Development of a Non-Melanoma Skin Cancer Detection Model

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\textbf{Key Words}
Skin cancer · Detection · Nurses

\section*{Abstract}
\textbf{Background:} The incidence and prevalence of skin cancer is rising. A detection model could support the (screening) process of diagnosing non-melanoma skin cancer. \textbf{Methods:} A questionnaire was developed containing potential actinic keratoses (AK) and basal cell carcinoma (BCC) characteristics. Three nurses diagnosed 204 patients with a lesion suspicious of skin (pre)malignancy and filled in the questionnaire. Logistic regression analyses generated prediction models for AK and BCC. \textbf{Results:} A prediction model containing nine characteristics correctly predicted the presence or absence of AK in 83.2\% of the cases. BCC was predicted correctly in 91.4\% of the cases by a model containing eight characteristics. The nurses correctly diagnosed AK in 88.3\% and BCC in 90.9\% of the cases. \textbf{Conclusions:} Detection or screening models for AK and BCC could be made with a limited number of variables. Nurses also diagnosed skin lesions correctly in a high percentage of cases. Further research is necessary to investigate the robustness of these findings, whether the percentage of correct diagnoses can be improved and how best to implement model-based prediction in the diagnostic process.

\section*{Introduction}
Because of the rapidly rising incidence of non-melanoma skin cancer, a new disease management strategy will be necessary for this new chronic disease. To manage the inflow of patients in the skin cancer management model, it is essential to get the true-positive skin cancer patients into the system and to reduce the false-positive and false-negative patients \cite{1}. Improvements could be made on the level of referral by general practitioners (GPs) and prioritization of patients. In an earlier study a triage system to identify suspicious skin lesions by a telephone screening method showed a decrease in waiting time \cite{2}. Teledermatology has shown both an improvement of prioritization and a decrease in waiting time \cite{3–5}. Attempts were made to educate the population by means of a brochure containing photographs for self-detection of melanoma. This was associated with a favorable impact on self-surveillance in 13\% of the study population. Unfortunately, the campaign was not even recalled by 62\% of the people \cite{6}. Quereux et al. \cite{7} developed a questionnaire to assess melanoma risk factors. The tool seemed to be useful for GPs, but was difficult for the patients themselves to fill in.
To the best of our knowledge, no risk assessment questionnaires or prediction models for non-melanoma skin cancer exist. A skin cancer detection model could help nurses (with the proper training) to make a preselection of patients before they enter a certain healthcare process.

The present study was set up to develop a skin cancer detection model as part of a new skin cancer management strategy [1, 8] and to investigate the potential of nurses in diagnosing skin (pre-)malignancies. In this study we focused on actinic keratosis (AK) and basal cell carcinoma (BCC), as these represent the major part of non-melanoma skin cancer and pre-malignancies [9, 10].

**Patients and Methods**

The study was performed by researchers of the Eindhoven University of Technology at the outpatient clinic of dermatology of the Catharina Hospital Eindhoven, in collaboration with the Department of Dermatology.

The first step in this study was to determine the characteristics of non-melanoma skin cancer, with a focus on AK. 20 patient- and clinical lesion-related characteristics were obtained from the literature (table 1) [11–14]. In addition, one dermatologist and three residents of dermatology were interviewed at the dermat-oncology unit of the Catharina Hospital Eindhoven. They were asked to list further characteristics that might predict or rule out AK. This resulted in an additional 15 characteristics (table 1). To be able to score these 35 characteristics, a questionnaire was developed (Appendix).

A total of 204 patients, all over the age of 18, who had been referred to the outpatient clinic by a GP with a lesion suspicious of AK or skin cancer, were asked to participate. The study was performed with three nurses working at the outpatient clinic of dermatology, with varying levels of experience. The first nurse, who examined 64 cases, was an all-round dermatology nurse who had been working at the clinic for years. The second nurse had been working at the dermat-oncologic outpatient clinic for several years. She examined a total of 70 cases. The third nurse, who also examined 70 cases, had had clinical experience at the dermatologic outpatient clinic in the past and had recently started a traineeship as a physician assistant.

