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Original Research

Increasing time trends of thin melanomas in The Netherlands: What are the explanations of recent accelerations?

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Abstract ***Background:*** A disproportional increase in *in situ* or thin melanomas may point at underlying causes such as increased melanoma awareness, as well as 'overdiagnosis' of melanoma in diagnostically equivocal small lesions.
Objectives: The purposes of this study were to estimate trends in melanoma incidence by sex, Breslow thickness (thin melanomas subdivided into four subgroups: <0.25 mm, 0.25–0.49 mm, 0.50–0.74 mm, and 0.75–1.0 mm), age and location, and to compare these with trends in subgroups of thicker melanomas.
Methods: Data on all histologically confirmed *in situ* and invasive melanomas diagnosed between 1994 and 2010 were retrieved from the Netherlands Cancer Registry. Trends in European standardised rates (ESRs) were assessed using joinpoint analysis, and expressed as estimated annual percentage change (EAPC).
Results: Between 1994 and 2010, 34,156 persons were diagnosed with an *in situ* or thin melanoma. The ESR of *in situ* melanomas doubled for males and females with a recent steeper rise in incidence (EAPC 12% (95% confidence interval [CI]: 8.1–16) and 13% (95% CI: 5.9–20), respectively). ESR for thin melanomas amongst males approximately doubled with a steep,

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but non-significant acceleration compared to other thickness categories since 2006 for <0.25 mm melanomas (EAPC 26% (95% CI: 2.1–35)). For female patients with thin melanomas the ESRs increased almost two-fold, except for <0.25 mm melanomas.
Conclusions: The incidence rates of *in situ*, thin and thick melanomas increased similarly between 1994 and 2010. Recently steep increases were found for *in situ* melanomas and thin melanomas in men. Explanations are 'overdiagnosis' in conjunction with increased ultraviolet exposure (natural and artificial) and therefore a 'true' increase, increased awareness, early detection, diagnostic drift and changed market forces in the Dutch health care system.

1. Introduction

The incidence of cutaneous melanoma is rising in the Netherlands and has doubled in the last two decades amongst all Breslow categories [1,2]. In other countries, such as Northern Ireland and Australia, the incidence of thin [3] and *in situ* melanomas [3,4] increased faster than thick melanomas. The majority of the first invasive melanomas in the Netherlands currently have a Breslow thickness of less than 1 mm [2].

Intermittent excessive exposure to ultraviolet (UV) radiation, especially in people with fair skin (phototypes 1 and 2), has undoubtedly played a role in this rise of melanoma incidence [5–7]. Various skin cancer campaigns, aiming to increase public awareness in the general population, have probably contributed as well [2].

Increased awareness among both patients and physicians may induce 'overdiagnosis' (i.e. diagnosing a lesion that has some macroscopic and microscopic features of melanoma, but lacking the potential of progression to metastasise). Further possible causes of the rise in incidence of thin melanomas could be a diagnostic drift towards a more conservative approach (lowering threshold to classify a lesion as malignant) in the pathological diagnosis of suspicious melanocytic lesions or inappropriately diagnosing lesions as malignant (i.e. 'misdiagnosis') [8]. If overdiagnosis explains a large proportion of the increment of melanoma incidence, we hypothesised that the increase would be the largest in thin and *in situ* melanoma.

Our aim was to investigate whether the increase of thin melanomas (<1 mm subdivided in four subgroups and *in situ*) is steeper compared to thicker melanomas, which could be suggestive of increased awareness and overdiagnosis. Furthermore, Breslow thickness of first and subsequent melanomas was compared to show influence of follow-up visits on Breslow thickness. These results add to the debate on underlying causes of the rising incidence of thin melanomas.

2. Methods

Population-based data from the Netherlands Cancer Registry (NCR) were used to include all cutaneous melanomas diagnosed between 1994 and 2010. The NCR started in 1989 and is based on all diagnosed malignancies in the Netherlands by the automated pathological archive (PALGA, Pathologisch Anatomisch Landelijk Geautomatiseerd Archief), the comprehensive national registry of pathology diagnoses. Information about patient and tumour characteristics was obtained from the medical records. The completeness of the NCR data is estimated to be at least 98% on all cancers and 93% on skin cancers (excluding basal cell carcinoma) [9,10]. However, we assume that melanoma completeness was 100%, because melanoma requires a pathological diagnosis.

2.1. Patient selection

All patients diagnosed in the Netherlands with an *in situ* or thin (≤1 mm) invasive cutaneous melanoma between 1994 and 2010 were included and compared with data of thicker melanomas and subsequent melanomas. Systematic registration of Breslow thickness in the NCR started in 1994. As the Comprehensive Cancer Centre Rotterdam started registering Breslow thickness in 1999, this region was excluded from the analysis and eight regions remained in the analysis. For the analysis of time trends of first primary thin and *in situ* melanomas, only first primary melanomas with a Breslow thickness of ≤1 mm were included. Four time periods were constructed: 1994–1997, 1998–2001, 2002–2005 and 2006–2010. The data were stratified by sex and divided in three age groups (0–44, 45–64 and ≥65 years). Anatomical sites were categorised according to the International Classification of Diseases for Oncology-3 [11](C44): head and neck (C44.0–C44.4), trunk (C44.5), arms (C44.6), legs (C44.7), and other sites (C44.8–C44.9). The melanomas were divided in the following histopathological subtypes: lentigo maligna (LM), melanoma *in situ* (MEL *in situ*), superficial spreading melanoma, nodular melanoma, acrolentiginous melanoma, LM melanoma, and other subtypes. In order to investigate any possible changes over time in melanoma stage at diagnosis, the regional and distant metastatic status was ascertained according to the tumour lymph node metastasis classification; to answer the main research question of this study, melanomas with a Breslow thickness ≤1 mm were subcategorised into four