

Striking Increase of Thin Melanomas Contrasts With Stable Incidence of Thick Melanomas

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Objective: The aim of this study was to analyze the temporal evolution of melanoma incidence in the department of the Bas-Rhin, France, and to study the evolution of tumor thickness.

Design: Retrospective study including all histologically proven melanomas recorded at the cancer registry of the department of the Bas-Rhin between January 1980 and December 1992 and at the Cutaneous Histopathology Department of the University Hospitals, Strasbourg, between January 1980 and December 1997.

Setting: Population-based cancer registry and academic cutaneous histopathology department.

Patients: A total of 1254 patients with histologically proven melanomas.

Intervention: None.

Main Outcome Measures: Temporal evolution of melanoma incidence and tumor thickness.

Results: The mean (SD) and median tumor thicknesses were 1.48 (1.59) mm and 0.87 mm, respectively, and they decreased during the study period. The increase in the number of melanomas was mainly related to an increase of superficial spreading melanomas in both sexes. The number of intermediate melanomas (1-2 mm) in both sexes and the number of melanomas with a Breslow index between 2 and 4 mm in women increased only slightly. The number of melanomas with a Breslow index greater than 2 mm in men and greater than 4 mm in women remained stable during the reference period.

Conclusion: A striking increase in incidence of thin melanomas contrasts with a stable incidence of thick melanomas.

Arch Dermatol. 1999;135:1451-1456

MELANOMA incidence is increasing worldwide between 3% and 7% per year in populations of European origin.¹⁻⁹ Metastatic melanomas usually lead to death, whereas many persons with a thin stage I lesion can be cured.^{10,11} In most Western countries, this has encouraged prevention and early detection.¹²⁻¹⁹ Detection is primarily aimed at the early diagnosis of thin melanomas,^{12,13} which is consistent with a common histopathologic

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entity, namely, the radial growth phase on the skin surface of the most common histologic type, the superficial spreading melanoma.^{12,20,21} Efficient screening for melanoma requires precise epidemiological data. Very few data are known for France.⁹ To address this question and to see how France compares with other Western countries, we studied the melanoma incidence in the department of the Bas-Rhin, France,

and we evaluated the evolution of the Breslow index since 1980 in a cutaneous histopathology department in which all cases of melanoma were confirmed by 2 dermatopathologists (E.M.G. and B.J.C.).

RESULTS

GLOBAL EPIDEMIOLOGY OF MELANOMA IN THE DEPARTMENT OF THE BAS-RHIN, 1980 TO 1992 (DATA FROM THE CANCER REGISTRY OF THE DEPARTMENT OF THE BAS-RHIN)

The annual melanoma incidence, adjusted for age to the local standard population, increased in both women and men during the reference period. In women, world standardized incidence increased from 4.7 per 100 000 in 1980 to 8.46 per 100 000 in 1992 ($P < .001$) and in men from 3.33 per 100 000 to 6.24 per 100 000 ($P < .001$) (**Figure 1**). The highest standardized incidences were 10.18 per 100 000 for women in 1989 and 10.91 per 100 000 for men in 1990.

MATERIALS AND METHODS

This study describes the epidemiology of cutaneous melanoma between January 1980 and December 1997 in the department of the Bas-Rhin, France. All melanomas recorded in the population-based cancer registry of the Bas-Rhin (Registre des cancers du Bas-Rhin) between January 1980 and December 1992 were included. Investigators from the registry conduct a survey each year in all private and public pathology laboratories and record every new case of melanoma. The data recorded include year of diagnosis and sex and age of the patient. Mortality related to melanoma in the department of the Bas-Rhin was available for the study period through exhaustive reviewing of death certificates.

