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Detection Rate and Lead Times for Diagnosis of Cutaneous Malignant Melanoma – a Cross-Sectional Study at Two Dermatology Clinics in Sweden

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Abstract

Background: Cutaneous Malignant Melanoma (CMM) has, together with the other skin cancer types, the steepest incidence increase in Sweden. Since CMM prognosis is strongly associated with tumour thickness, early diagnosis is key. It is shown that dermatologists can diagnose CMM faster and to a lower cost than primary care physicians.

Objective: To characterize CMM patients diagnosed at two dermatology clinics, to calculate and compare lead times for patients found to have CMM with those with benign nevi and to calculate the melanoma detection rate.

Methods: A retrospective, cross-sectional study at two dermatology clinics in Sweden. All patients diagnosed with CMM at these clinics were included; 102 in Stockholm and 22 in Malmö. A control group consisting of patients with benign pigmented lesions were age and gender matched with the CMM group. Data were collected from medical records.

Results: Patients with CMM had shorter lead times than control patients from first visit to excision (median 5 vs 17 days, p = 0.003) and from first visit to histopathological diagnosis (27.5 vs 40 days, p = 0.003). Females waited longer than males from referral/booking to first visit (25 vs 15.5 days, p = 0.014). The CMM detection rate was 1.4 %.

Conclusions: Our results imply that the dermatologist can shorten lead times when a CMM is suspected. The CMM detection rate was higher than reported from Euro melanoma weeks. Together this indicates that a health care system with easy access to dermatologists can be effective. The CMM patients had shorter waiting times than nationally, suggesting that general improvements in Sweden are possible.

Key words: melanoma; early diagnosis; waiting times; secondary prevention

Introduction

Cutaneous Malignant Melanoma (CMM) has continuously increased in incidence over the last decades [1]. The yearly increase is approximately 5 %, measuring one of the fastest increasing cancer types in Sweden [2]. Even though the majority are cured with surgery only, the mortality of CMM of 5 deaths per 100,000 cases is significantly higher than that of the other skin neoplasm basal cell cancer and squamous cell cancer. CMM constitutes the only cancer type with rising mortality in Sweden [3]. The most prominent prognostic factor is the thickness of the tumour, with a 5-year survival of 95% for thin CMM (≤ 1.00 mm). The 5-year survival for patients with the thickest CMM (> 4 mm) is 53% [4]. Secondary prevention strategies aim to decrease morbidity and mortality by means of early detection of suspect lesions and diagnosis of thinner lesions [5]. Delayed diagnosis of CMM is, however, not uncommon, mainly due to failure of recognizing new or changing skin lesions, either by professionals or by the patients and their relatives [6].

A patient who seeks medical attention for a pigmented skin lesion is, in current practice in most parts of Sweden, primarily managed by the Primary Care Physicians (PCPs). The PCPs are, in turn, expected to refer the patient to specialist care in case of high clinical suspicion of skin cancer [7]. Studies have, however, shown that dermatologists are better at diagnosing pigmented skin lesions than PCPs regarding diagnostic accuracy, lead times and costs [7,8]. The difficulties in diagnosing skin lesions in primary care often result in surgical excision of benign naevi, which increases the health care costs [9]. In Sweden, the yearly direct costs of removing benign skin lesions amount to approximately 300 million SEK (36.7 million USD). The costs for treatment of CMM are estimated to 166 million SEK (20.3 million USD) per year [9].

In addition to being cost-beneficial, the better diagnostic accuracy among dermatologists may contribute to shorter time to diagnosis and treatment of CMM, and thereby result in reduced morbidity and mortality. A Swedish study [10] found that CMM patients primarily examined by dermatologists had shorter lead times to primary excision and histopathological diagnosis, compared to patients first consulting a PCP. A US retrospective

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single-centre study showed that patients having an established contact with a dermatologist had thinner CMM or CMM *in situ*, than those irregularly visiting a dermatologist [11].

The median lead time in Sweden from first doctor's examination to diagnosis of CMM is 37 days [12]. Swedish recommendations state that 80% of patients should receive a definite diagnosis within 28 days from their first medical visit [13]. Data from 2010-2013 show that this was due for only 40% of CMM patients [13].

