

## Effect of Histopathological Explanations for Dermoscopic Criteria on Learning Curves in Skin Cancer Training: a Randomized Controlled Trial

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**Authorship:** All authors have contributed significantly to this publication.

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**ABSTRACT Introduction:** Case-based training improves novices pattern recognition and diagnostic accuracy in skin cancer diagnostics. However, it is unclear how pattern recognition is best taught in conjunction with the knowledge needed to justify a diagnosis.

**Objectives:** The aim of this study was to examine whether an explanation of the underlying histopathological reason for dermoscopic criteria improves skill acquisition and retention during case-based training in skin cancer diagnostics.

**Methods:** In this double-blinded randomized controlled trial, medical students underwent eight days of case-based training in skin cancer diagnostics, which included access to written diagnosis modules. The modules dermoscopic subsections differed between the study groups. All participants received a general description of the criteria, but the intervention group additionally received a histopathological explanation.

**Results:** Most participants (78%) passed a reliable test in skin cancer diagnostics, following a mean training time of 217 minutes. Access to histopathological explanations did not affect participants' learning curves or skill retention.

**Conclusions:** The histopathological explanation did not affect the students, but the overall educational approach was efficient and scalable.

## Introduction

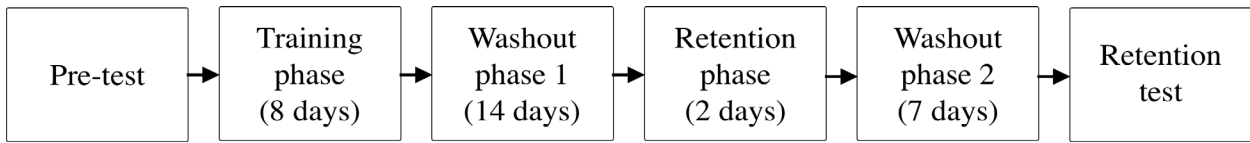
Skin cancer is the most common malignancy among fair-skinned people worldwide [1,2]. Early detection and treatment of skin cancers reduce patient mortality and the associated socioeconomic costs [3]. In most countries, skin cancer triage is performed by personnel without standardized training in the domain [4,5]. Courses that teach structured checklists for skin cancer diagnostics such as the ABCD (Asymmetry, Borders, Colour, and Diameter) algorithm improve novices short-term accuracy, but frequent refresher courses are needed to maintain the skill [6,7]. It is unclear if the training effect is caused by the structured checklists or the simultaneous exposure to many skin lesion images. A Cochrane review recently stated that structured checklists do not improve clinicians accuracy in skin cancer diagnostics [8]. Case-based training improves novices accuracies in skin cancer diagnostics significantly more than structured checklist practice [9-11]. Exposure to annotated skin lesion images improves novices pattern recognition, which is the primary diagnostic strategy of experts [12-14]. It is unclear how pattern recognition and the declarative knowledge needed to justify a diagnosis, are best taught in conjunction. Related work from odontology suggests that teaching the underlying biomedical reason for visual criteria improves the students ability to recognize and remember the criteria [15,16].

## Objectives

This study investigated a novel approach towards teaching skin cancer diagnostics through a mobile educational application. Our primary objective was to examine whether an explanation of the underlying histopathological reason for the dermoscopic criteria used in skin cancer diagnostics affects medical students' learning curves and skill retention. We hypothesized that a deeper biomedical understanding of the dermoscopic criteria would improve the students' ability to recognize and remember them.