For each patient, the questionnaire was filled in by one of these nurses. The patient was asked about the patient-related characteristics present in the questionnaire. The nurse then judged the lesion-related characteristics and diagnosed the lesion. Afterwards, one of the dermatologists received all materials and judged and diagnosed the lesion as well.

A biopsy of the lesion was performed if the dermatologist suspected a malignancy or if the clinical diagnosis was unclear (45 cases; 22%). The histological outcome was recorded. If no biopsy was taken, the clinical diagnosis given by the dermatologist was recorded as the definite diagnosis. Although the initial research focused on characteristics of AK, we realized that the set of characteristics could be used for a prediction model for BCC as well, because we could not find characteristics in the literature that were suggested as predictive for BCC that were not already included in our list for AK. For example, shininess can be considered a relevant characteristic for both AK and BCC, with a shiny lesion expected to make BCC more and AK less likely.

The data were analyzed in Stata 13 [15] by means of logistic regression procedures. Different approaches for selecting variables (enter all variables, forward stepwise, backward stepwise) yielded highly similar results (we got the same set of significant predictors and almost identical accuracy in predicting presence and absence of AK and BCC). We therefore only report the results of the method of variable selection where we first entered all variables and then retained the variables with p values <0.20. Due to missing data, seven cases had to be deleted, leaving 197 cases for the analyses.

**Results**

**AK**

An initial regression model without predictors predicted that AK was absent in all 197 cases, which was correct in 139 of 197 cases (70.6%). The eventual statistical prediction model for AK consisted of nine predictors.

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**Table 1. Characteristics of AK found in the literature and mentioned by doctors**

<table>
<thead>
<tr>
<th>Characteristics from the literature (20) [5–8]</th>
<th>Additional characteristics mentioned by doctors (15)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient-related</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>History of skin cancer</td>
</tr>
<tr>
<td>Gender</td>
<td>Frequent sun exposure &lt;65 years</td>
</tr>
<tr>
<td>Skin type</td>
<td>Frequent sun exposure &gt;65 years</td>
</tr>
<tr>
<td>Excessive sun exposure</td>
<td>Liked sun tanning</td>
</tr>
<tr>
<td>Profession outdoors</td>
<td>Spent time in tropics</td>
</tr>
<tr>
<td>Immunosuppressant use</td>
<td>Frequent holidays with sun exposure</td>
</tr>
<tr>
<td>Organ transplant patients</td>
<td>Sunburned as a child</td>
</tr>
<tr>
<td><strong>Lesion-related</strong></td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td>Itching</td>
</tr>
<tr>
<td>Scaliness</td>
<td>On top of the epidermis</td>
</tr>
<tr>
<td>Keratotic surface</td>
<td>Shininess</td>
</tr>
<tr>
<td>Confinement</td>
<td>Presence other signs of sun damage</td>
</tr>
<tr>
<td>Elevation</td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td></td>
</tr>
<tr>
<td>Speed of enlargement</td>
<td></td>
</tr>
<tr>
<td>Induration</td>
<td></td>
</tr>
<tr>
<td>Ulceration</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>Localization</td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td></td>
</tr>
<tr>
<td>Widened blood vessels</td>
<td></td>
</tr>
</tbody>
</table>

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van der Geer/Kleingeld/Snijders/Rinkens/Jansen/Neumann/Krekels

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Table 2. Comparison of three prediction models for AK and BCC

