

# **Cancer registration in Belgium: experience from a melanoma registration programma in the province of East-Flanders**

by

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## **Abstract**

*This paper presents the results of a study investigating melanoma registration in Belgium.*

*Incidence rates reported by the National Cancer Registry were low compared to other European countries. Over the period 1989-1994 a decrease in reported melanoma incidence was observed, which was not reported in any other country and is most probably artificial. A melanoma registration programme in East-Flanders obtained a higher registration*

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compared to the National Cancer Registry in females, especially in the age group < 50. In these younger females, 6 of 22 (27%) melanomas were in situ compared to 5 in 29 (17%) in the other group ( $p = 0.39$ ). Additionally thinner invasive melanomas (median Breslow thickness 0.94mm versus 1.56mm,  $p = 0.019$ ) were reported in this group compared to females aged over 50. Such early-stage melanomas are more likely to be treated on an outpatient basis.

*These data suggest that the lower registration by the National Cancer Registry is most probably related to its hospital-based reporting system. Incorporation of registration procedures including pathology laboratories and the direct reporting by treating physicians, are currently being investigated in a cancer registration network in Flanders.*

## Keywords

Belgium, cancer registration, melanoma incidence, melanoma registration.

## Introduction

Reliable cancer statistics are indispensable to assess the burden of cancer, and the international variation in occurrence and time trends. They are also an indispensable instrument for the evaluation of cancer control activities ranging from health care planning and prevention campaigns to etiological research. They benefit both the individual and society. Data collection on cancers in a defined population attributes to the in-depth study of cancers, while reducing the risk of selection bias found in clinical series.

The aim of this study was to investigate melanoma registration in Belgium. In the first part of this paper melanoma incidence rates reported for Belgium are compared with the data of other European countries. In a second part, the time trends in melanoma incidence for Belgium are compared with the trends reported in the literature. A third part of this paper compares the melanoma registration by the National Cancer Registry with the results obtained by a melanoma registration programme in the province of East-Flanders. In the last part of the paper these results are compared with the findings of other cancer registration systems in Belgium. The possible explanations and implications of the results are discussed.

## Methods

Age-standardized melanoma incidence rates for Belgium for the period 1988-1992 were compared to those of other European countries. World-standardized incidence rates for several European countries were taken from the 7<sup>th</sup> volume of *Cancer Incidence in Five Continents* (1). World-standardized rates for Belgium were calculated using the direct method of standardization (2).

To evaluate trends in cancer incidence rates, the 1984-1994 data as reported by the National Cancer Registry were age-standardized to the European reference population (2). Multivariate modelling using Poisson regression models was used to evaluate the trends.

In November 1996, a melanoma registration programme was started in East-Flanders (approximately 1.300, 000 inhabitants). The registration started at the University Hospital of Ghent. Additionally, the dermatologists, plastic surgeons and pathologists of East-Flanders and the nearby provinces (644 physicians altogether) were sent a registration form three times a year and were asked to report all patients residing in East-Flanders with a first manifestation of cutaneous melanoma since 1 January 1995. Stamped envelopes with address label on them were included to encourage response. Dermatologists, plastic surgeons and physicians mentioned by the pathologists received information leaflets to inform their patients about the registry and ask their consent. In order to protect individual privacy, each patient was registered by a code. The registration form also asked for the patient's gender and year of birth, the date of the histological diagnosis and whether it concerned an invasive or an in situ melanoma. In the case of invasive melanoma, the Breslow thickness (this is the microscopically measured depth of the tumour, and is the most important prognostic factor in local disease) was registered. All reported cases were histologically confirmed.

The Chi-squared test was used to test equality of proportions (3). The Mann-Whitney U test was used to compare the medians of two populations (4).