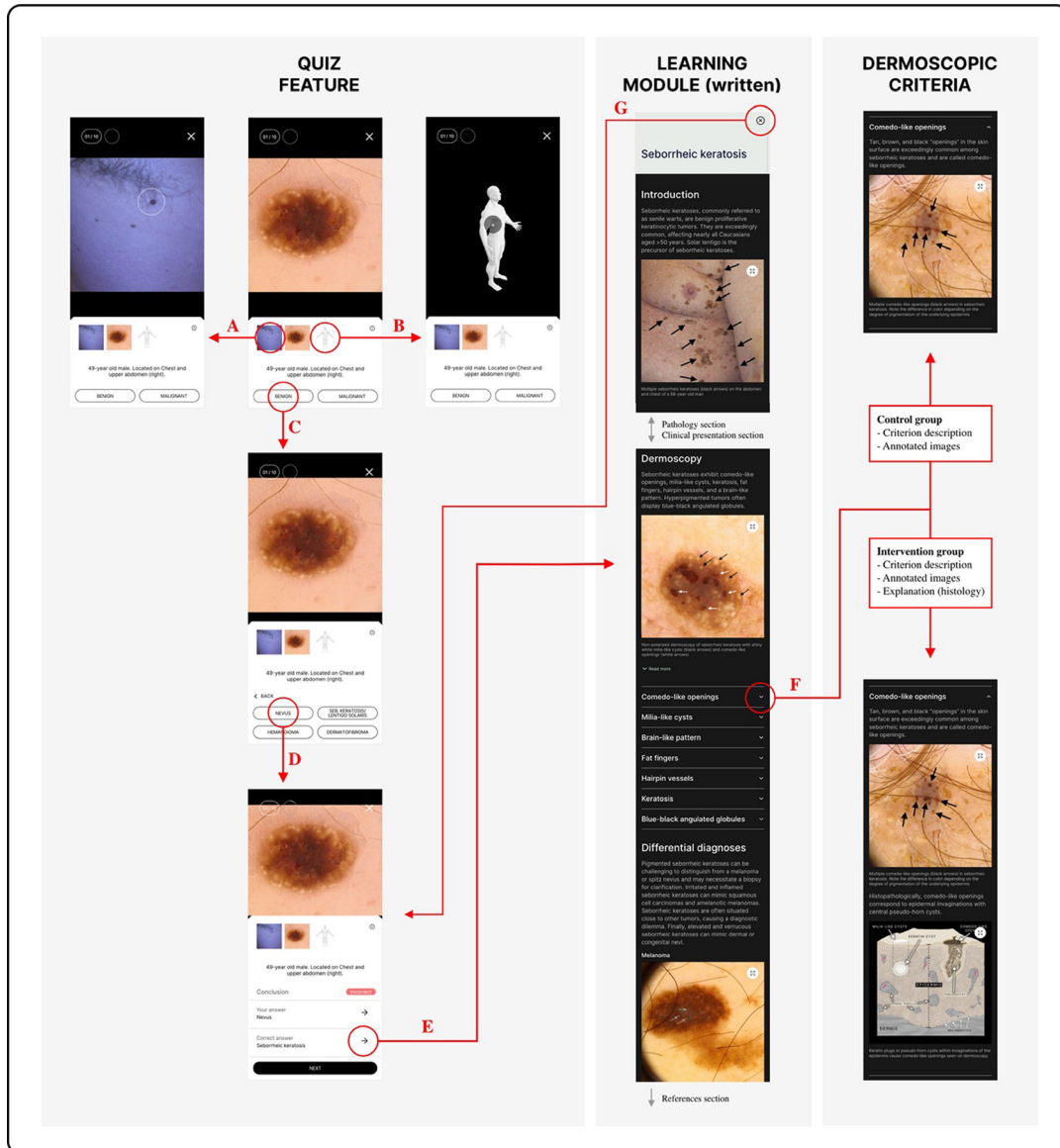
## Methods

In this double-blinded randomized controlled trial (allocation ratio 1:1), we enrolled medical students with no prior experience in skin cancer diagnostics that had previously passed an exam in general histology. The students were invited to participate through a Facebook group for Danish medical students. Participants were enrolled through virtual meetings between the 8<sup>th</sup> and 27<sup>th</sup> of July 2021. During inclusion, we helped participants download and get started in the educational application (onboarding process). Participants were automatically and randomly (simple randomization) assigned to the intervention or control group during the onboarding process. The principal investigator (N.K.T.), a student assistant (S.K.), and participants were all blinded towards trial group allocation. Following the onboarding process, all participants underwent a pre-test and were instructed to diagnose 500 skin lesion cases (including the pre-test cases) over 8 days (training phase), pause for 14 days (washout phase 1), diagnose another 100 cases in 2 days (retention phase), pause for another 7 days (washout phase 2), and finally, complete a retention test (Figure 1). All participants received daily reminders during the training and retention phases, and those that completed the entire study received a certificate of completion. During the training and retention phase, participants had access to written learning modules that described the most common skin lesion diagnoses. The learning modules included a dermoscopy subsection that differed between the trial groups. Participants in the control group saw a brief description of the dermoscopic criteria, while the intervention group saw the same description supplemented with a histopathological explanation (Figure 2). Neither group were informed about the group-dependent learning module differences. We planned and conducted the study per the principles of the Declaration of Helsinki. Participants were informed about the study before participation and gave informed consent. The study was voluntary, held no consequences for the participants, and received a waiver from the Regional Ethics Committee