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Model 1 AK</th>
<th>Model 2 AK</th>
<th>Model 3 AK</th>
<th>Model 4 BCC</th>
<th>Model 5 BCC</th>
<th>Model 6 BCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratotic</td>
<td>1.344 (3.60)</td>
<td>1.349 (5.00)</td>
<td>0.559 (0.91)</td>
<td>-1.521 (-2.95)</td>
<td>-0.951 (-1.73)</td>
<td></td>
</tr>
<tr>
<td>Shape: elevated</td>
<td>-2.259 (-3.79)</td>
<td>-2.615 (-4.96)</td>
<td>-1.089 (-1.79)</td>
<td>1.204 (1.83)</td>
<td>1.552 (1.90)</td>
<td></td>
</tr>
<tr>
<td>Light-red color</td>
<td>1.075 (2.19)</td>
<td>0.360 (0.59)</td>
<td>1.942 (2.65)</td>
<td>0.301 (1.64)</td>
<td>0.336 (1.37)</td>
<td></td>
</tr>
<tr>
<td>Frequent holidays with sun exposure</td>
<td>-0.320 (-2.07)</td>
<td>-0.223 (-1.22)</td>
<td>1.268 (2.25)</td>
<td>0.112 (-0.15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shininess</td>
<td>-2.000 (-2.04)</td>
<td>-1.894 (-1.82)</td>
<td>2.164 (2.63)</td>
<td>1.147 (1.47)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulceration</td>
<td>-0.706 (-1.09)</td>
<td>0.559 (0.63)</td>
<td>3.01 (2.43)</td>
<td>0.25 (0.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Widened blood vessels</td>
<td>1.563 (1.53)</td>
<td>0.455 (0.64)</td>
<td>1.139 (1.95)</td>
<td>0.25 (0.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Located on sun-exposed part of body</td>
<td>1.400 (2.13)</td>
<td>0.455 (0.64)</td>
<td>1.139 (1.95)</td>
<td>0.25 (0.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequent sun exposure before 65 years of age</td>
<td>0.986 (2.04)</td>
<td>3.01 (2.43)</td>
<td>1.139 (1.95)</td>
<td>0.25 (0.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AK diagnosis of nurses</td>
<td>1.400 (2.13)</td>
<td>0.455 (0.64)</td>
<td>1.139 (1.95)</td>
<td>0.25 (0.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCC diagnosis of nurses</td>
<td>3.911 (4.76)</td>
<td>3.911 (4.76)</td>
<td>3.911 (4.76)</td>
<td>3.911 (4.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeds easily</td>
<td>1.353 (3.01)</td>
<td>1.597 (4.56)</td>
<td>1.366 (2.70)</td>
<td>2.931 (3.71)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.0648 (2.83)</td>
<td>0.0595 (2.28)</td>
<td>0.0595 (2.28)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCC diagnosis of nurses</td>
<td>1.353 (3.01)</td>
<td>1.597 (4.56)</td>
<td>1.366 (2.70)</td>
<td>2.931 (3.71)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>-3.294 (-1.92)</td>
<td>-0.0676 (-0.12)</td>
<td>-6.806 (-3.30)</td>
<td>-13.160 (-4.80)</td>
<td>-4.977 (-6.57)</td>
<td>-12.43 (-3.87)</td>
</tr>
<tr>
<td>Observations</td>
<td>197</td>
<td>197</td>
<td>197</td>
<td>197</td>
<td>197</td>
<td>197</td>
</tr>
<tr>
<td>Pseudo R²</td>
<td>0.37</td>
<td>0.26</td>
<td>0.55</td>
<td>0.49</td>
<td>0.21</td>
<td>0.58</td>
</tr>
<tr>
<td>AIC</td>
<td>171.6</td>
<td>182.2</td>
<td>129.7</td>
<td>110.8</td>
<td>149.9</td>
<td>95.8</td>
</tr>
<tr>
<td>AUC</td>
<td>0.89</td>
<td>0.84</td>
<td>0.93</td>
<td>0.93</td>
<td>0.78</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Models 1 and 4 show the result of entering all predictor variables and then re-estimating the model with the (almost) significant predictors. Models 2 and 5 show base models with two of the most frequently mentioned predictors (for AK and BCC). Models 3 and 6 include the nurses’ diagnosis as a predictor to models 1 and 4.

In each cell, the first number represents the regression coefficient B. These are the values for the logistic regression equation for predicting the dependent variable (outcome) from the independent variable (predictor). The second number (in parentheses) represents the t statistic. Superscripts represent the two-tailed p value used in testing the null hypothesis that the coefficient equals zero.