The results of the melanoma registration programme were compared to melanoma incidence rates observed by other cancer registration systems in Belgium. Estimates on the expected number of melanoma cases in East-Flanders were based on the data of the Eindhoven Cancer Registry. The Eindhoven Cancer Registry is a regional cancer registry covering the south-east of the Netherlands, near the Belgian border

(population 2.1 million in 1988). In the 1980s, it was admitted to the International Association of Cancer Registries (IACR) (5). It has data on all cancer patients diagnosed since 1955. For comparison of the incidence rates of different registration systems confidence intervals were calculated (6).

The Belgian *National Cancer Registry* (NCR) includes incident cases of all kinds of cancer in Belgian inhabitants (approximately 10 million) since 1983. Data are collected by the sickness funds, of which more than 99% of the population is member because membership is mandatory. The overall underestimation of incident cancer cases is estimated at 20-25%, with a probably larger underregistration among males (7). Some of the causes of underreporting are the hospital-based reporting system and the lack of response of physicians who received a registration form. In the past years many efforts have been made to achieve a more complete cancer registration by including other data sources. The Belgian Work against Cancer started a cancer registration network in Flanders (8).

In 1990, a cancer registration programme called *AKR (Antwerps Kankerregister)* was started in the province of Antwerp (approximately 1.600, 000 inhabitants). Registration is performed by 6 full-time registration co-workers and includes patients from 10 of the 34 provincial hospitals. The quality of the collected data is excellent; there is information on tumour staging ((p)TNM classification (9)), treatment and follow-up (vital status). In 1996, registration covered 71% of the incident cancer cases reported by the NCR for the province of Antwerp (10). Registration is better for tumours treated with radiotherapy (e.g. lip, oral cavity, pharynx) and bronchuscarcinoma. On the other hand, tumours of the gastrointestinal tract, the urinary system, the skin and hematological malignancies are underrepresented (10).

In 1993, the Cancer Foundation of Limburg (*LIKAS, Limburgse Kanker Stichting*) decided to start a cancer registry in the province (approximately 800, 000 inhabitants) with the help of all provincial pathology laboratories and some laboratories outside the province. All cytologically and/or histologically confirmed tumours diagnosed in residents are entered in the register. This should theoretically lead to a complete registration of incident cancer cases, with the exception of tumours diagnosed only clinically and of hematological malignancies. One difficulty of the registration procedure is to discriminate between prevalent and incident cancer cases. A first report on the 1996 results is available (11).

There is a network of voluntary general practitioners (sentinel practices) who have been collecting various data, including incident cases of

some cancers for some years. This network tries to cover at least 1% of the Belgian population.

Finally, the reporting of data on hospitalization time and duration by different diagnostic groups has become mandatory for all hospitals since 1990. These MCD (minimal clinical data) are gathered to determine the financial needs of different patient populations. Disease registration from an epidemiological point of view is not an objective.

## Results

- 1) ***Melanoma incidence rates in Belgium (NCR): compared to other European countries, reported melanoma incidence rates in Belgium are low.***

In accordance with the hypothesis that sunlight is a major factor in the etiology of melanoma, melanoma incidence generally increases with increasing proximity to the equator. An exception to this pattern is found in Europe at latitudes higher than 50 degrees north, where increasing incidence rates are reported with increasing distance from the equator. Melanoma incidence rates in the Scandinavian countries are therefore higher than those observed in Mediterranean countries (12). This typically European phenomenon has been attributed to the skin colour ranging from dark in the south to light in the north, giving rise to a different susceptibility to melanoma. An exception to this European phenomenon is England (latitude 50-60° north), where melanoma incidence increases with decreasing latitude. This is probably related to a rather homogeneous skin complexion of the British population (13).

Compared to its neighbouring countries (the Netherlands, France and Germany) and countries at a similar latitude (e.g. United Kingdom), incidence rates in Belgium for the period 1988-92 are low in both males and females (fig 1). In both men and women for example, incidence rates in the Eindhoven Cancer Registry, the Netherlands, are more than twice as high as those reported in Belgium.