Sixty percent of the melanomas were diagnosed in a single pathology center, the Department for Cutaneous Histopathology, University Hospitals, Strasbourg, France. The diagnosis of melanoma was confirmed in all cases by 2 dermatopathologists. The melanomas diagnosed in this center were further analyzed for anatomic site, histopathology, tumor thickness, Clark level, and the delay in diagnosis of melanoma, which was defined as follows: (1) for a newly appearing lesion, the time from when the patient first noticed an abnormal lesion to the date of excision of the lesion; (2) for preexisting lesions that remained unchanged for at least 5 years, the time between the first clinical changes the patient noticed and excision. This information was obtained by personal interview of the patient. This detailed analysis also included the period from January 1993 through December 1997, which was not recorded in the cancer registry at the time of the present study.

Log-linear regression with Poisson error in an age \times period model and χ^2 tests were applied where appropriate, using GLIM 4, 1994.²² World standardized incidences were estimated using the EUROCLIM 1.1 database 1998, International Agency for Research on Cancer (IARC).

The annual mortality rate for melanoma in the same period ranged from 1.34 per 100 000 to 1.63 per 100 000 in men and from 0.83 per 100 000 to 1.26 per 100 000 in women. There was no significant increase of mortality during the study period ($P = .13$).

DETAILED ANALYSIS OF MELANOMAS DIAGNOSED AT THE DEPARTMENT FOR CUTANEOUS HISTOPATHOLOGY, UNIVERSITY HOSPITAL, STRASBOURG BETWEEN 1980 AND 1997

Data included in this analysis also include the melanomas diagnosed between 1993 and 1997, which were not yet exhaustively recorded in the cancer registry data bank. During the reference period, 1294 melanomas were diagnosed in 1254 patients. Twenty-eight patients had more than 1 melanoma. There were 734 women and 520 men

(woman-man ratio, 1.4) with a mean (SD) age of 54 (17) years. The number of melanomas diagnosed each year in this laboratory increased in both men and women during the study period (**Figure 2**). The mean (SD) and median tumor thicknesses were 1.48 (1.59) mm and 0.87 mm, respectively. Mean and median tumor thicknesses decreased steadily in both sexes between 1980 and 1997 (**Figure 3**). Clark level was known in 1082 melanomas; 119 (11%) were in situ Clark level I; 281 (26%) were Clark level II; 378 (35%), Clark level III; 239 (22%), Clark level IV; and 65 (6%), Clark level V. The 119 melanomas in situ occurred mainly in women (76%). The **Table** shows the anatomic sites of the melanomas according to sex. Most melanomas were located on the back in men (19%) and the legs in women (19%). There were 699 (54%) superficial spreading melanomas; 272 (21%) were nodular melanomas; 130 (10%), lentigo maligna melanomas; 90 (7%), acrolentiginous melanomas; and the growth pattern was unknown in 103 (8%). The median Breslow index was 2.6 mm in the group of nodular melanomas compared with 0.65 in superficial spreading melanomas, 1.15 in acrolentiginous melanomas, and 0.58 in lentigo maligna melanomas. The increase in the number of melanomas was largely related to an increase of superficial spreading melanomas in both sexes (**Figure 4** and **Figure 5**).

The number of thin melanomas (<1 mm) increased dramatically ($P < .001$). The number of intermediate melanomas (1-2 mm) increased slightly in both sexes ($P < .001$) as well as the number of melanomas between 2 and 4 mm in women ($P < .001$). The number of melanomas between 2 and 4 mm in men ($P = .15$) and larger than 4 mm in both sexes ($P = .38$) remained stable during the reference period (**Figure 6** and **Figure 7**).

The delay in the diagnosis of melanoma was known in 445 patients. The mean (SD) and median values were 30 (32) months and 24 months, respectively. This delay was significantly shorter in thick (>2 -mm) melanomas (mean [SD] delay, 18 [29] months; median delay, 12 months) than in thin (<1 -mm) melanomas (mean [SD] delay, 35 [34] months; median delay, 24 months) ($P < .001$). There were more women in the group of subjects for whom information about the delay to diagnosis was available than in the rest of the study population (woman-man ratios, 1.5:1.3). The Breslow index in this group was slightly thinner (1.35 mm vs 1.5 mm; $P = .04$), but there was no significant statistical difference in age between the 2 groups.