Pseudo R²: A measure of the amount of variance explained in the outcome by the predictor variables. AIC: Akaike information criterion, representing the relative quality of the models, with lower scores representing a better fit of the model. AUC: Area under the curve, an index of accuracy of the model (as the pseudo R²). Higher values (maximum = 1) are better.

( model 1 in table 2) and achieved a substantially higher percentage of correct diagnoses: 83.2% (164 of 197 cases) (table 3). The sensitivity of the prediction – its ability to identify AK correctly – is 69.0%. The specificity – the ability to exclude AK correctly – is 89.2%. The pseudo R² value equals 0.37 and the AUC is 0.89. Correlations among predicting variables and variance inflation factors were low, indicating that there were no problems with multicollinearity.

Figure 1a contains the specificities and sensitivity curves for the prediction of AK, showing the changes in sensitivity and specificity as a function of the cut-off score. The standard cut-off value employed in this study was 0.5. This means that cases with a predicted probability of AK of ≥50% were classified as positives, those with a probability <50% as negatives. A lower cut-off score leads to higher sensitivity and lower specificity, whereas a higher cut-off score leads to lower sensitivity and higher specificity, with overall accuracy decreasing in both cases. To illustrate, suppose that correctly establishing the presence of AK is more important than correctly establishing the absence of AK. In such a case increasing the number of true positives to 57 out of 58 (sensitivity 98.3%), instead of the original 40 out of 58 (sensitivity 69.0%), would require using a cut-off score of 0.15, resulting in an increase of false positives from 15 to 49 of the 139 negatives, which decreases specificity from 89.2 to 64.7% and overall accuracy from 83.2 to 74.6%. Such arguments are typically of use when considering the use of diagnostic tools in practice. For instance, one could imagine using a prediction model as a screening device with an emphasis on finding cases that are not likely to be AK or BCC. A positive diagnosis might then be made by other means, such as diagnosis by a dermatologist or a biopsy.

Of the nine characteristics in the final model, four had a significant positive prediction value, indicating an increased probability that AK is present (table 2); the lesion is keratotic, the lesion has a light-red color, the patient had frequent sun exposure before the age of 65, and the lesion is located on sun-exposed areas of the skin. Three characteristics had a negative prediction value, indicating...
a decreased probability that AK is present: the lesion is elevated, the lesion is shiny, and patient had frequent holidays with sun exposure. Two characteristics did not meet the commonly used significance value of 0.05: widened blood vessels (positive) and ulceration (negative). They were retained because they slightly improved the overall prediction accuracy and might be of importance if a larger number of cases will be included in the future. The two strongest predictors of AK are a keratotic lesion (positive) and an elevated lesion (negative). When these are used as sole predictors (model 2 in table 2), the overall accuracy of the prediction decreases slightly to 81.7% (table 3). As a benchmark, we tested a model with two of the most often mentioned predictors for AK, whether the spot is keratotic and whether it is elevated. The AUC value then decreases to 0.84 and the pseudo $R^2$ value to 0.26 (compared to the full model’s 0.89 and 0.37). To assess whether there is any evidence for over-fitting, we compared the AUC value and the overall accuracy for a training set consisting of two-thirds of the original data and a test set consisting of one-third of the original data. The AUC value slightly decreases to 0.82 and the pseudo $R^2$ value to 0.25.