- 2) ***Trends in melanoma incidence rates (NCR): observed trends are not in agreement with the trends reported in literature.***

After the start of the National Cancer Registry in 1983, there was an initial rise in melanoma incidence followed by a subsequent decrease

Fig. 1: Melanoma incidence rates in different European countries (1988-1992)  
(world-standardized rates per 100, 000)

Sources: Cancer Incidence in Five Continents, vol VII,  
IARC & the Belgian National Cancer Registry

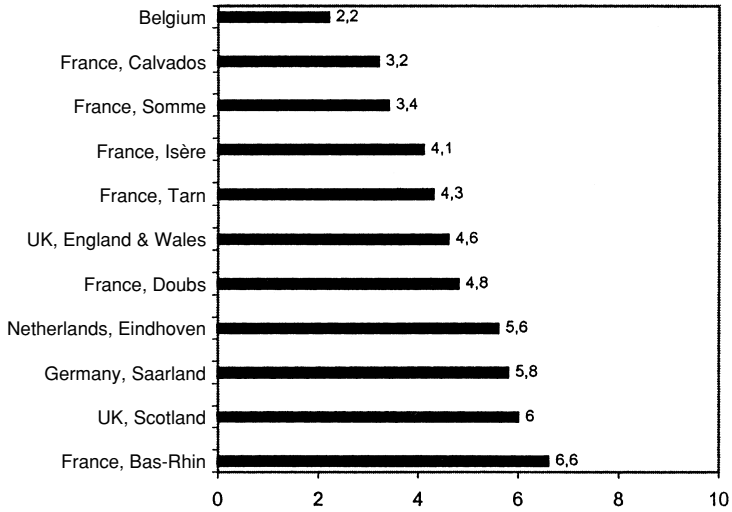


Fig. 1a: males

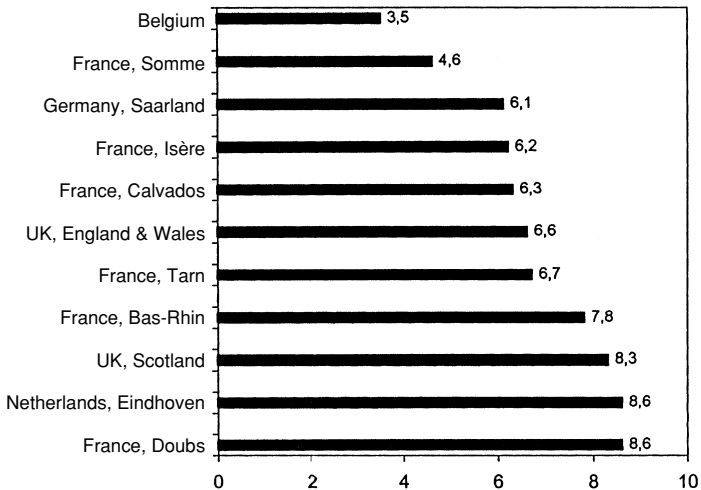


Fig. 1b: females

after 1989 (fig 2a). The initial rise in melanoma incidence was most probably due the gradual development of a more complete cancer registration. An upward trend in the period 1984-1988 was also observed for cancer in general (fig 2b). There was a subsequent decrease of melanoma registration in the period 1989-1994 ( $p < 0.05$ ). This decrease amounted to 5% annually (CI 1-9%) in males and 4% (CI 1-6%) in females. To date such a fall in melanoma incidence has not been reported in melanoma literature. In Scotland, melanoma incidence rates seem to have stabilized since 1986 in females under 65 years of age and in the USA a slight decrease in overall incidence has been observed in females. Moderation or cessation of the increase in mortality in the younger generations, and absence of a similar change in incidence trends is the pattern most commonly observed in populations of mainly European origin (14). Trend analysis of melanoma mortality in Belgium from 1972 to 1992 demonstrated continuously rising rates (to the extent of a 20% increase every 5 years) in both sexes, irrespective of birth cohort (15). These data suggest that the observed decrease in melanoma incidence is likely to be artificial, rather than real.