**Figure 1.** Trial flow.

Participants performed a pre-test (12 cases) at the beginning and a retention test (25 cases) at the end of the trial. During the training and retention phases, each participant practiced skin lesion diagnostics on 500 (including the pre-test cases) and 100 training cases, respectively, while accessing the learning modules of their own accord. We instructed participants to abstain from any training during both washout phases.



**Figure 2.** Educational intervention (mobile application).

The educational intervention consisted of an educational mobile application that included quizzes and written learning modules. The red circles within the figure indicate where users “press” the mobile screen to proceed towards the next screen, indicated by the red arrow. The “Quiz feature” presents skin lesions for diagnostics. The small images representing the clinical image (A) and the avatar (B) are buttons that open the clinical image and 3D avatar. When users press “Benign” (C) or “Malignant”, an array of new buttons representing the various benign or malignant differential diagnoses appear. When users press one of the diagnosis buttons (D), they receive immediate feedback. The feedback consists of the chosen diagnosis, the correct diagnosis, and access to learning modules on both the chosen and correct diagnoses (E). Each learning module consists of the following sections: introduction, pathology, clinical presentation, dermoscopy, differential diagnoses, and references. The dermoscopy sections included an overview and subsections describing the primary dermoscopic criteria. Each subsection included a detailed description of the dermoscopic criterium (F). Users from both trial groups received descriptions and annotated images representing the dermoscopic criteria. However, the subsections presented to the intervention group participants also explained the underlying histopathological correlation for the dermoscopic criteria. When the learning modules in the application are closed (G), users return to the previous training case feedback page.

of Region Hovedstaden, Denmark (jr nr. H-20066667). The Danish Health Data Authorities and Data Protection Agency approved access, anonymization, handling, and storage of the skin lesion cases (jr. nr. 21/5103 and 18/53664). We submitted a study protocol on [clinicaltrials.gov](https://clinicaltrials.gov) prior to initiating the study (identifier: NCT05087485).

### Skin Lesions Library

We developed a case library consisting of 2,376 anonymous skin lesions for this study. Each lesion belonged to one of the following seven diagnostic groups: nevus, seborrheic keratosis/solar lentigo, dermatofibroma, hemangioma, melanoma, basal cell carcinoma, and squamous cell carcinoma. Each case included a clinical and dermoscopic image of the lesion, the lesion location on a human 3D avatar, a diagnosis, and the patient age and gender. The lesions diagnoses were based on either a histopathological assessment (N = 1,293) or a clinical consensus (N = 1,083), consisting of a joint judgment by 2-3 clinicians. All images were captured by nurses and doctors at the Department of Dermatology and Allergy Centre, Odense University Hospital, in Denmark, from the 1<sup>st</sup> of September 2010 until the 8<sup>th</sup> of May 2021. Dermoscopic images were photographed using digital dermoscopes (Medicam 800 and 1000, Fotofinder Systems GmbH).

### Written Learning Modules

The mobile application's written content consisted of 38 diagnosis (eg melanoma) and sub-diagnosis learning modules (eg superficial spreading melanoma). Each sub-diagnosis module included the following subsections: introduction, pathology, clinical presentation, dermoscopy, differential diagnoses, and references (Figure 2). We created two versions of each dermoscopic sub-section; one described the dermoscopic criteria with annotated images (control group), and another version that additionally explained the histopathological correlation for each dermoscopic criterion (intervention group) (Figure 2). All diagnosis and sub-diagnosis modules were written by the first author (N.T.) and reviewed by content experts in pathology, dermatology, and skin cancer surgery (co-authors: A.C., P.G., T.V., R.S., L.H., and J.S.).