**Table 3.** Sensitivity, specificity and overall accuracy in predicting AK and BCC of statistical prediction models, nurses’ diagnosis, and a prediction model with nurses’ diagnosis as an additional predictor (n = 197)

<table>
<thead>
<tr>
<th>Model in table 2</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensitivity TP/(TP + FN)</th>
<th>Specificity TN/(TN + FP)</th>
<th>Overall accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>AK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prediction model (all predictors)</td>
<td>1</td>
<td>40</td>
<td>124</td>
<td>15</td>
<td>18</td>
<td>69.0%</td>
<td>89.2%</td>
</tr>
<tr>
<td>Prediction model (two best predictors only)</td>
<td>2</td>
<td>43</td>
<td>118</td>
<td>21</td>
<td>15</td>
<td>74.1%</td>
<td>84.9%</td>
</tr>
<tr>
<td>Nurses’ diagnosis</td>
<td>3</td>
<td>50</td>
<td>124</td>
<td>15</td>
<td>8</td>
<td>86.2%</td>
<td>89.2%</td>
</tr>
<tr>
<td>Prediction model, including nurses’ diagnosis</td>
<td>4</td>
<td>50</td>
<td>128</td>
<td>11</td>
<td>8</td>
<td>86.2%</td>
<td>92.1%</td>
</tr>
<tr>
<td>BCC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prediction model (all predictors)</td>
<td>4</td>
<td>22</td>
<td>158</td>
<td>5</td>
<td>12</td>
<td>64.7%</td>
<td>96.9%</td>
</tr>
<tr>
<td>Prediction model (two best predictors only)</td>
<td>5</td>
<td>15</td>
<td>152</td>
<td>11</td>
<td>19</td>
<td>44.1%</td>
<td>93.3%</td>
</tr>
<tr>
<td>Nurses’ diagnosis</td>
<td>6</td>
<td>27</td>
<td>152</td>
<td>11</td>
<td>7</td>
<td>79.4%</td>
<td>93.3%</td>
</tr>
<tr>
<td>Prediction model, including nurses’ diagnosis</td>
<td>7</td>
<td>24</td>
<td>158</td>
<td>5</td>
<td>10</td>
<td>70.6%</td>
<td>96.9%</td>
</tr>
</tbody>
</table>

TP = True positive; TN = true negative; FP = false positive; FN = false negative.

**Fig. 1.** Sensitivity and specificity curves for AK (a) and BCC (b). a The curves refer to model 1 in table 3. b The curves refer to model 4 in table 3.
of the remaining third. Repeating this procedure 100 times gives an average AUC value for the training set of 0.89 (SD = 0.02) and an overall accuracy of 83.2% (SD = 2.0). For the test set, we find an AUC value of 0.85 (SD = 0.05) and an overall accuracy of 80.0% (SD = 4.3). Hence, over-fitting is hardly apparent, given the small decrease in AUC value and overall accuracy.

**BCC**

The initial regression model without predictors predicted the absence of BCC correctly in 163 of 197 cases (82.7%). The final statistical prediction model, which included eight characteristics as predictors (model 4 in table 2), achieved a substantially higher percentage of correct diagnoses (91.4%; 180 of 197 cases) (table 3). The sensitivity of the prediction is 64.7. The specificity is 96.9%. The pseudo R² value equals 0.49 and the AUC is 0.93. Correlations among predictors and variance inflation factors were low, indicating that there were no problems with multicollinearity. With the standard cut-off value of 0.5, 91.4% of the cases were predicted correctly (table 3). Of the eight characteristics in the final model, five had a positive prediction value, indicating an increased probability that BCC is present: the lesion has a light-red color, shininess, age of the patient, ulceration of the lesion, and the lesion bleeds easily. One variable had a negative prediction value, indicating a decreased probability that BCC is present: the lesion is keratotic (table 2, model 4). Two characteristics did not meet the commonly used significance of 0.05: the lesion is elevated and the patient had frequent holidays with sun exposure. Both were retained because they slightly improved the percentage of correct diagnoses.