3) ***Comparison of the National Cancer Registry data with the findings of a population-based melanoma registration programme in the province East-Flanders.***

For 1995-1997 a total of 263 melanoma cases were reported to the East-Flanders melanoma registration programme. About 57% of these cases were reported through the registration forms. The other patients were recruited at the university hospital in Ghent. In East-Flanders overall response rates were 64% among dermatologists, 44% among plastic surgeons and 52% among pathologists.

Comparison of the 1995 melanoma incidence rates in East-Flanders reported by the National Cancer Registry and the melanoma registration programme led to the following observations (16):

- In females, the melanoma registration programme registered a clearly higher incidence than the National Cancer Registry (fig 3b). The Eindhoven Cancer Registry data for the period 1988-1992 were used to estimate the expected incidence rates (table 1). The expected and observed incidence rates were used to calculate underregistration. Estimated underregistration for melanoma was 36% for the National Cancer Registry and 13% for the melanoma registration programme.
- The higher number of reported females referred mainly to women aged under 50; in this subgroup there was a higher proportion of in situ

Fig. 2: Cancer incidence rates in Belgium (1984-1994)  
 (age-standardized rates per 100,000 (reference: European population))

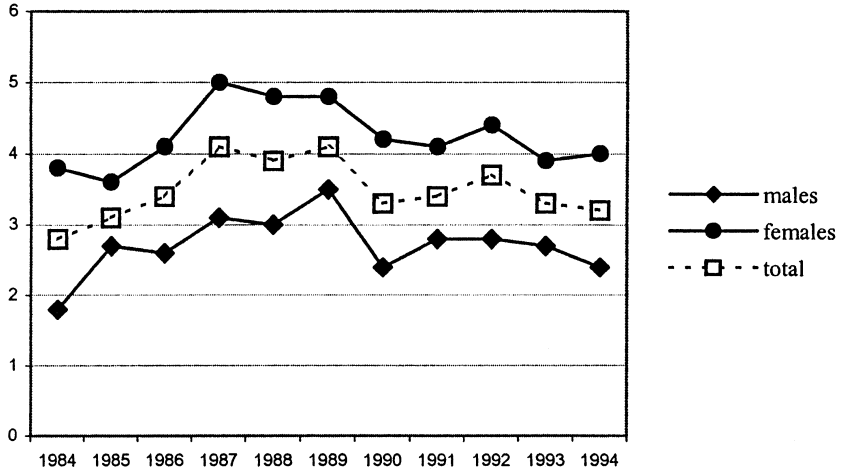


Fig. 2a: melanoma

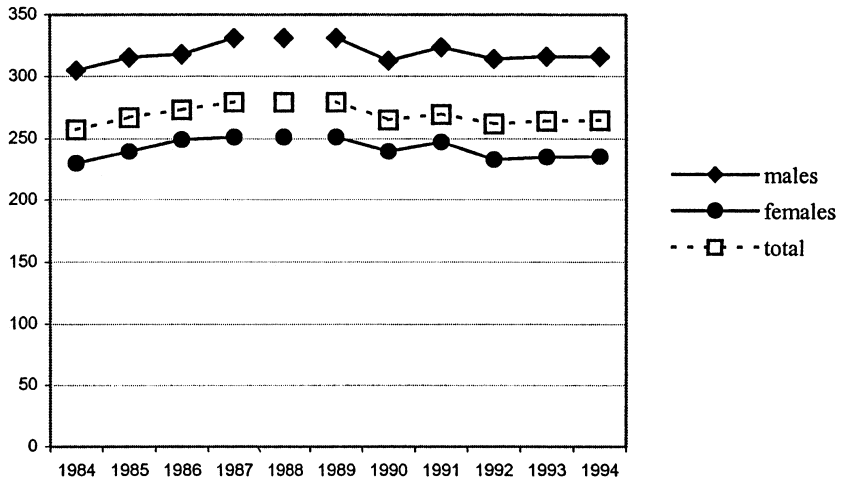


Fig. 2b: all cancers



melanomas (6/22 (27%) versus 5/29 (17%),  $\chi^2 = 0.74$ ,  $p = 0.39$ ) and the median Breslow-thickness of invasive melanomas was significantly lower (0.94mm versus 1.56mm, Mann-Whitney U Test,  $p = 0.019$ ). In situ melanomas and thin invasive melanomas can be treated on an out-patient basis and are therefore more prone to be missed by the National Cancer Registry, which in 1995 only had a hospital-based registration system.