In 2012 in Stockholm, and two years later in Skåne, the so-called Health Choice Dermatology ("VårdvalHud") was introduced in Sweden. This model allows patients to turn directly to a dermatology clinic bypassing primary care, and enabled the start of Diagnostiskt Centrum Hud (DCH). DCH comprise of two open-care dermatology clinics, one located in Stockholm and one in Malmö. Due to the positive association between early detection and patient prognosis, together with the tendency described above of higher efficiency when patients can access dermatology specialists directly, we aimed to explore lead times and detection rates for CMM patients in this new model, "Health Choice Dermatology".

Materials and Methods

Participants

The study design was retrospective and cross-sectional, including consecutive CMM patients at two Swedish dermatology clinics, in Stockholm and Malmö, respectively. The patients were identified from the clinics' reports to the Swedish National Cancer Registry (NCR) and captured both invasive and *in situ* CMM diagnosed at DCH in Stockholm from the opening in March 2012 to March 2015, and in Malmö from the opening in July 2014 to March 2015. Each CMM case in Stockholm was age and gender matched with two randomly selected control patients with suspect pigmented skin lesions that had been diagnosed as benign. The control patients were identified from the clinic's health care statistics, using the code for dermatoscopy as a proxy for suspect pigmented skin lesions. Due to difficulties in using the clinic's statistics in Malmö, control patients were only obtained from Stockholm. Thus, there were three separate cohorts of patients: 1) All consecutive CMM patients from Stockholm, 2) Gender and age matched controls from Stockholm and 3) All consecutive CMM patients from Malmö.

Data collection

After retrieving the CMM patients' personal identification number from the NCR reports and for the matched control patients from the clinic's statistics, all data were collected through retrospective viewing of the patients' medical records. Data included age, gender, type of CMM, tumour characteristics (TNM, Breslow thickness, presence of ulceration and Clark level), anatomical site and whether the patient had been referred from a PCP or was self-referred. In addition, the different time points of the patient management were collected from the patient's medical records in order to calculate lead times, as illustrated in Table 1. The total lead times were calculated from referral

Table 1: Health care events used for lead times.

	Event
A	Referral or booking [1]
B	First visit at clinic
C	Primary excision
D	Preliminary histopathological report
E	Final histopathological report
F	Referral for wide excision
G	Wide excision at clinic
[1] Referral from primary care or self-referral via website or by phone (booking).	

or booking (A) to either referral for wide excision (F) or wide excision at the clinic (G). Similar data were collected from the control patients, except for tumour characteristics.

Statistics

Statistical analyses were performed using SPSS (Statistical Package for the Social Sciences), version 22.0. Descriptive statistics were used to calculate proportions for categorical variables and means, medians and standard variation (SD) for continuous variables. All continuous variables were analysed for normal distribution using skewness, Shapiro-Wilkes test, histograms and Q-Q-plots. When a variable was not normally distributed, the non-parametric *Mann-Whitney U test* was used.

When comparing patient and tumour characteristics between the three study groups, Chi-square test for categorical data (or Fischer's exact test when categories contained less than 5 subjects) and Mann-Whitney *U* test for continuous data were performed. Patient and tumour characteristics were likewise tested for potential associations with age (divided in patients ≤ 60 and > 60 years), gender and presence or absence of referral from other health services. The Mann Whitney *U* test was used to compare differences in lead times as well as to test for potential association between patient and tumour characteristics, including gender, age, and presence or absence of referral from a PCP. The significance level was set to $p < 0.05$.

To calculate the melanoma detection rate, the number of diagnosed CMM at the clinic in Stockholm between March 2012 and August 2014 were divided with the total number of individual consecutive patients undergoing dermatoscopy during the same period. This was done using the monthly reports sent to the Stockholm County Council from DCH, containing all billable medical services.