### Mobile Application

In this study, we employed a mobile application for training skin lesion diagnostics, called Dermloop Learn (Melatech ApS), developed in cooperation with our group (Figure 2). A continuously updated version of the application can be accessed online (<https://training.dermloop.io/>) or through the app store ("Dermloop Learn"). The application included three functionalities: skin lesion quizzes, written learning modules, and user tracking. Each quiz consisted of ten randomly sampled skin lesion cases from the case library.

Participants received immediate feedback on their quiz diagnoses, including the correct diagnosis and access to the aforementioned learning modules. Time spent reading the learning modules and diagnosing the quiz cases were automatically registered throughout the study.

### Pre- and Retention Test

The pre- and retention tests consisted of skin lesion cases from a test item library with validity evidence previously described by our group [4]. The pre-test consisted of 12 randomly sampled test items (Generalizability coefficient of 0.7), while the retention test included all 25 test items (Cronbach  $\alpha$  of 0.83). A former pass-fail test revealed a pass-fail limit of twelve, ie a score above 12/25 is enough to pass the test [4].

### Statistics

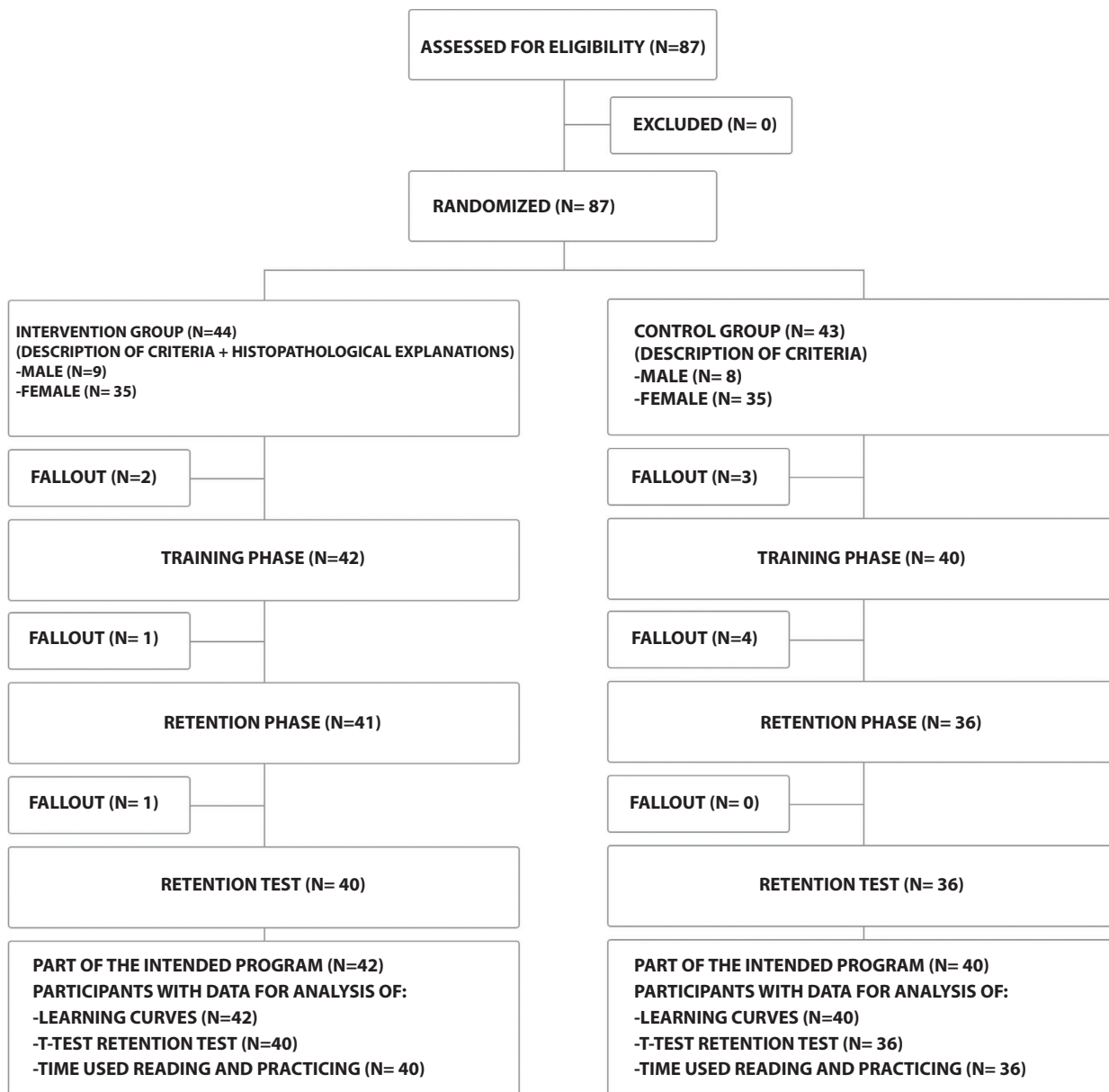
Data was divided into a training (0-500 cases) and a retention phase (501-600 cases). A mixed-effects logistic regression model with correct or false case-answers as an outcome and a random intercept and slope for each individual was applied to estimate the learning curves on the log-odds scale. We sought the most straightforward description of the participants learning curves by comparing (likelihood-ratio tests) cubic and linear spline models with four, one, or zero knots. The retention phase data were described using a simple line. Once we had located the optimal statistical equation for describing the training phase, we compared the control and intervention groups training and retention learning curves using likelihood-ratio tests. The control group retention test results were compared to those of the intervention group using the Welch t-test. For exploratory post hoc analyses, we used the participants test scores on the retention test to divided them into three equally big performance groups; low- (1<sup>st</sup> tertile), intermediate- (2<sup>nd</sup> tertile) and high- (3<sup>rd</sup> tertile) performance. We compared the learning curves, time spent reading, and time spent diagnosing training cases between the 1<sup>st</sup> and 3<sup>rd</sup> tertile using likelihood ratio tests and Welch t-tests. All statistical analyses were performed in R version 4.1.0 (R Foundation for Statistical Computing).