- There were no obvious differences in melanoma incidence rates reported for males between the melanoma registration programme and the National Cancer Registry (fig 3a). Based on the Eindhoven data the underregistration in males was estimated at 43% for the National Cancer Registry and 49% for the melanoma registration programme (table1).

4) **Comparison to the findings of other (cancer) registration systems**

The melanoma incidence rates reported by LIKAR for 1996 seem to be higher than those observed by the melanoma registration programme – especially in males –, without reaching statistical significance (6.6/100,

Fig. 3: Melanoma incidence rates reported by different registration systems in Belgium (age-standardized rates per 100,000 (reference: 1991 East-Flanders population))  
 NCR: East-Flanders (1986-95) Melanoma registration programme: East-Flanders (1995-97) LIKAR: Limburg (1996)  
 AKR: Antwerp (1993-96) MCD: hospitalizations in Belgium (1993-96)

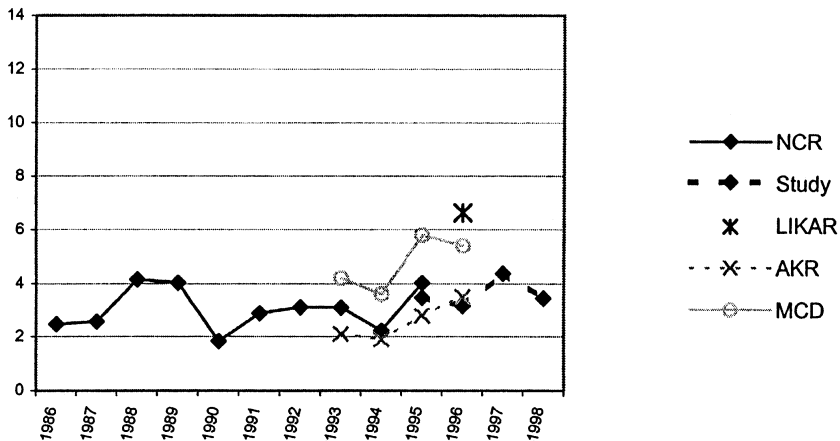


Fig. 3a: males

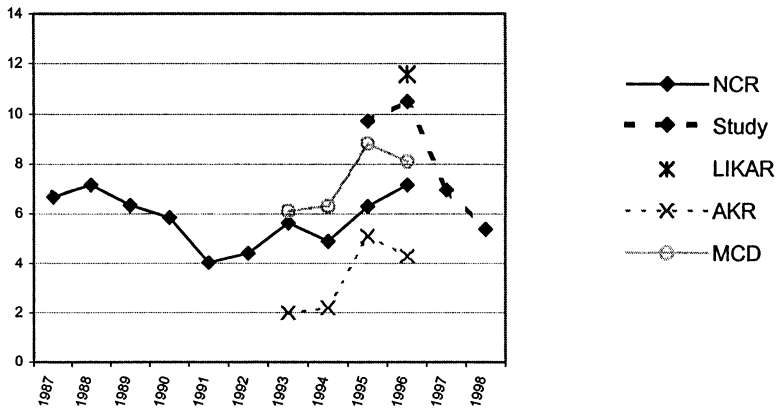


Fig. 3b: females

000 (CI 4.1-9.2) versus 3.2/100, 000 (CI 1.8-4.5)) (fig 3). Estimated underregistration by LIKAR, based on the 1988-1992 Eindhoven Cancer Registry data, is 5% in females and 11% in males (table1).