Figure 1b contains the specificity and sensitivity curves for the prediction of BCC, showing the changes in sensitivity and specificity as a function of the cut-off score. A prediction with only two strong predictors of BCC (light-red color, bleeds easily; table 2, model 5) has a prediction accuracy of 84.8%, which is 6.6 percentage points lower than model 4 with all predictors. As a benchmark, we tested a model with two of the most often mentioned predictors for BCC, whether the spot has a light-red color and whether the spot bleeds easily. The AUC value then decreases to 0.78 and the pseudo R² value to 0.21 (compared to the full model’s 0.93 and 0.49). To assess whether there is any evidence for over-fitting, we compared the AUC value and the overall accuracy for a training set consisting of two-thirds of the original data and a test set consisting of the remaining third. Repeating this procedure 100 times gives an average AUC value for the training set of 0.87 (SD = 0.02) and an overall accuracy of 82.8% (SD = 2.2). For the test set, we find an AUC value of 0.83 (SD = 0.05) and an overall accuracy of 79.5% (SD = 4.4). Hence, once again over-fitting is hardly apparent, given the small decrease in AUC value and overall accuracy. However, given the size of the data set and the low prevalence of BCC (roughly 1 in 6 cases), the standard deviations of the accuracy in the test set are quite large, which makes it difficult to accurately assess whether there is a decrease in precision.

**Nurses’ Diagnoses**

A direct comparison of the nurses’ diagnoses with the biopsy results/dermatologists’ diagnoses revealed that the nurses obtained a high percentage of correct diagnoses. For AK a correct diagnosis was given in 88.3% of the cases (sensitivity 86.2%; specificity 93.3%) (table 3). For BCC the percentage of correct diagnoses was even higher: 90.9% (sensitivity 79.4.2%; specificity 93.3%) (table 3). The overall accuracy scores obtained by the nurses are similar to the statistical prediction model, with a sensitivity that is higher than the specificity for both AK and BCC.

**Combining the Statistical Prediction with the Nurses’ Diagnoses**

Additionally, we incorporated the diagnoses made by nurses as a predictor in the models of AK and BCC. By adding this predictor, the total percentage of correct predictions increased substantially for AK (from 83.2 to 90.4%) and slightly for BCC (from 91.4 to 92.4%) (table 3). Next to this predictor, other variables are important for the correct prediction of the diagnosis, as is shown in models 3 and 6 of table 2. These variables can be interpreted as corrections to the nurses’ diagnosis. For example, model 3 in table 2 shows that in predicting AK, widened blood vessels is a strong additional predictor to the nurses’ diagnosis, indicating that in their diagnosis these nurses may have underestimated the importance of widened blood vessels as a characteristic of AK.

**Comparison to GP and Dermatologist Predictions**

In a small retrospective study (unpublished data) performed at our dermatology outpatient clinic, 109 medical records of patients with AK were screened to identify the referrals made by the GPs. In this sample, GPs had correctly diagnosed only 16 cases of AK as AK (a sensitivity of 14.7%). This is substantially lower than the range of sensitivity scores observed in this study (69.0–86.2%; table 3). In a recent study we found that in patients with BCC, dermatologists clinically diagnosed BCC correctly...
in 894 of 953 cases (sensitivity 93.8%; 894 true positives, 59 false negatives) [10]. This is higher than the sensitivity scores found in this study (prediction model: 64.7%; nurses: 79.4%; table 3).

Discussion

With a rapidly rising incidence of non-melanoma skin cancer, an increasing number of patients are referred to dermatologists for evaluation of lesions suspicious of skin cancer or pre-malignancies. Healthcare systems have not yet adjusted to this increased demand on chronic skin cancer care [1]. A disease management system that provides a new skin cancer management strategy on several levels is needed to provide adequate control and treatment of patients [1]. The burden on the healthcare system will be reduced if screening methods improve [16, 17].

With this study we have shown that developing prediction models for AK and BCC with only a limited number of variables might be a useful way to improve the screening method. These models can be used to screen for AK and BCC with an emphasis on sensitivity or specificity, depending on the value of the cut-off point that is used.

This brings us to an important, ethical part of the discussion. What would be an acceptable cut-off point? In how many cases would it be acceptable to miss a diagnosis of AK or BCC? If missing even one single diagnosis is unacceptable, we will have to deal with a lot of false-positive cases, which will unnecessarily increase the burden on the healthcare system. One could argue that although missing an AK is not life-threatening, it could develop into a squamous cell carcinoma. Missing a BCC is not life-threatening either. However, early recognition is important since treatment of BCC is then less difficult and less expensive [16, 17].