Results

A total of 124 cases of CMM were diagnosed at DCH from March 2012 to March 2015. Of these, 102 (82%) were diagnosed in Stockholm and 22 (18%) in Malmö. Two hundred and four control patients with benign pigmented skin lesions were matched with the melanoma patients in Stockholm. Males accounted for 52% in Stockholm and 45% in Malmö (Table 2). The mean age was approximately 60 in all groups, with a range of 23-93 years in Stockholm and 24-88 in Malmö. Fifty-four percent of the CMM patients in Stockholm were referred from

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Table 2: Comparison of characteristics of study groups in Stockholm and Malmö. Tumour characteristics were not applicable (NA) for control patients.

| | Stockholm | | Malmö | | |
	Melanoma	**Control**	**Melanoma**	**p-value[1]**	**p-value[2]**
Total no. of patients	102	204	22		
Males, n (%)	53 (52)	106 (52)	10 (46)	1.000[3]	0.580[3]
Age, y					
Mean (SD)	60.0 (16.7)	59.4 (16.9)	61.5 (18.4)	0.927[4]	0.534[4]
Range	23-90	23-93	24-88		
Contact with clinic, n (%)				<0.001[3]	0.124[3]
Referral	55 (54)	61 (30)	8 (36)		
Self-appointment	46 (45)	143 (70)	14 (64)		
Not available	1 (1)				
Anatomical site, n (%)				<0.001[3]	0.664[5]
Trunk	45 (44)	67 (33)	11 (50)		
Head and neck	26 (26)	28 (14)	3 (14)		
Lower extremities	17 (17)	18 (9)	4 (18)		
Upper extremities	14 (14)	2 (1)	4 (18)		
Multiple sites		69 (34)			
Not available		20 (10)			
Melanoma subtype [6], n (%)		NA			0.167[5]
SSM	69 (68)		10 (46)		
LM	19 (19)		8 (37)		
LMM	5 (5)		1 (5)		
Other	9 (9)		3 (14)		
Invasive, n (%)	55 (54)	NA	12 (55)		0.927[3]
T-categories		NA			0.286[5]
Tis	47 (46)		10 (46)		
T1	41 (40)		7 (32)		
T2	8 (8)		2 (9)		
T3	5 (5)		2 (9)		
T4	0		1 (5)		
Breslow thickness[7], mm		NA			0.253[4]
Mean (SD)	0.89 (0.69)		1.52 (1.38)		
Median (range)	0.70 (0.10-3.40)		0.83 (0.30-4.15)		
Clark, n (%)		NA			0.446[5]
I	47 (46)		10 (46)		
II	17 (17)		4 (18)		
III	24 (24)		4 (18)		
IV	13 (13)		3 (14)		
V	0		1 (5)		
Ulceration, n (%)	5 (5)	NA	0		0.584[5]

[1] Comparison between melanoma group and control group in Stockholm. [2] Comparison between melanoma groups in Stockholm and Malmö. [3] Chi-square test. [4] *Mann Whitney U test*. [5] Fischer's exact test. [6] SSM = superficial spreading melanoma; LM = Lentigo Maligna; LMM = Lentigo Maligna Melanoma; [7] Of invasive cases.

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a PCP to the clinic, while only 30% were referred in the control group (p < 0.001). Additionally, there was a statistical significant difference in anatomical site between the CMM group and the control group in Stockholm (p < 0.001) (see Fig. 1 and Table 2). There were no statistically significant differences in patient and tumour characteristics between CMM patients in Stockholm and Malmö Table 2. The CMM subtypes are illustrated in Fig. 2. *In situ* tumours (Tis) and thin tumours (T1) were in majority at both clinics, accounting for 86% of CMM in Stockholm and 77% in Malmö. Among patients with CMM, 23% in Stockholm and 18% in Malmö initially underwent subtotal incisional biopsies. Of these, the majority were of Lentigo Maligna (LM) and Lentigo Maligna Melanoma (LMM) subtypes.

Among older patients (> 60 years of age), LMM were more common than among younger patients, observed at both clinics (p=0.001 for Stockholm; p = 0.039 for Malmö), Fig. 2.

CMM patients referred to the clinic in Stockholm were slightly older than those who were self-referred, mean age 61.5 years vs 57.0 years (p = 0.142). Corresponding figures for the control group were 63.5 years vs 57.5 years

(p = 0.018).