TABLE 1

*Absolute number of melanomas observed compared to the expected number of melanoma cases. Estimated underregistration by different registration systems. \* the expected number of melanoma cases was calculated by applying the age-specific melanoma incidence rates observed in the Eindhoven Cancer Registry from 1988 to 92 (5) to the population at risk. \*\* calculated as [(expected – observed)/expected] %*

	Observed	Expected*	"Underregistration"***
NCR 1995 East-Flanders			
Males	27	47	43%
Females	49	76	36%
Study 1995-96 East-Flanders			
Males	44	94	53%
Females	138	150	8%
LIKAR 1996 Limburg			
Males	25	28	11%
Females	41	43	5%

Melanoma incidence in females reported by the AKR is lower than that reported by the melanoma registration programme (e.g. 1995: 5.1/100, 000 (CI 3.5-6.7) versus 9.7/100, 000 (CI 7.4-12.1)) (fig 3). For males, the results are comparable (e.g. 1995: 2.8/100, 000 (CI 1.6-4.0) versus 3.5/100, 000 (CI 2.1-4.9)).

The MCD data reflect the annual number of hospitalization episodes for melanoma in Belgium, with the exclusion of a second hospitalization episode at the same institution within the same year. These data seem to be slightly higher than – but quite parallel (especially in males) to – melanoma incidence rates reported by the NCR (e.g. 1995, males: 5.8/100, 000 (CI 5.1-6.5) versus 4.0/100, 000 (CI 2.5-5.6); 1995, females: 8.8/100, 000 (CI 8.0-9.6) versus NCR 7.1/100, 000 (CI 5.2-9.2)) (fig 3). The problem with cancer incidence rates from MCD data is that prevalent cases are not excluded.

Sentinel practices constituted by general practitioners may not be the most effective way to estimate melanoma incidence: the low occurrence of melanoma in general practice (estimated 1 in 7 years (unpublished data)) and the relatively small population covered by the network result in rather large fluctuations in reported incidence rates and large confidence intervals. Overall reported melanoma incidence rates in 1990-1995 was 9.2/100, 000 in females (CI 5.3-14.8) and 4.4/100, 000 in males (CI 1.9-8.9) (world-standardized rates) (Personal communication, Dr Van Casteren – Wetenschappelijk Instituut Volksgezondheid-Louis Pasteur). They seem to exceed those registered by the National Cancer Registry in the same period, both in females (3.2/100, 000 (CI [3.0-3.4]) and in males (1.6/100, 000 (CI [1.4-1.7])).

## Discussion

Reliable cancer statistics are vital to our knowledge of cancer burden and to any attempt of cancer control. We demonstrated that there is an underregistration of melanoma in Belgium, both indirectly, by comparison of the NCR data with other European countries, and directly, by the results of a melanoma registration programme and the findings of some other cancer registration systems.

Underreporting of melanoma is a reality in a variety of countries (17-22). Estimates of the extent of underreporting vary from between 1 to 25% or more (17, 20). The underregistration is usually higher in *in situ* lesions and thin melanomas, compared to thick melanomas and late stage tumours (17). The widespread underregistration of melanoma skin cancer is attributed to the hospital-based reporting system of cancer registries. While a hospital-based reporting system is undoubtedly an effective way of registering cancers in general (since nearly all patients need hospital treatment at some stage of disease), it inevitably leads to problems when

cancers can be treated on an outpatient basis, like melanoma. This was also suggested by the findings of the melanoma registration programme in East-Flanders: compared with the NCR data, a higher number of melanoma cases was observed among women. The higher registration was mainly confined to women under 50 years of age. In these younger women a higher proportion of in situ lesions (although not significant) and a significantly lower median Breslow thickness of the invasive tumours were observed compared with the older age groups. These early stage melanomas are more likely to be treated on an outpatient basis.