COMMENT

This study showed a considerable increase in the number of thin melanomas in both sexes, which contrasted with only a slight increase of thick melanomas in women or even a stable number of thick melanomas in men. Strasbourg (located 48.35° N, 7.45° E) is the main city of the department of the Bas-Rhin, with about 1 million inhabitants. Data provided from the local and exhaustive cancer registry showed that melanoma incidence in the department of the Bas-Rhin increased in both sexes and reached more than 10 per 100 000 from the late 1980s on. This range of incidence is close to the incidence reported in other Western European countries.^{1,2,3,7,8}

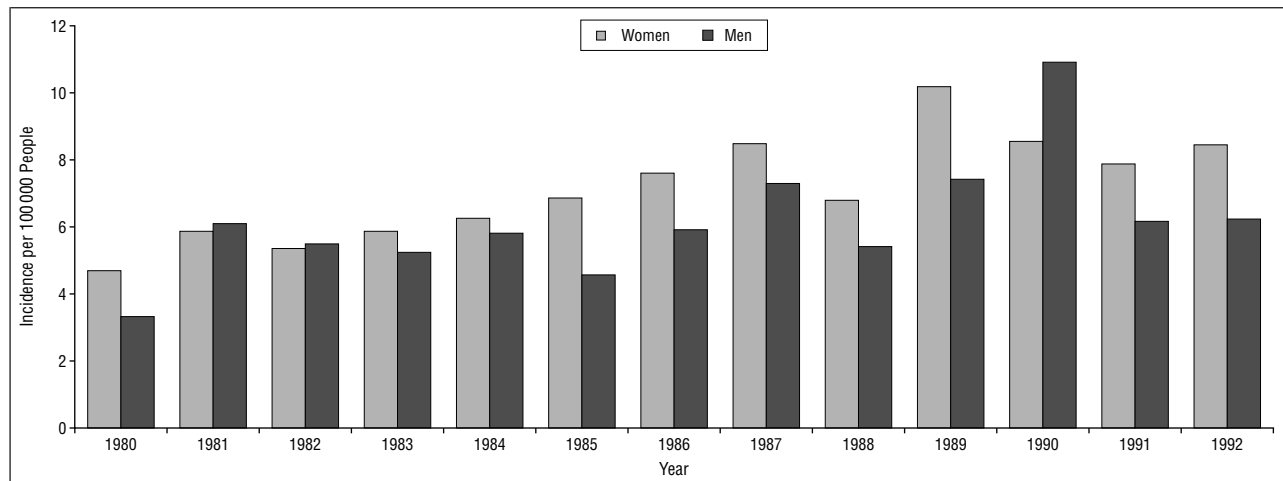


Figure 1. World-standardized incidence of melanoma in the department of the Bas-Rhin.