## Results

Eighty-seven medical students were enrolled, and 76 completed the entire trial, see the consort diagram in Figure 3.

### Retention Test

Results on the retention test were equal ( $t = 0.13$ , degrees of freedom ( $df$ ) = 71.3,  $P = 0.90$ ) for the intervention (mean: 13.8, SD: 3.06) and control (mean: 13.9, SD: 3.35) groups. Fifty-nine (78%) out of the 76 participants passed the retention test (>12/25 correct answers). The 76 participants



**Figure 3.** Consort diagram.

who completed the retention test were split into low-, intermediate-, and high-performance groups (N = 25, 25, and 26) based on their test results. Intervention and control participants were equally distributed across the low (N = 14/11) and high-performance (N = 14/12) groups.

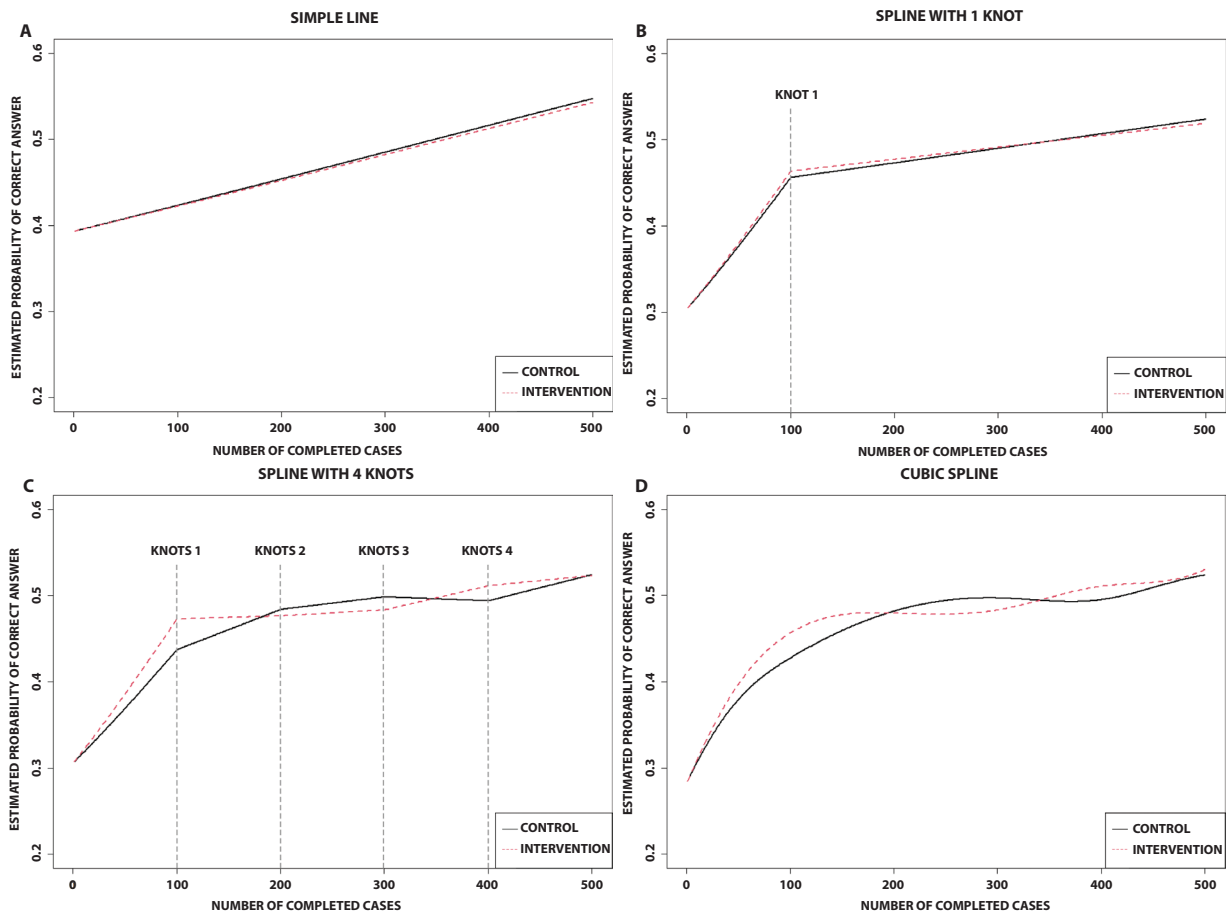
### Learning Curves and Time Spent Training

An almost straight line with a single knot, ie breaking point, at 100 cases provided a significantly better data-fit for the training phase than a straight line without knots ( $\chi^2= 125.0$ ,  $df = 2$ ,  $P = <0.01$ ). There was no added benefit from adding three additional knots at 200, 300, and 400 training cases ( $\chi^2= 7.5$ ,  $df = 6$ ,  $P = 0.28$ ), or performing a cubic transformation ( $\chi^2= 4.3$ ,  $df = 4$ ,  $P = 0.37$ ) (Figure 4).

There were no significant learning curve differences in the training or retention phase, when comparing the