Lead times

Lead times and total waiting times for all three studied groups are presented in Table 3. In comparison to the control group, the waiting times for CMM patients in Stockholm were shorter

from first visit (B) to primary excision (C), from excision (C) to preliminary histopathological report (D) and from first visit to final histopathological report (E).

Patients with CMM in Malmö had a significantly shorter waiting time than CMM patients in Stockholm for the period between preliminary (D) and final histopathological report (E). Furthermore, patients in Malmö waited shorter time from final histopathological report (E) to wide excision at the clinic (G).

In the CMM group in Stockholm, women waited longer than men from the date of referral or booking (A) to first visit at the clinic (B) (median 25 versus 15.5 days, p = 0.014). For the same lead time, patients older than 60 years waited longer than young patients. (26.5 vs 15 days, p = 0.027).Patients referred to the clinic waited longer than self-referred patients (27 versus 14 days, p=0.002). Patients with thick CMM (> 1.00 mm, n = 13) had significantly shorter lead times in Stockholm when compared to patients with thin CMM. The difference in lead times was significant between first visit (B) and primary excision (C) (median 0 versus 7.5 days, p = 0.009), excision (C) and preliminary histopathological report (D) (6 versus 16 days, p = 0.008) and between first visit (B) and final histopathological report (E) (13 versus 33 days, p = 0.001).