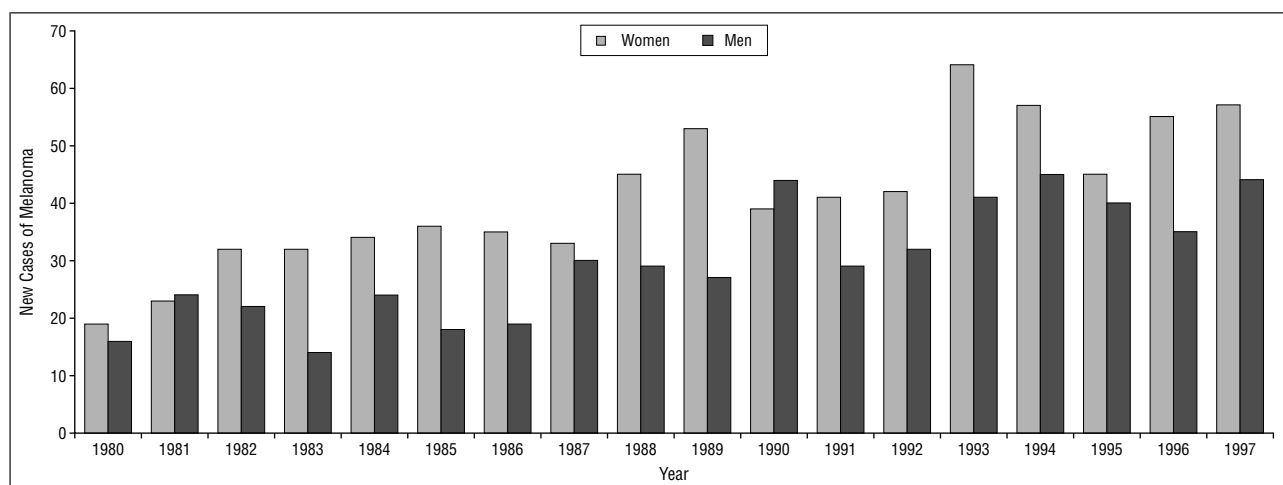


Figure 2. New cases of melanoma diagnosed at the Department for Cutaneous Histopathology, University Hospitals, Strasbourg, France, between 1980 and 1997.

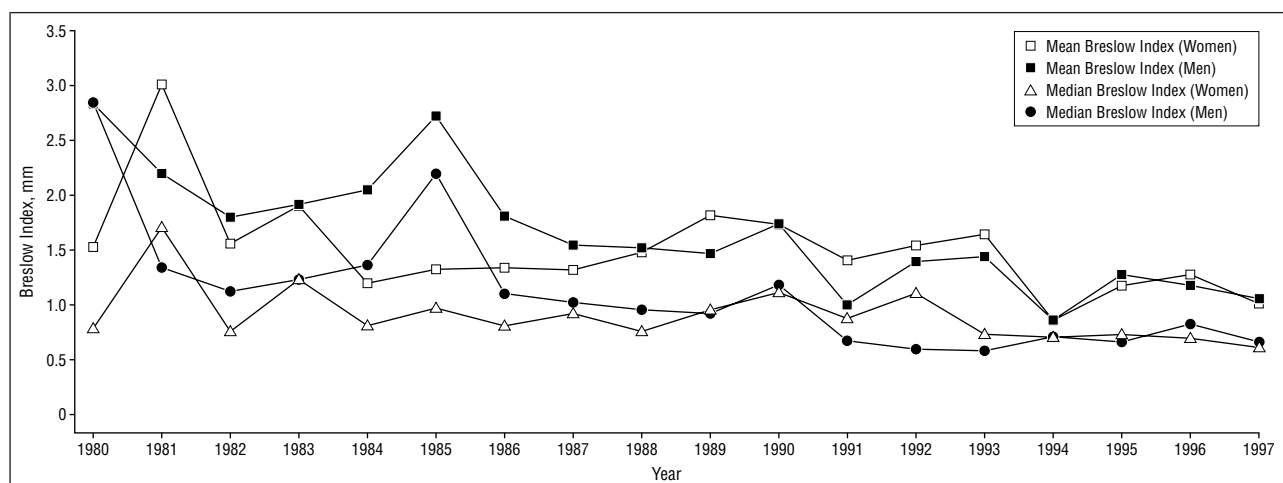


Figure 3. Tumor size as determined by mean and median Breslow index for both men and women.

Using the recently reviewed and critiqued optimal cutoffs of tumor thickness,¹¹ we evaluated incidence of tumors according to the Breslow index (Figures 6 and 7). Melanoma incidence overall increased mainly as a result of an increased incidence of thin melanomas. The

same senior dermatopathologist (E.M.G.) confirmed all diagnoses of melanoma in this study, using the same histopathologic criteria for all cases. These 2 facts combined suggest a real and not artifactual increase in incidence. Van der Esch et al²³ have already shown similar