We have no satisfying explanation why the registration programme failed to obtain a higher registration in males, compared to the NCR. One hypothesis is that more men refused to participate in the study. Another hypothesis is that men with melanoma come into contact with medical care through an alternative route than that used in the registration programme: in case of suspected melanoma they could be more likely to see general practitioners, general surgeons, oncologists, ... . A lower proportion of early-stage melanomas in males could also be a possible explanation. However we have no hard data to confirm either of these hypotheses: for 2/24 (8%) of the registered melanomas in males, the physician who performed the excisional biopsy was no dermatologist or plastic surgeon. In females this was 7/67 (10%). The median Breslow thickness of invasive melanomas was 1.40mm in males, compared to 1.24mm in females (difference not statistically significant). Two of the 24 (8%) registered melanomas in males were in situ, compared to 11/67 (16%) in females (difference not statistically significant).

Reports in other countries show that the proportion of melanoma patients treated outside the hospital is increasing (18, 19, 22). The only alterations that took place in melanoma treatment, is that surgery has become less aggressive, which reduced the number and duration of hospitalizations (23). Economic factors could further favour this evolution. When surgery is not extensive (without graft), outpatient treatment could be an option that is worthwhile, reducing the costs for the community. In dermatology, the possibility of intensive outpatient treatment of some extensive skin diseases like psoriasis is also being explored. Increased treatment of outpatients with melanoma, possibly triggered by an earlier detection of (thinner) melanomas, could be one explanation for the decrease in registration of incident melanoma cases by the NCR after 1989. Since a decrease of total cancer incidence has also been observed since 1989 (fig 2b), a general diminished supply of data to the NCR could be another explanation.

To improve melanoma registration in Belgium, there may be a need to include other data sources apart from the hospital-based registration procedure. This is currently being explored by the NCR.

The melanoma registration programme in East-Flanders was realized with the help of certain groups of physicians who were thought to deal most frequently with melanoma. As response rates and estimates on the extent of underregistration show, clinicians and surgeons often lack the motivation and time to participate in such a reporting system. At present physicians are already overburdened with paperwork and it would probably be a little naïve to hope for their continuous engagement in a registration procedure, unless this could also produce other data, for instance for MCD. The involvement of registration co-workers could lead to high-quality data, but is expensive. Rewarding or the obligation to report cancers could also contribute to better registration. The Danish Cancer Registry, a long-standing and one of the most complete cancer registries in Europe, started back in the 1940s on a voluntary basis with a small fee for each notification form received. In 1987 cancer reporting became mandatory (24). In Belgium, the collection of MCD and mortality data is compulsory. Unfortunately, MCD data only focus on defining the financial needs of different patient populations and in its present form are of little use to make a significant contribution to cancer registration.

Pathologists occupy a key position with regard to the diagnosis of most malignant diseases. The systematic involvement of pathology laboratories in a cancer reporting system could significantly increase completeness of registration. This is supported by the results of melanoma registration obtained by LIKAR. In the Netherlands, the National Cancer Registry receives a substantial part of its information through a network constituted by all the pathology laboratories (PALGA-system) (<http://telescan.nki.nl/palga.html>). The cancer registration network in Flanders that is currently being tested involves pathology laboratories in its registration procedure. A possible problem of including this data source is to distinguish prevalent from incident cases, especially during the starting period of the registration. There is also a lack of clinical information, for instance on staging, treatment and date of death.

An important obstacle for pathologists participating in the East-Flanders melanoma registration programme was that they had no direct patient contact, which made the informed consent procedure rather stringent. If pathology laboratories systematically participated in cancer registration, there would be a need for a legal basis.

A population of 10 million (approximate number of Belgian inhabitants) is probably too large to obtain complete and reliable data (25). Most cancer registries operate with a source population of about 1 to 5 million. Therefore independent regional registries e.g. at a provincial level could provide better manageable source populations. If they were linked, they could all contribute to a national registration. Efforts and costs of more extensive cancer research could then be concentrated on a smaller e.g. provincial area or on specific tumours.