Melanoma Detection Rate

The number of individual "mole check" patients in Stockholm, using dermatoscopy as a proxy for suspicion of CMM, was estimated to 5,906 up until August 2014. The number of CMM
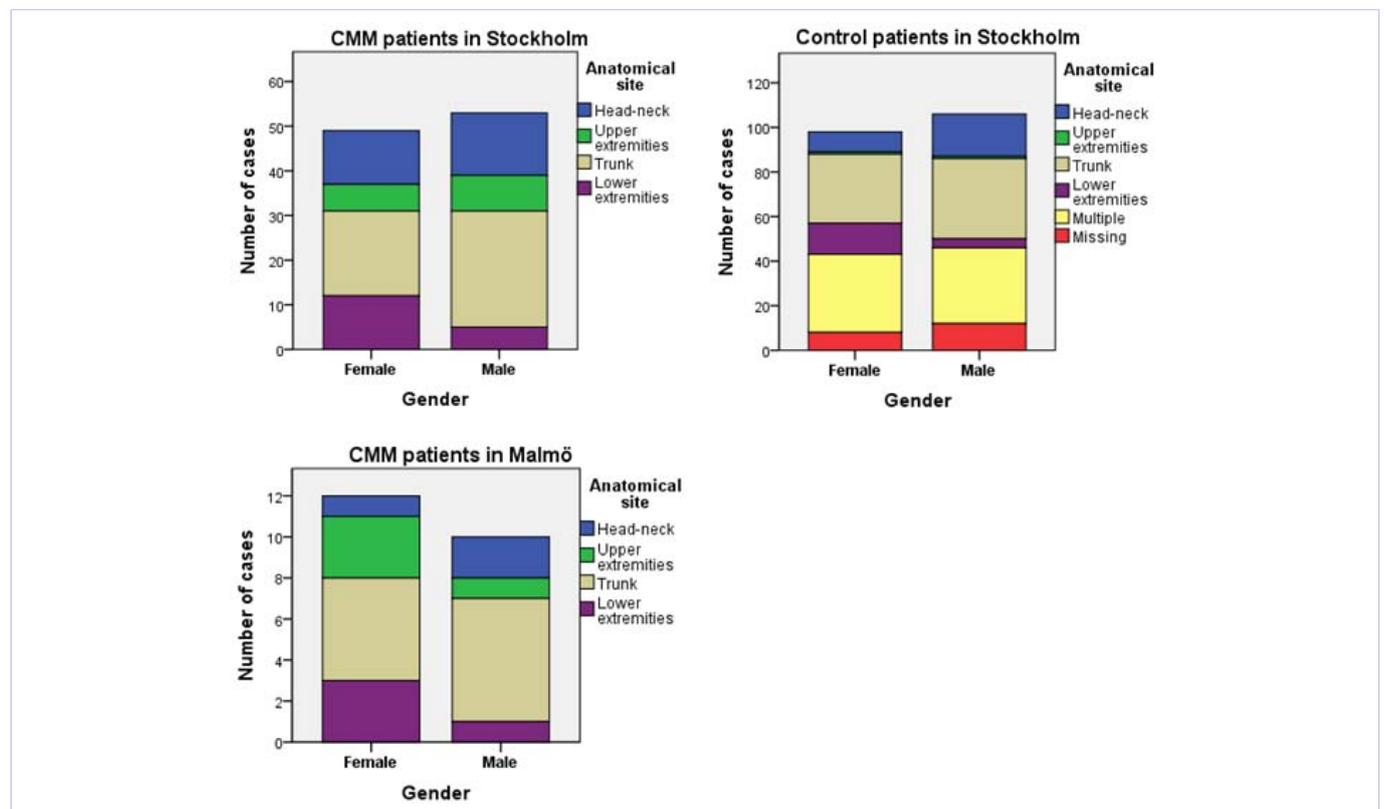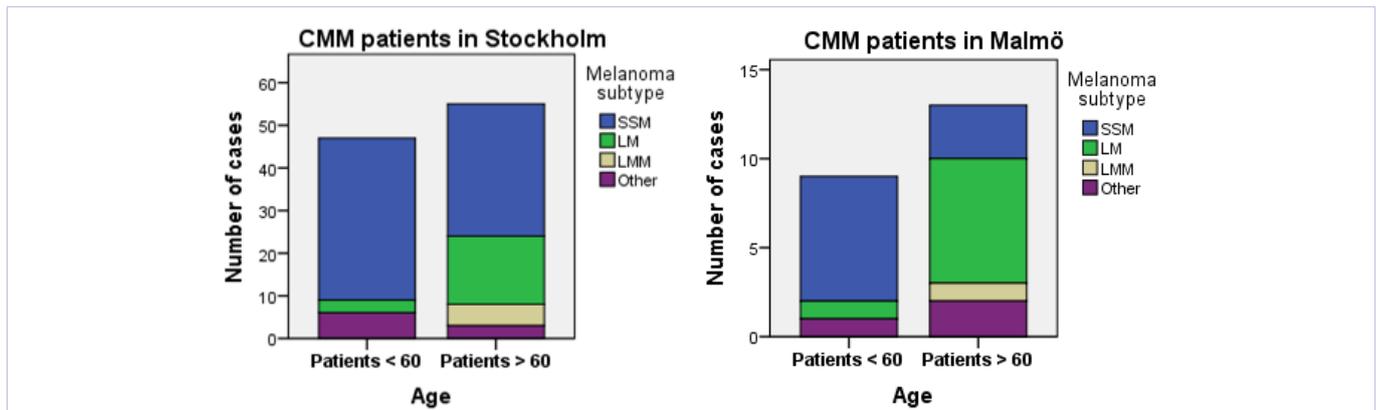

Figure 1: Differences in anatomical sites for males and females in all three study groups. CMM = cutaneous malignant melanoma.

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Figure 2: Differences in melanoma subtypes for patients below and above 60 years of age. CMM = Cutaneous Malignant Melanoma; SSM = Superficial Spreading Melanoma; LM = Lentigo Maligna; LMM = Lentigo Malignant Melanoma; Other = spitzoid, acral, desmoplastic and nodular melanomas.

Table 3: Comparison of lead times between study groups. P-values were calculated with a *Mann-Whitney U te*st.

Interval	Melanoma, Stockholm		Control, Stockholm		Melanoma, Malmö		p-value[1]	p-value[2]
	Mean	Median (range)	Mean	Median (range)	Mean	Median (range)		
A → B	26.5	20.0 (0-192)	22.3	21.0 (0-97)	23.9	21.5 (8-46)	0.588	0.678
B → C	18.1	5.0 (0-153)	28.9	17.0 (0-242)	11.7	6.5 (0-55)	0.003	0.881
C → D	15.0	15.5 (3-34)	20.0	19.0 (6-34)	16.7	15.0 (5-45)	<0.001	0.539
D → E	5.0	3.5 (0-39)	0.8	0.0 (0-14)	2.7	0.0 (0-29)	<0.001	0.006
E → F	9.5	8.0 (-10-40)	NA[3]		4.0	4.0 (1-9)		0.131
E → G	30.5	24.0 (3-91)	NA[3]		18.9	19.0 (7-36)		0.050
B → E	38.3	27.5 (4-166)	51.4	40.0 (11-263)	31.1	27.5 (6-71)	0.003	0.772
A → F	74.1	59.0 (5-366)	NA		46.0	46.0 (33-59)		0.499
A → G	95.6	84.5 (27-231)	NA		67.8	65.5 (56-84)		0.180

