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Introducing teledermoscopy of possible skin cancers in general practice in Southern Denmark

Teledermoscopy in Denmark (short title)

Article category: Health Service Research

Tine Vestergaard[abc], Sumangali C Prasad[a], Annette Schuster[a], Rasa Laurinaviciene[a], Anette Bygum[a], Anders Munck[b], Merethe K Andersen[b]

[a] Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark

[b] Audit Project Odense, Research Unit of General Practice, University of Southern Denmark, Odense, Denmark

[c] OPEN, Odense Patient data Explorative Network, Odense University Hospital, Odense, Denmark

www.sdu.dk/ki/open

Corresponding author:

Dr. T Vestergaard

Department of Dermatology and Allergy Centre

Odense University Hospital

Kløvervænget 15

5000 Odense C

Denmark

Tine.vestergaard@rsyd.dk

Key messages:

- Teledermoscopy was practically feasible in general practices in Denmark
- The photo quality achieved in this study was acceptable
- General practitioners were uncertain about their diagnoses in over 40% of cases
- Over 70% of patients with suspected skin cancers had benign lesions
- Over 30% of patients could potentially avoid an in-person dermatology appointment

Keywords: Dermatology, Dermoscopy, Malignant melanoma, Primary Care, Skin cancer, Telemedicine

Abstract

Background: The increasing incidence of skin cancers poses a burden to health care systems. General practitioners (GPs) play an important role in triaging these diseases and referring relevant patients to specialists. It is challenging to distinguish benign from malignant skin lesions, and GPs may benefit from diagnostic support from teledermoscopy. Objectives: To assess whether the introduction of teledermoscopy in general practice was feasible and might reduce the number of unnecessary referrals to specialists, and to assess the diagnostic accuracy and confidence of participating GPs. Methods: Fifty general practices in Southern Denmark participated. Adult patients presenting to their GP with suspected skin cancer could be included. Images including dermoscopy were taken by the GP and sent for evaluation by specialized dermatologists at a university hospital. Patients were simultaneously referred for a face-to-face evaluation at the university hospital. Diagnoses proposed by the GPs and by teledermoscopy were compared to the final diagnoses obtained by histopathology or, if not available, face-to-face evaluation. Results: 519 patients with 600 suspected skin cancers were included. The final diagnosis was benign in 72.3%. The photo quality was good or fair in 90.5%. GPs reported uncertainty about their diagnoses in

41.5% of cases. The GPs' positive predictive values for any malignancy and for malignant melanoma were 49.5% and 26.3%, respectively. On evaluation by teledermoscopy, 31.5% of lesions did not need further in-person assessment. Conclusion: Useful images of suspicious skin lesions were obtained from general practice, and GPs could benefit from teledermoscopy to improve their diagnostic accuracy and confidence.

Background

The incidence of malignant melanoma (MM) and non-melanoma skin cancer (NMSC) is rising in fair skinned populations in Europe and other parts of the World, due to increasing sun exposure as well as growing and ageing populations, and these cancers are among the six most common cancers in Denmark. (1-4) While NMSC primarily affects older individuals and is rarely life threatening MM is a potentially lethal disease that can occur even in adolescence or childhood. Early diagnosis is essential to reduce morbidity and mortality. On the other hand, overtreatment of benign skin lesions misdiagnosed as malignancies poses significant costs to the health care system as well as possible adverse effects for the patients.(5,6) Denmark has a well-established gatekeeper function through the general practitioners (GPs), who assess, refer and treat many skin lesions. It could therefore be helpful for the GPs to have access to telemedical assistance in their evaluation of suspicious skin lesions. Previous studies from other countries have shown this is feasible, aids earlier diagnosis and reduces unnecessary referrals to dermatologists or plastic surgeons (7-9). However, this has not been investigated in Denmark so far.

The main aim of this study was to assess whether the introduction of teledermoscopy (TD) in general practice was feasible and could potentially reduce the number of unnecessary referrals to a dermatologist or plastic surgeon. Furthermore, we assessed the diagnostic accuracy and confidence of the participating GPs.

Methods

In November 2017 an invitation to participate in this study was sent to all 364 general practices in the Region of Southern Denmark, a geographic area with approximately 1.2 million inhabitants. Fifty general practices were included on a first come first serve basis, but a representative distribution throughout the whole Region, and general practices with more than one GP were prioritized.

