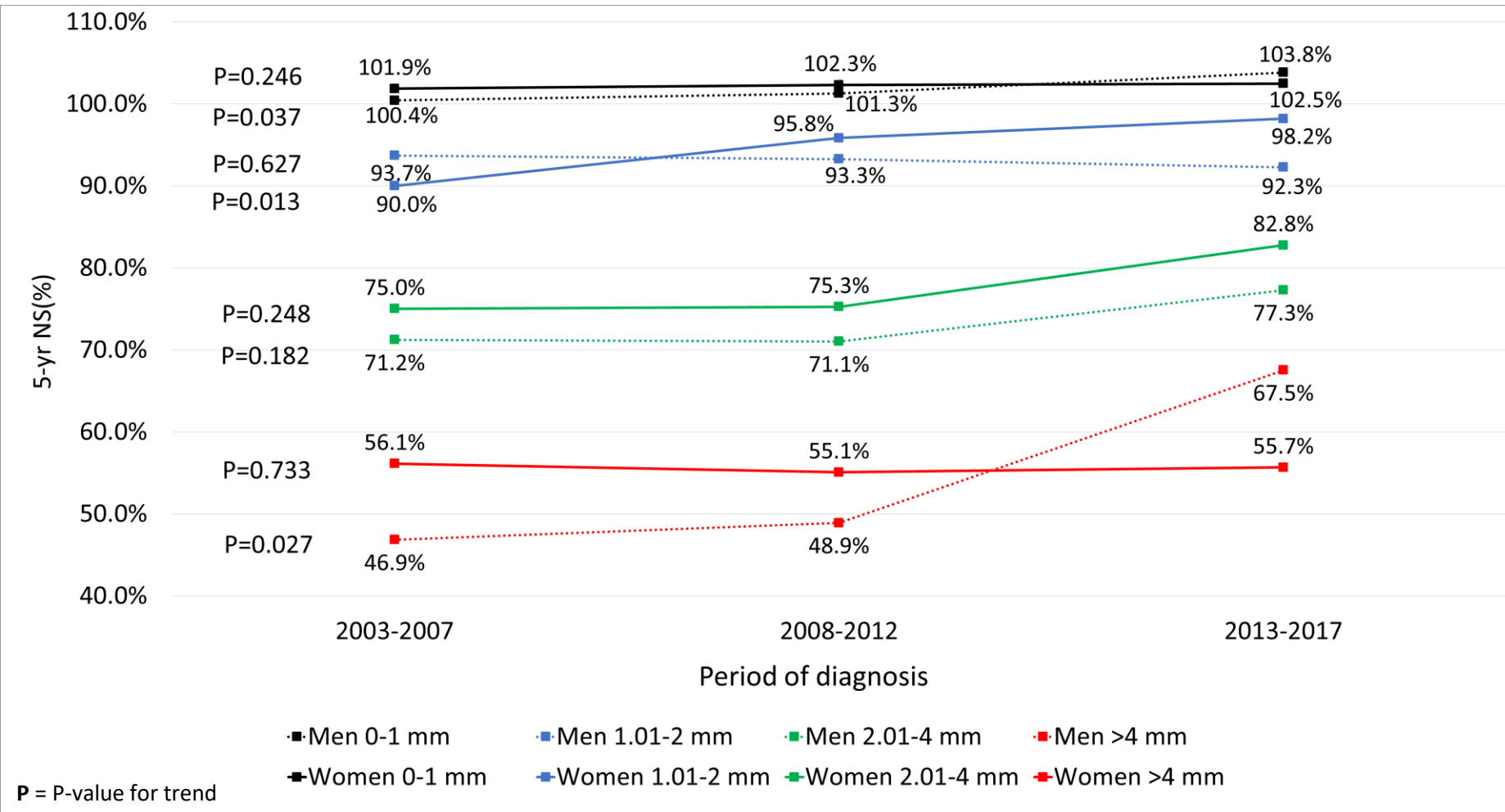
TIME TREND IN 5-YEAR NS



- ✓ **Decrease** in median tumour thickness, steeper for **men** and with a more pronounced variation in 2013-2017.
- ✓ **Borderline** significance of trend for **women**, due to their high baseline NS in 2003-2007.
- ✓ **Marked increase** in 5-years NS in 2013-2017 for **men** → they had no longer any survival gap despite their higher median tumour thickness