Anatomic Site Distribution of Melanomas According to Sex

Site	Women	Men	Total
Arm	93	53	146
Forearm	32	16	48
Hand	20	13	33
Total Upper Limb	145	82	227
Buttock	5	5	10
Thigh	50	33	83
Leg	211	39	250
Foot	65	31	96
Total Lower Limb	331	108	439
Scalp	4	6	10
Face	104	67	171
Neck	18	18	36
Total Head and Neck	126	91	217
Thorax	20	47	67
Abdomen	18	28	46
Back	85	166	251
Total Trunk	123	241	364
Mucosa	6	2	8
Unknown	24	15	39
Total	755	539	1294

results, although they did not include melanomas with a thickness less than 0.75 mm in the earliest period examined, which makes the relevance of their observations on thin tumors questionable. However, in our study the number of thick melanomas remained stable during this 18-year period. The contrast between a striking increase in incidence of thin melanomas and a stable incidence of thick melanomas has been reported by others.^{2,3,4} MacKie et al² showed a major increase in incidence of thin melanomas in both sexes, while incidence of intermediate and thick melanomas was stable in women and increased only slightly in men. In the study by MacKie et al,² incidence of melanoma stabilized in women younger than 65 years after 1986, which was not the case in our study (data not shown).

An increase in melanoma incidence has been reported in most Western countries.^{1-8,24} This might be related to many factors, including increased longevity, increased exposure to risk factors, increased concern in the general population, more accurate diagnosis, and increased use of immunochemistry to better diagnose poorly differentiated malignancies more specifically as

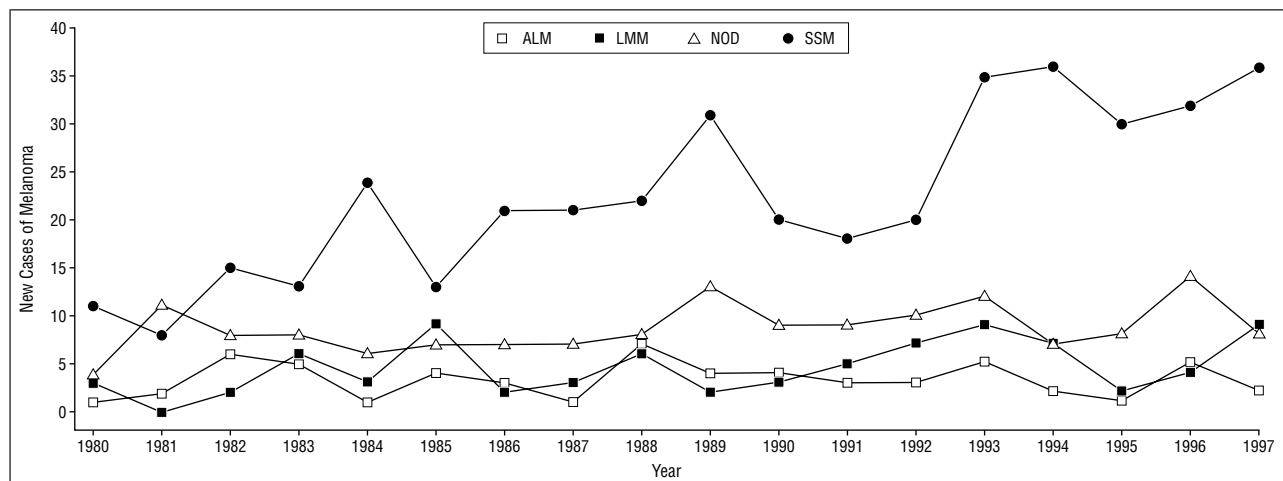


Figure 4. New cases of melanoma in women according to histologic subtype. ALM indicates acrolentiginous melanoma; LMM, lentigo maligna melanoma; NOD, nodular melanoma; and SSM, superficial spreading melanoma.