GPs and/or other staff from each participating general practice joined a half day introduction to the study, the equipment and dermoscopy immediately before study start. All GPs were asked to answer a short questionnaire on demographics and prior interests in dermatology and dermoscopy. Each participating general practice received an IPhone6® (Apple Inc., USA) and a dermoscope that was easily attached to the smartphone (Handyscope®, FotoFinder Systems GmbH, Germany). After the first four weeks of the study all participants were encouraged to join a 1.5 hour brush-up session in order to solve any technical or organizational difficulties.

The participating GPs were asked to include consecutive adult patients with skin lesions suspicious of MM or NMSC, which they would usually refer for a specialist evaluation. Lesions located in anatomic regions inaccessible to dermoscopy or too large to fit in one dermoscopic image, could not

be included. Informed consent was gained from the patient before taking three photographs of the suspicious lesion: an overview, a close-up and a dermoscopic image. These images were sent securely using the Handyscope® application and FotoFinder Hub® (FotoFinder Systems GmbH, Germany) for evaluation at the Department of Dermatology and Allergy Centre, Odense University Hospital by one of four participating dermatologists with a special interest and clinical experience in skin cancer. The GPs filled in a short audit template on patient symptoms (growing lesion, itch, change in colour, new lesion, non-healing wound, patient worry) and risk factors (previous MM, previous NMSC, fair skin, sun exposure/solarium use, family members with MM, more than 50 nevi), clinical findings (asymmetry, poorly defined border, more than one colour, diameter ≥ 6mm, ulceration, elevated lesion), diagnosis (atypical nevus, MM, basal cell carcinoma, squamous cell carcinoma, Bowen's disease, actinic keratosis), and diagnostic confidence (completely confident, fairly confident, unconfident). In order to make this registration feasible and valid, the template was set up according to the APO (Audit Project Odense) Method, with which the GPs have experience and confidence. (10) A similar template was filled in by the dermatologist evaluating the photographs for image quality (good, fair, poor/useless), diagnosis, treatment plan, and diagnostic confidence (completely confident, fairly confident, unconfident). The templates were pilot tested by GPs and dermatologists, respectively, prior to the registration. Concurrently with sending the photos, patients were referred to the skin cancer clinic at the department of dermatology for a face-to-face (FTF) evaluation and management of the suspicious skin lesions as per standard procedure. This was performed by one of the four participating dermatologists, excluding the dermatologist performing the TD evaluation of the same lesions. Patients with suspected MM were seen FTF within seven days, patients with suspected NMSC were seen FTF within 28 days. The evaluations obtained by the GPs and by TD were compared to the final diagnosis obtained by histopathology or, if not available, by FTF evaluation. In line with the APO Method, audit results were presented at a

follow up meeting, where the experienced obstacles were addressed and discussed with the participating GPs.

Data from evaluation sheets were typed into REDCap (Research Electronic Data Capture) hosted at OPEN (Open Patient data Explorative Network), Odense University Hospital using double entry and data comparison. (11,12) Descriptive statistics using STATA version 15.0 were applied.

Results

The study was conducted between January 9th and October 31st 2018. Of the fifty included general practices, two dropped out after the initiation of the study, and one general practice included no patients. GP characteristics are shown in Table 1. Participating GPs were younger and more likely to employ GPs in training than the background population of GPs in the Region of Southern Denmark.

A total of 562 patients were referred for this study, of which 43 were excluded due to unfulfilled inclusion criteria (Figure 1). Finally 519 patients with 600 suspicious lesions were included for TD evaluation of which 64 patients had more than one skin lesion photographed, ranging from 2 to 5. A majority of the patients (57.0%) were women and the mean age was 55 years (range 19-94).

The GPs registered 442 patients with a total of 458 suspicious lesions. Fourteen patients had two lesions registered, one patient three lesions. Most patients were women (57.7%) and the mean age was 56 years (range 20-94). Every general practice registered an average of 9.5 lesions (range: 0-30) and submitted photos of 12.5 lesions for TD evaluation (range: 0-41) during the study period.

Photos of 142 lesions were received, where the corresponding GP registration was lacking. In many cases the GP had registered one lesion in a patient, but sent photos of several lesions for TD evaluation. A comparison between the diagnoses proposed by the GPs and the final diagnoses is shown in table 2.