The quality of cancer registration could also benefit from a universally applied unique personal coding system for different data base systems. In Denmark for instance, the national cancer registry makes use of a unique personal identifying number allocated to every Danish resident at birth or when taking up permanent residence in Denmark. This unique personal code enables linkage to the Central Population Registry, where information on certain socio-economic aspects and date of death is available (24). At present the use of such a universal unique identification is not allowed in Belgium because privacy legislation is too stringent. Such a registration system would certainly have its scientific value, but it remains a delicate question how far the rights of privacy should go.

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## Résumé

Cette étude porte sur l'enregistrement du mélanome cutané en Belgique.

Comparée aux autres pays européens, l'incidence du mélanome rapportée par le Registre National du Cancer est basse. Au cours de la période 1989-1994 on a observé

une diminution de l'incidence des mélanomes notifiés. Une diminution comparable n'a pas été observée par d'autres pays, probablement à cause d'un enregistrement incomplet. Un sondage organisé en Flandre Orientale a enregistré plus de mélanomes chez les femmes en comparaison avec le Registre National du Cancer, surtout dans la catégorie des femmes de moins de 50 ans. Dans ce groupe de femmes, il y avait 6 mélanomes *in situ* sur 22 (27%) comparé à 5 sur 29 (17%) dans le groupe de femmes de plus de 50 ans ( $p = 0.39$ ). Dans ce groupe de femmes plus jeunes on a aussi enregistré plus de mélanomes invasifs d'épaisseur réduite (épaisseur de Breslow médiane 0.94mm versus 1.56mm,  $p = 0.019$ ). Les mélanomes minces sont souvent traités en ambulatoire.

Ces observations suggèrent que l'enregistrement moindre par le Registre National du Cancer est probablement lié à la procédure d'enregistrement (patients hospitalisés). Actuellement des efforts sont faits pour intégrer d'autres procédures d'enregistrement dans un réseau flamand qui tient compte autant des laboratoires d'anatomo-pathologie que des cas rapportés par des médecins traitants.

## Samenvatting

Dit artikel bespreekt de resultaten van een studie die de registratie van melanoom in België onderzocht.

In vergelijking met enkele andere Europese landen is de door het Belgisch Nationaal Kankerregister gerapporteerde melanoomincidentie laag. Over de periode 1989-1994 deed zich een daling voor in de gerapporteerde melanoomincidentie. Een dergelijke daling werd niet gemeld voor andere landen en is het meest waarschijnlijk te wijten aan een verminderde registratie. Een melanoompeiling in Oost-Vlaanderen registreerde meer melanomen bij vrouwen dan het Nationaal Kankerregister, vooral in de leeftijdsgroep < 50 jaar. In deze groep waren 6 van de 22 melanomen *in situ* versus 5 op 29 (17%) in de leeftijdsgroep > 50. Bovendien werden in deze jongere leeftijdsgroep dunnere invasieve melanomen (mediane Breslow dikte 0.94mm versus 1.56mm,  $p = 0.019$ ) geregistreerd. Deze vroege stadia van het melanoom worden vaak behandeld op poliklinische basis.

Deze gegevens laten vermoeden dat de lagere registratie door het Nationaal Kankerregister verband houdt met de op-hospitalisatie-gerichte registratieprocedure. Het includeren van andere registratieprocedures wordt momenteel geëxploreerd in een Vlaams kankerregistratienetwerk, dat ook pathologielaboratoria en een directe rapportering door de behandelende arts bij de registratie betreft.

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## **Remark**

We would like to mention that since the preparation of this manuscript the AKR has published its 1997 report (1) and the LIKAR its 1996-1998 report (2).

- (1) Kankerregistratie in de provincie Anwerpen, incidentiejaar 1997 – Vlaamse Liga tegen Kanker, Antwerps kankerregister-AKR, Antwerpen, 2000.
- (2) BUNTINX F, CLOES E, DHOLLANDER D et al. Incidence of cancer in the Belgian Province of Limburg 1996-1998 – Limburgse Kankerstichting, Hasselt, 1999.