[1] Comparison between CMM group and control group in Stockholm. [2] Comparison between CMM groups in Stockholm and Malmö. [3] Wide excision not performed on control patients. A = referral or booking; B = first visit at clinic; C = primary excision; D = preliminary histopathological report; E = final histopathological report; F = referral for wide excision; G = wide excision at the clinic

diagnosed that period was 84, resulting in a melanoma detection rate of 1.4 % at the Stockholm clinic during the studied period.

Discussion

This retrospective cross-sectional study was conducted at two dermatology clinics in Sweden, comparing lead times for CMM patients with matched patients having benign nevi and calculating CMM detection rate. Lead times were also analysed for potential associations with patient characteristics, and by comparing the two separate clinics. Waiting times were significantly shorter for the CMM patients, than for the patients with benign nevi. This result is encouraging and indicates that when a dermatologist suspects a CMM, the health care process is quickened. This could also explain the shorter lead times for patients with thick CMM.

Patients in Malmö waited a significantly shorter time than patients in Stockholm between preliminary and final histopathological report. The reasons for this may relate to differences between the two cities in regards to histopathological workload or working processes. The difference in lead time

between final histopathological report and wide excision, where patients in Malmö waited fewer days in median, approached statistical significance. There were no differences in patient and tumour characteristics between the clinics explaining the differences in waiting times. Considering the relatively small cohort in Malmö, due to the shorter study period there, our results should be analysed with caution, but indicate that lead times, especially regarding the histopathology review, could potentially be shortened in Stockholm.

Women with CMM waited a longer time than men in Stockholm from referral or booking to first visit at the clinic. This is interesting considering a study by Hajdarevic *et al.* [10], reporting that women waited shorter times than men. In that study, however, the case mix was different from ours, with women having significantly more *in situ* tumours and thinner invasive CMM [10]. For the same lead time, we also found that CMM patients > 60 years waited longer than younger patients in Stockholm. According to the Swedish NBHW, older people with cancer, including CMM, wait longer for examination and

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treatment than younger people [14]. This inequality needs to be addressed, as there is an association between age and tumour thickness, with thicker tumours especially seen among older men living alone [15]. Thus, early detection is of outmost importance also among older patients.

The observation that referred patients, compared to the self-referred, in both groups in Stockholm had longer lead times from first contact to first visit could be influenced by the handling of self-referrals at the clinic. A handful of self-referred patients were scheduled for a visit the same day, due to last-minute cancellations from other patients. There were also a few days, *e.g.* at the Melanoma Week in May, when the clinic was open for drop-in appointments for patients with pigmented skin lesions.

For year 2013, the Swedish NBHW reported that the waiting time for melanoma patients from first visit to definitive diagnosis was in median 38 days in Stockholm and 28 days in Skåne [12]. In our study, the median waiting time from first visit to final histopathological diagnosis was 27.5 days in both Stockholm and Malmö. However, there was a difference between the national report and our study in how the date of the definitive diagnosis was defined. The national report used the date when the patient received information about their diagnosis [12]. In our study, such information was often missing in the medical records. We therefore used the date of the final histopathological report as the date of diagnosis. In reality, the time until the patient received information about the definitive diagnosis is longer. The Swedish NBHW states that 80 % of patients should receive a diagnosis within four weeks from their first doctor's visit [13]. In our study, 54% of the CMM patients in Stockholm and 50% of the patients in Malmö had a waiting time of less than four weeks for the interval between first visit and final histopathological report. These results do not fulfil the recommendations, but still exceed the all-country data from 2010-2013, where 40 % of patients met the criteria, with reservation for the mentioned divergence in definitions of lead times [13].