Of the 600 suspicious lesions referred by the GPs 434 (72.3%) were benign and 166 (27.7%) were malignant or premalignant. In this study, premalignant and malignant lesions included 51 actinic keratoses, 2 cases of bowen´s disease, 6 squamous cell carcinomas, 2 keratoacanthomas, 1 atypical fibroxanthoma, 81 basal cell carcinomas, 17 invasive melanomas and 6 cases of melanoma in situ. Benign lesions included 167 benign nevi/lentigenes, 122 seborrheic keratoses, 46 atypical nevi and 99 “other”, covering a variety of benign diagnoses including dermatofibroma, angioma, lichenoid keratosis, cysts, verruca vulgaris and inflammatory skin diseases.

Photo quality was evaluated by the participating dermatologists as good in 58.9%, fair in 31.6% and poor/useless in 9.5% of cases. Poor/useless photo quality was due to out of focus images, missing overview or dermoscopic image, or missing agreement between overview and dermoscopic image.

Dermatologists were completely confident in their diagnosis in 37.2% of cases, fairly confident in 42.8%, unconfident in 19.8%, and data were missing in 0.2% of cases. There was a clear correlation between the quality of the images and the dermatologists’ confidence in the TD diagnoses. (Figure 2)

On TD, the dermatologists evaluated that 31.5% of lesions did not need any further treatment or follow-up. Of all lesions, 34.0% were evaluated for biopsy or excision, 19.5% for clinical follow-up

or sequential digital dermoscopy and 14.3% for other treatments (i.e. cryotherapy, topical, photo dynamic therapy). In 0.7% of lesions, this data was missing.

The concordance between TD evaluation and FTF found in this study has been reported elsewhere (13).

For GPs, we found a positive predictive value (PPV) for malignancy/premalignancy of 49.5%, and for MM of 26.3% (table 3). The GPs' sensitivity and specificity in regards to any malignancy/premalignancy was 87.8% and 59.6%, respectively, and for MM 52.6% and 93.6%, respectively.

GPs were completely confident in their diagnosis in 5.5% of cases, fairly confident in 44.5%, unconfident in 41.5%, and this information was missing in 8.5% of cases. The GPs reported the highest degree of diagnostic confidence for actinic keratosis (12.5% completely confident) and basal cell carcinoma (9.0% completely confident) and the lowest degree of diagnostic confidence for MM (73.7% unconfident).

Discussion

The APO method is well known by GPs in Denmark and elsewhere, and our data provide knowledge on in-situ clinical assessments. This prospective study succeeded in producing images of a useful quality for TD evaluation, which is in accordance with previous studies evaluating photo quality of images obtained by GPs (14-16). Furthermore, this study showed that GPs are uncertain in diagnosing a group of patients suitable for TD. Low confidence in diagnosing MM and NMSC

has formerly been reported for GPs. (17,18) However, the GPs' PPVs were high and for MM similar to that of TD (Table 3).

Almost 75% of referred lesions were benign; the most common final diagnoses were benign nevus/lentigo and seborrheic keratosis, hence there is potential to avoid unnecessary FTF consultations for these ordinary conditions. This is in accordance with previous studies. (7, 8, 19)

In retrospective studies of GPs' diagnostic accuracy, PPVs for malignancy of 53.8%, for BCC of 48.4%-72.7%, for actinic keratosis of 30.9%-73.5%, and for MM of 33.3%-66.7% have been reported. (19-21) In a study by Menzies et al., with an inclusion process similar to ours, 63 GPs from 19 practices included 374 suspicious pigmented lesions (22). A PPV of 40.0% for malignancy and 34.0% for MM was found for GPs. In a study by Argenziano et al. 36 GPs screened 1197 patients' skin lesions as suspicious or banal. Both suspicious and banal lesions were subsequently evaluated in a specialist setting. With the specialist evaluation as the reference standard, a PPV for malignancy of 16.1% was reported (23).

Since PPV is dependent on the prevalence of the disease, it is difficult to directly compare these results. Menzies et al. found a sensitivity and specificity for malignancy of 55.0% and 89.0%, respectively, and for MM of 53.1% and 89.0%, respectively. (22) Unlike the above mentioned study by Argenziano et al. we do not have the complete number of false negatives and true negatives dismissed initially by the GPs and hence not included in this study. We tried including all lesions evaluated by GPs in a smaller pilot study, but this was not practically feasible, as GPs were reluctant to spend time on the inclusion of benign lesions, and patients were not willing to travel to the department of dermatology for the evaluation of a lesion conceived as benign. For the GPs in

our study the true sensitivities are probably slightly lower and the true specificities are higher. Argenziano et al. reported a sensitivity and specificity for malignancy of 79.2% and 71.8%, respectively. (23)