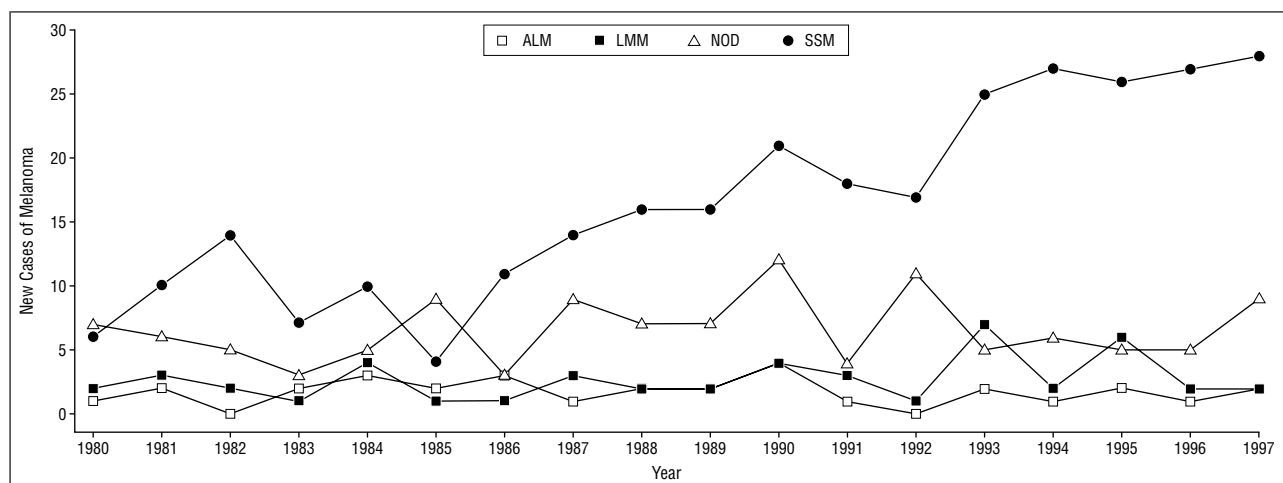


Figure 5. New cases of melanoma in men according to histologic subtype. ALM indicates acrolentiginous melanoma; LMM, lentigo maligna melanoma; NOD, nodular melanoma; and SSM, superficial spreading melanoma.

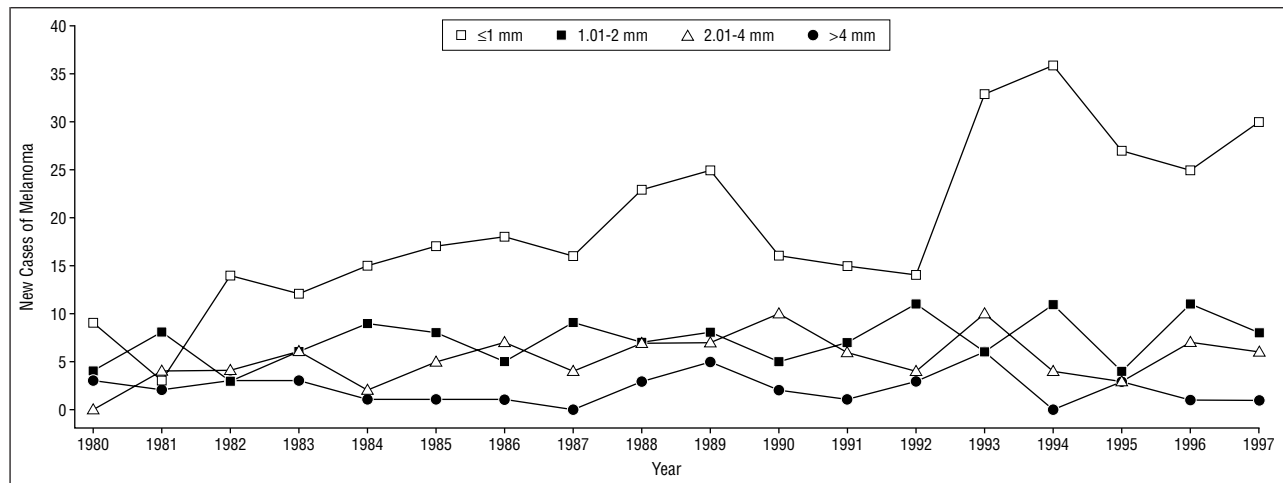


Figure 6. New cases of melanoma in women according to tumor thickness.