One should bear in mind that the prediction model is just an additional tool; the nurses (nurse practitioners or physician assistants) need to be trained in the recognition of skin cancer and treatment options. They will need to stay alert and not just depend on the model. When in doubt, they should always ask the opinion of the dermatologist. In addition, we would suggest using this questionnaire for chronic non-melanoma skin cancer patients who are undergoing follow-up screening.

In our study all three nurses diagnosed a high percentage of cases correctly, 88.3% for AK and 90.9% for BCC. They did, however, not have any experience in diagnosing lesions and had had no extra training on assessing and diagnosing AK or BCC. The high percentage of correct diagnoses by nurses is comparable to the one obtained with the statistical prediction model, which was 83.2% for AK and 91.4% for BCC. The questionnaire they used might have made the nurses more aware of certain characteristics, which might have helped them to diagnose the lesions.

From the additional analysis we conclude that the total of correct predictions of AK and BCC by the model can be improved by adding the diagnoses made by nurses as a predictor. From this model it becomes clear that widened blood vessels were not given enough weight by nurses when diagnosing AK (table 2, model 3). For BCC, the nurses appear to have underestimated the impact of light-red color, bleeds easily and age (table 2, model 6). On the basis of these models, nurses might improve their percentage of correct diagnoses if they were trained to attenuate the weight they attach to these predictors. It is supported by the literature that nurse practitioners can be trained to accurately identify and triage suspicious skin lesions [18].

The evaluation of the nurses’ results suggest that nurses diagnose AK and BCC substantially better than GPs, in line with the literature on GPs’ diagnoses of skin malignancies. Pockney et al. [19] concluded that GPs missed 30% of skin malignancies. An internet-based tutorial for primary care physicians to improve skin cancer triage skills unfortunately did not have a sustaining result. In addition, the response rate was low – 83% of physicians did not start with the tutorial and many did not complete the program [20]. The results of dermatologists for BCC are also comparable to figures found in the literature [19]. When these are compared to the results of the model and nurses, we see that they are close but not completely at the same level as dermatologists.

There are some limitations to this study. It included patients who were seen at the outpatient clinic of dermatology. This means that a GP had already referred a large number of the patients, and a certain preselection had taken place. Therefore, our results cannot be generalized for patients outside the dermatology clinic (unless one is willing to assume that GPs refer almost everybody with a suspicious lesion). Nevertheless, it is likely that diagnostic models for patients who arrive at GPs would include similar predictors.

Another limitation is that the characteristics used in the questionnaire are not evidence-based. No questionnaire exists to compare our results. In the literature, there is no evidence on the strength of the characteristics; it is limited to observations and descriptions of AK [11–14]. Additional characteristics were provided by (only) four
physicians (dermatologists or residents) of the dermatology unit, and there might be more.

The predictors found in the model are, however, commonly known characteristics of AK and they can be traced in the literature. The conclusions about the model on BCC need to be interpreted carefully, as in the initial phase of the study the search for diagnostic characteristics focused on characteristics of AK. Nevertheless, the prediction model for BCC has a high overall accuracy and contains some predictors that distinguish it from AK, such as keratotic surface (negative) and shininess and whether the spot bleeds easily (positive). Although the study was performed with only 204 cases, the implementation of the prediction model and the support of nurses in diagnosing AK and BCC seem promising. More patients will be needed to be able to strengthen the conclusions and to determine the robustness of our results. In this sense, one should consider this study indicative of the promise of model-based prediction, more than a definitive list of the crucial predictors for AK and BCC. Other types of non-melanoma skin cancer, such as Bowen’s disease and squamous cell carcinoma, will need to be incorporated to complete the detection model.