There are some limitations to this study. The included GPs volunteered to participate and probably have a higher degree of interest in telemedicine or dermatology than GPs in general, as indicated by the fact that 45% of participating GPs already had access to a dermoscope prior to this study and 47% stated a special interest in dermatology. In a UK survey, 89% of dermatology-interested GPs had access to a dermoscope in their practice. (24) A study conducted in France reported that 8% of GPs had access to a dermoscope, and GPs using dermoscopy had a significantly higher diagnostic confidence than dermoscopy non-users. (25) Furthermore, the use of dermoscopy in general practice has been shown to increase the diagnostic accuracy. (22, 23, 26) Indeed, the included GPs differed from the general population of GPs in The Region of Southern Denmark by being younger and being more likely to have GPs in training employed, the latter indicating a special interest in teaching and quality development. However, this difference would only strengthen the results of this study; we speculate that the diagnostic accuracy and confidence of Danish GPs as a whole might be lower than reported here.

There is a risk of selection bias in this study, as we do not know how many eligible patients were not included by the GPs, either because the patients declined or the GPs missed the opportunity to include them. However, by feedback from the GPs in this study, patients primarily declined to participate due to logistic factors, such as preferring referral to a local dermatologist closer to the patient´s home than the skin cancer clinic. This may imply that the benefits of TD depend on the patients' residence and the accessibility of dermatologists in the area.

A major reason for the discrepancy between the number of TD and GP registrations was the fact that GPs sent photos of several lesions in the same patient but only registered one lesion. Many GPs let the practice nurse take the photos after they had registered the patient's lesion(s), this may have led to the nurse photographing extra lesions. If TD is to be implemented, it is essential that there is clear agreement between the referral and the number of lesions photographed. Also, it would be preferable with a platform that could be directly incorporated in the electronical medical records of both the GPs and the skin cancer clinic as this was a general obstacle reported by the GPs at the follow-up audit meeting. Interestingly, many GPs had used the equipment provided to show photos of selected skin lesions to colleagues and residents in their practice and used the opportunity for academic sparring.

In conclusion, this study shows that it is feasible to obtain useful images of suspicious skin lesions from general practice. Over 30% of lesions evaluated by TD did not need further follow-up or treatment. GPs had high PPVs even though their level of diagnostic confidence was low. However, other issues such as the diagnostic accuracy of TD, the risk of missing incidental lesions on TD due to the lack of total body skin examination, patient and provider satisfaction and socioeconomic factors need to be considered before the implementation of this technology.

Declarations/ Acknowledgements

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Table 1. Background information on general practitioners participating in teledermoscopy study in Denmark, 2018

Characteristics of included GPs based on replies from 42 practises				**All 785 GPs in Region of Southern Denmark (27, 28)**
Male sex	42	49%$^{n.s.}$	n=86	51%
Age (years)	**47.5**$^{p=0.0002}$ (mean)	27-69 (range)	n=86	51.9 (mean)
Years as GP	10.8 (mean)	0-30 (range)	n=85	N/A
Have a special interest in dermatology	39	47%	n=83	N/A
Had a dermoscope before this study	38	45%	n=84	N/A
Distance to nearest dermatologist (km)	9.5 (mean)	0-37 (range)	n=86	N/A
Number of GPs per practice	2.4 (mean)	75%$^{n.s.}$ in practice with ≥2 GPs	n=85	81% in practice with ≥2 GPs
Have GPs in training employed	77	**91%**$^{p<0.0001}$	n=85	38.5%
Number of patients	1549$^{n.s.}$ (mean)	517-4373 (range)	n=81	1566 (mean)

n.s.: non significant N/A: not available

Table 2. Comparison between diagnoses proposed by general practitioners in a teledermoscopy study in Denmark, 2018 and the final diagnoses established at a department of dermatology at a university hospital. GP: general practitioner MM: malignant melanoma

	Final diagnosis (% confirmed by histopathology)									
GP diagnosis	Atypical nevus	MM/ in situ	Basal cell carcinoma	Sq. cell carcinoma	Bowen's disease	Actinic keratosis	Nevus/ lentigo[$]	Seborrheic keratosis[$]	Other[¤]	**Total**
Atypical nevus	**24**	7	5	0	0	3	81	37	18	175
Melanoma/in situ	1	**10**	5	0	0	0	12	6	4	38
Basal cell carcinoma	1	0	**43**	2	0	12	7	16	19	100
Squamous cell carcinoma	0	1	4	**2**	1	4	1	3	2	18
Bowen's disease	0	0	0	0	**0**	1	0	1	3	5
Actinic keratosis	0	0	3	1	0	**17**	2	23	10	56
Other	2	0	3	0	0	1	10	9	14	39
Missing diagnosis	2	1	5	0	0	0	6	7	4	25
Total	30 (26.7)#	19 (100)	68 (98.5)	5 (100)	1 (100)	38 (21.1)	119 (19.3)	102 (14.7)	74 (39.2)	456* (38.4)

[#] A further 16 (53.3%) atypical nevi were followed up by sequential digital dermoscopy, showing no change.