RESULTS [3/4]

TIME TREND IN 5-YEAR NS



- ✓ **Improvement** in survival more pronounced with increasing tumour thickness category.
- ✓ For **women**, the increase was **limited** to lesions 2.01-4.00 and >4.00 mm thick.
- ✓ For **men**, dramatic **improvement** in survival from the thickest CMMs in the last time period.

RESULTS [4/4]

STEPWISE MULTIVARIATE ANALYSIS OF SURVIVAL

Sex	Model	Variable	LR Test	P-Value	RERs and 95% CI		
					2003-2007	2008-2012	2013-2017
Men	A	Period			1.00	0.94 (0.64-1.36)	0.65 (0.41-1.01)
	B	Model A plus age	B vs A	<0.001	1.00	0.91 (0.66-1.26)	0.62 (0.42-0.91)
	C	Model B plus histologic subtype	C vs B	<0.001	1.00	0.90 (0.68-1.19)	0.63 (0.45-0.88)
	D	Model C plus subsite	D vs C	0.057	1.00	0.89 (0.67-1.19)	0.64 (0.46-0.90)
	E	Model D plus thickness	E vs D	<0.001	1.00	0.94 (0.76-1.18)	0.72 (0.56-0.93)
Women	A	Period			1.00	0.86 (0.54-1.38)	0.62 (0.36-1.10)
	B	Model A plus age	B vs A	<0.001	1.00	0.88 (0.59-1.31)	0.66 (0.41-1.05)
	C	Model B plus histologic subtype	C vs B	<0.001	1.00	0.94 (0.67-1.30)	0.81 (0.54-1.21)
	D	Model C plus subsite	D vs C	0.020	1.00	0.92 (0.66-1.28)	0.82 (0.55-1.21)
	E	Model D plus thickness	E vs D	<0.001	1.00	0.98 (0.76-1.26)	0.86 (0.65-1.15)

DISCUSSION_[1/3]

PRINCIPAL FINDINGS

- ✓ Strong prognostic significance of tumour thickness
- ✓ Increasing incidence of *thin* CMM.
- ✓ Increasing survival from CMM in the last 20 years, more pronounced among men.
- ✓ Increasing survival gain with increasing tumour thickness
- ✓ Larger survival gain among men with the thickest lesions

DISCUSSION_[2/3]

PRINCIPAL FINDINGS

- ✓ The decrease in tumour thickness explained only part of the survival gain among patients diagnosed in 2013 and after.
 - ✓ **Men:** the decrease in tumour thickness accounted for approximately one fourth of the survival improvement occurring in 2013 and after
 - ✓ **Women:** better baseline survival and weakly significant increasing time trend. In sensitivity analysis, however, they showed a pattern of results comparable to that seen among men and at a borderline level of significance.

DISCUSSION _[3/3]

INTERPRETATION

- ✓ The most likely factor accounting for the rest of the survival gain: **the enhancement of treatment strategies for CMM** taking place in the last decade (targeted therapies and immune checkpoint inhibitors for advanced-stage, thick, unresectable, and metastatic CMM)
- ✓ **Early detection**: still an important but complementary strategy for improving clinical outcomes of patients

CONCLUSIONS

The decreasing tumour thickness accounted for one fourth of the improvement in survival observed in 2013-2017. The introduction of immunotherapy and targeted therapy in the last decade is the most likely explanation for the remaining component.

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Thank you very much for your attention



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