The characteristics of the CMM's found were in concordance with published data. Tumours on the trunk were more common among men, and tumours on the lower extremities more common among women. Similar results have been presented in quality reports for Sweden since the early 90s and the differences are thought to correspond to the sunbathing and clothing habits for each sex [16]. Patients > 60 years had more lentigo subtypes and more CMM in the head- and neck region, when compared to younger patients. Since lentigo subtypes usually appear in regions chronically exposed to sunlight, *i.e.* the head and neck, these two findings are linked to one another [17]. Additionally, because of the slow growth pattern of LM and LMM, these subtypes are more common among older patients [17].The majority of the CMM diagnosed at the two clinics were *in situ* or thin tumours (T1). This finding is encouraging as identifying CMM at an early stage minimizes the risk of local recurrence and metastasis [4].

An unexpected finding was that about 20% of patients in both CMM groups underwent subtotal incisional biopsies before or instead of primary excision. This treatment option is not recommended in guidelines as previous studies have shown an increased risk of incorrect staging in the histopathological analysis [16, 18]. Our results exceed that in another Swedish study, where 10% of patients underwent biopsies [10], but can be explained and motivated by the fact that most biopsied CMM were of lentigo subtypes.

Melanoma detection rate

The melanoma detection rate was 1.4% at the clinic in Stockholm between March 2012 and August 2014. This kind of data is unique, since it is collected after the introduction of a new model, "Health Choice Dermatology". Thus, there is a lack of an optimal comparator. In a Swedish setting this relatively high access to a dermatology specialist is historically most comparable to the Euromelanoma campaign. Published data from Sweden 2009 and 2010 state a detection rate of 1.1 % [19].The differences in detection rate between Euromelanoma week and our study can partly be explained by DCH receive 30% of the patients admitted from a PCP, who has already performed a medical examination. The referred patients have thus been selected.

A detection rate of 1.4% might be considered fairly low. With the potential benefit in having high access to dermatologists not being limited to identifying the more obvious CMM, but also to find the more obscure, early cases of thin CMM or even *in situ* cases, there is obviously still a need to excide a high number of benign lesions in order not to miss a CMM. As mentioned above, there are indications of dermatologists being more effective than PCPs [10] and, when consulting a dermatologist, the efficiency is higher if the patient regularly sees the same dermatologist [11]. In regions with low access to dermatologists, tele-dermatoscopy could help to triage the patients that really needed to be examined by a specialist [20].

Clinical implications

Our results show that the use of so-called fast tracks in health care, including early primary excision and response from the pathologists, lead to shortened processes for patients with CMM. Such implementations ought therefore to be expanded further. The individual physicians decide, however, on whether a lesion is warrant a quick management. Even though the results are positive in a national comparison, further improvements are possible. The largest room for improvement among the lead times is likely to be the time from excision to final histopathological report, and is, at least partly, a result of a shortage of experienced dermatopathologists. Given the difficulties, even for a trained dermatologist using dermatoscopy, to rule out a suspected nevus, there is still a need for excisions to confirm or disconfirm a CMM diagnosis. It would therefore be helpful with a large health economic analysis, collecting data on costs for diagnostic procedures at the PCP, "Health Choice Dermatology" and hospital levels, as well as the costs for early versus delayed diagnosis, in terms of morbidity and mortality.

Conclusions

The study demonstrates that patients diagnosed with CMM had shorter lead times than patients with benign pigmented skin lesions, indicating that existing strategies for quick management

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of CMM are potentially effective in "Health Choice Dermatology". Women and older patients had longer waiting times. The waiting times for CMM patients were shorter from first visit to diagnosis, compared to data from Sweden as a whole. Still, the national recommendations are not yet fulfilled and more studies, including health technology assessments, and improvements are needed to further shorten the total waiting times for CMM patients. The inequalities in terms of age and gender also need to be addressed.

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Declarations

Ethical approval. Ethical permission was obtained from the Regional Ethical Review Board in Stockholm with the review number 2014/1050-31/4.

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