[$]These diagnoses were not available to the GPs, as they could only refer lesions, they suspected could be malignant.

[¤]Included 1 keratoacanthoma, 1 atypical fibroxanthoma and a variety of benign diagnoses including dermatofibroma, angioma, lichenoid keratosis, cysts, verruca vulgaris and inflammatory skin diseases.

*Two lesions registered by the GPs could not be paired with a dermatological diagnosis because there were several different dermatological diagnoses for the same patient.

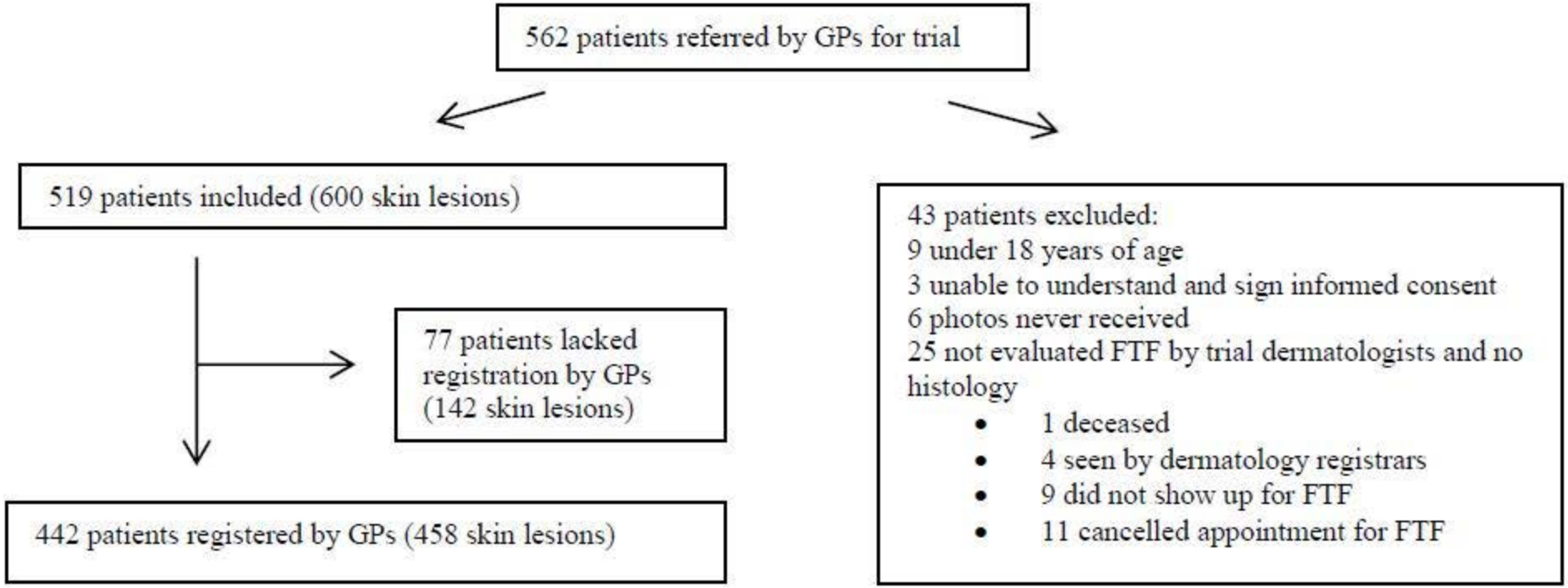
Table 3. Positive predictive values of general practitioners and dermatologists at a university hospital using teledermoscopy (Denmark 2018). PPV: positive predictive value GP: general practitioner TD: teledermoscopy CI: confidence interval AK: actinic keratosis SCC: squamous cell carcinoma