Conclusions

We have developed a skin cancer detection model that can predict and rule out a certain number of AK and BCC cases with a limited number of variables. Interpretation of the data and the choice of a cut-off point on false-negative and false-positive outcomes need to be further discussed, but the case for including model-based prediction for the diagnosis of AK and BCC is promising. Nurses correctly diagnosed a high percentage of lesions, comparable to the detection model, and including the nurses’ diagnosis in the prediction models led to an additional improvement in the overall prediction accuracy. Further research is necessary to investigate the robustness of the results when a larger number of cases is included. Moreover, an attempt should be made to increase the number of correctly predicted or diagnosed lesions.

Disclosure Statement

There are no conflicts of interest. The work was not supported by any funding sources.

Appendix

Questionnaire containing potential characteristics of AK and BCC

Patient-related characteristics

1. Name of the patient: ......................................................
2. Sex
   □ Male  □ Female
3. First visit to the dermatology clinic?
   □ Yes  □ No
4. Did you have an outdoor profession? (with sun exposure >5 h/day)
   □ Yes  □ No  □ Do not know
5. Did you have a lot of sun exposure <65 years of age?
   □ Yes  □ No  □ Do not know  □ Not 65 years of age yet
6. Did you have a lot of sun exposure >65 years of age?
   □ Yes  □ No  □ Do not know
7. Do you or did you like sun tanning?
   □ Yes  □ No  □ Do not know
8. Have you been in the tropics for more than 3 months?
   □ Yes  □ No  □ Do not know
9. How often have you been on a vacation with a lot of sun exposure?
   □ Often  □ Regularly  □ Sometimes  □ Seldom  □ Never
10. Did you often get sunburned as a child?
    □ Often  □ Regularly  □ Sometimes  □ Seldom  □ Never  □ Do not know
11. Did you often get sunburned as an adolescent?
    □ Often  □ Regularly  □ Sometimes  □ Seldom  □ Never  □ Do not know

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12. Do you/did you use a solarium?
  □ Yes  □ No

13. If you do/did, how often?
  □ Daily  □ Weekly  □ Monthly  □ Yearly

14. For how many years did you use the solarium?
  ...... years

15. At what age did you start using the solarium?
  ...... years of age

16. Did you have an organ transplant?
  □ Yes  □ No

17. If you did, in what year?
  Year: .............

18. Do you use immunosuppressant medication?
  □ Yes  □ No

19. If you do, what type of medication?
  □ Prednisolone  □ Imuran  □ Prograft  □ Cellcept  □ Cyclosporine  □ Other

20. Are there members of your family who have/had skin cancer?
  □ Yes  □ No  □ Do not know

21. If there are, how many persons in your family have/had skin cancer?
  Number: ......

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**Lesion-related characteristics**

22. For how long has the lesion been present?
  □ Days  □ Weeks  □ Months  □ Half a year  □ Years  □ Do not know

23. Does the lesion bleed easily?
  □ Yes  □ No  □ Do not know

24. Does the lesion itch?
  □ Very much  □ A little  □ No

25. Is the lesion located at the scalp, ears, in the face, at the forearms or the back of your hands?
  □ Yes  □ No

26. Skin type of the patient:
  □ I  □ II  □ III  □ IV

27. Largest diameter of the lesion:
  ...... mm

28. Does the lesion increase in size?
  □ Yes  □ No

29. Redness of the lesion
  □ Skin color  □ Light-red  □ Dark-red  □ Intense-red  □ Brown
  □ Other color: ......................

30. Shape of the lesion
  □ Flat  □ Elevated

31. Scaliness of the lesion
  □ None  □ Little  □ Much

32. Keratotic surface?
  □ No  □ Feels rough  □ Feels and looks rough  □ Thick keratotic surface

33. Is there induration?
  □ Yes  □ No

34. Is the lesion sharply demarcated?
  □ Yes  □ No

35. Is the lesion shiny?
  □ Yes  □ No
36. Is the lesion painful when it is touched? □ Yes □ No
37. Are there widened blood vessels present in the lesion or in the surrounding skin? □ Yes □ No
38. Is there ulceration? □ Yes □ No
39. Are there other signs of sun damage in the skin? (wrinkles, pigment, widened blood vessels) □ Yes □ No

References