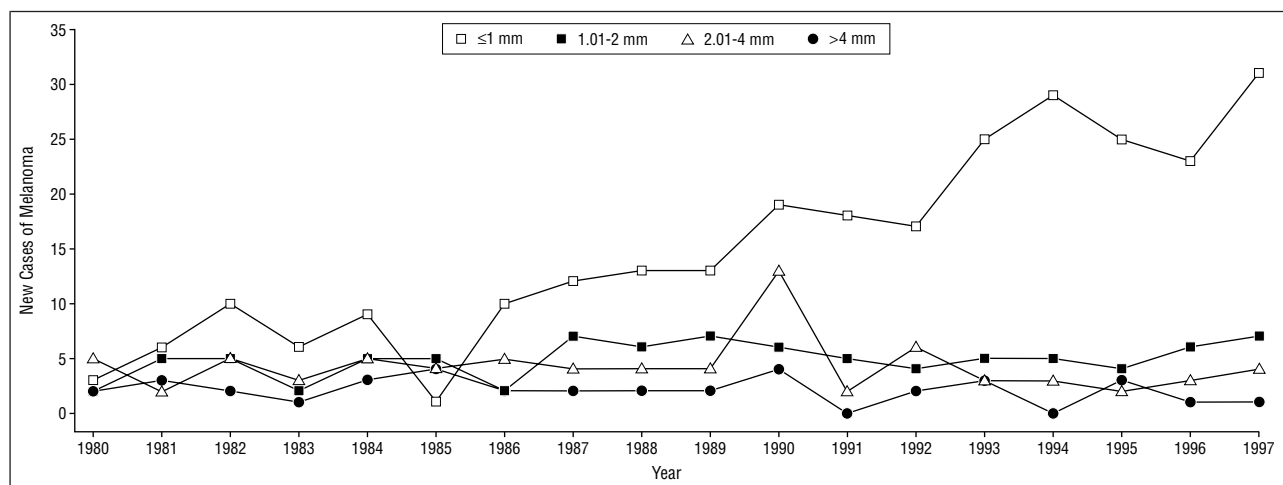


Figure 7. New cases of melanoma in men according to tumor thickness.

melanomas.²⁴ However, the increased incidences of thick and thin melanomas are different, and it seems that the excision of a growing number of thin melanomas has no effect on the incidence of thick melanomas, which are responsible for most of the mortality and morbidity. This fact suggests that thin (mainly superficial spreading) and thick (mainly nodular) melanomas might have different epidemiological features. In our study, the absence of a fall in incidence of thick melanomas after 18 years of observation may indicate that there has also been an increasing recognition of a form of melanoma that appears innocuous clinically and is unlikely to cause death if not treated. Other authors have suggested this possibility.^{25,26} The stability of the mortality related to melanoma in this population during the same period, which mimics the rate of thick melanomas, further supports this hypothesis.

We found an inverse association between the delay in diagnosis and tumor thickness. Indeed, the delay was shorter in the group with thick tumors. This finding has also been reported by others.^{3,27,28} Because this is a retrospective study, this delay was only approximate. Herd et al³ stated that "it is impossible to carry out a prospective study of delay to obtain hard data. There is too great a dependency on patients' memories, which are at best

unreliable, and at worst quite random." We share this point of view. Nevertheless, in this study, thick melanomas seemed to be mostly fast-growing tumors leading to prompt excision with a mean delay of 18 months, while the mean delay of excision of thin tumors was 35 months. This inverse association between diagnostic delay and tumor thickness reflects the variability of melanoma biology, which, along with the fast-growing nodular melanomas, is the main pitfall for an overall efficient early detection program, even if the entire population were well informed.

Accepted for publication April 28, 1999.

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