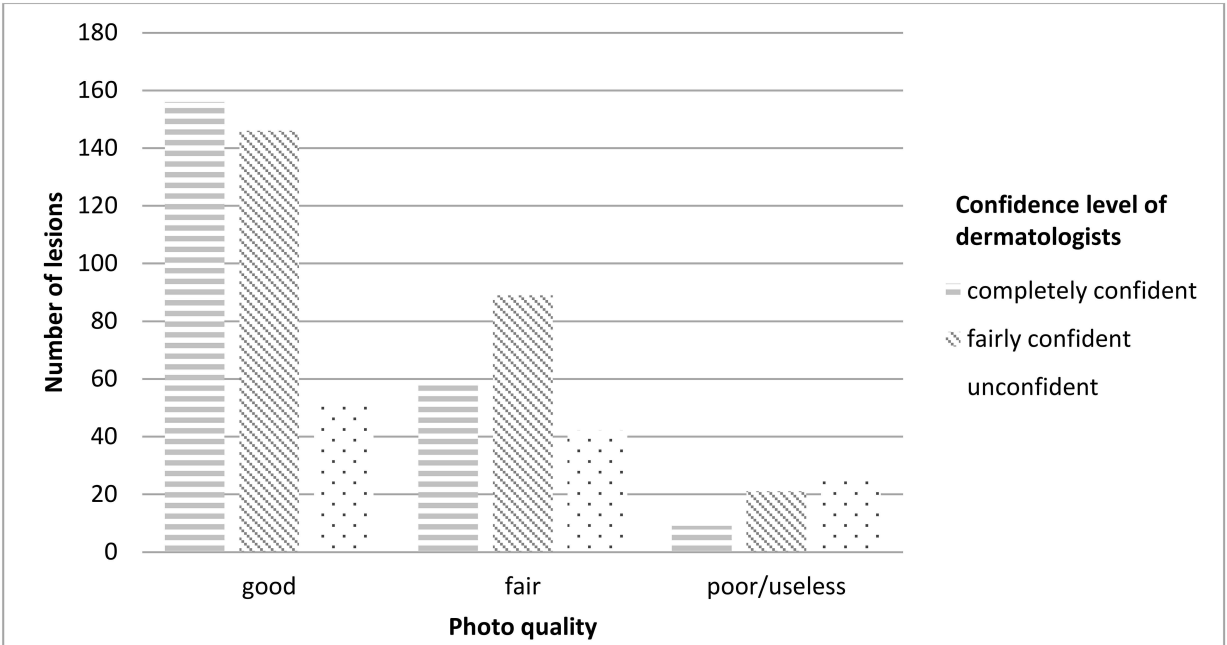
Diagnosis	PPV of GPs (95% CI) n=456	PPV of TD (95% CI) n=600
Malignancy/premalignancy	49.5% (42.7-56.4)	66.2% (59.4-72.5)
Melanoma/in situ	26.3% (13.4-43.1)	32.0% (19.5-46.7)
Squamous cell carcinoma	11.1% (1.4-34.7)	18.8% (4.0-45.6)
Basal cell carcinoma	43.0% (33.1-53.3)	78.9% (68.1-87.5)
Bowen's disease	0% (0-52.2)*	0% (0-84.2)*
Actinic keratosis	30.4% (18.8-44.1)	58.3% (44.9-70.9)
Atypical nevus	13.7% (9.0-19.7)	36.5% (23.6-51.0)
Nevus (benign + atypical)	60.0% (52.3-67.3)	88.0% (82.2-92.4)
AK, Bowen, SCC combined	35.4% (25.0-47.0)	53.8% (42.2-65.2)

*one sided, 97.5% confidence interval

Figure 1. Flowchart of inclusion of patients for teledermoscopy study in Denmark, 2018. GP: general practitioner FTF: face-to-face evaluation

Figure 2. Correlation between photo quality obtained by teledermoscopy in Denmark in 2018 and the diagnostic confidence of the dermatologists evaluating 598 images of suspected skin cancers


562 patients referred by GPs for trial
519 patients included (600 skin lesions)
77 patients lacked registration by GPs (142 skin lesions)
442 patients registered by GPs (458 skin lesions)
43 patients excluded:
9 under 18 years of age
3 unable to understand and sign informed consent
6 photos never received
25 not evaluated FTF by trial dermatologists and no histology
1 deceased
4 seen by dermatology registrars
9 did not show up for FTF
11 cancelled appointment for FTF


180
160
140
120
100
80
60
40
20
0
Number of lesions
good
fair
poor/useless
Photo quality
Confidence level of dermatologists
completely confident
fairly confident
unconfident