intervention and control groups (training phase:  $\chi^2= 0.35$ ,  $df = 2$ ,  $P = 0.83$ , retention phase:  $\chi^2=0.94$ ,  $df = 1$ ,  $P = 0.33$ ). The learning curves of the intervention and control group participants were also equal within the low- and high-performance groups (training phase:  $\chi^2= 0.80$ ,  $df = 2$ ,  $P = 0.67$ , retention phase:  $\chi^2=0.15$ ,  $df = 1$ ,  $P = 0.70$ ). However, there was a significant difference between the overall (intervention + control) learning curves of the low- versus high-performance groups, (training phase:  $\chi^2= 25.71$ ,  $df = 1$ ,  $P = <0.01$ , retention phase:  $\chi^2=15.29$ ,  $df = 1$ ,  $P < 0.01$ ).

The mean time spent training was 217 minutes, 117 minutes diagnosing training cases, and 100 minutes reading the learning modules. There was no difference in time spent diagnosing cases ( $t= -0.03$ ,  $df = 51.9$ ,  $P = 0.98$ ) or reading ( $t= -0.02$ ,  $df = 73.9$ ,  $P = 0.98$ ) between the intervention and control participants. The high-performance



**Figure 4.** Learning curve models for the training phase.

The figure depicts the various statistical equations applied to the data. Red dashed, and solid black lines represent the intervention and control groups, respectively. (B) An almost straight line with one knot provided a simple yet reliable fit for the data. (C,D) Increasing the complexity of the model by introducing additional knots (C) or a cubic function (D) did not provide any additional value compared to model B.

**Table 1.** Time spent training within the mobile application.

Activity	Time spent reading (min)				Time spent diagnosing training cases (min)			
	Intervention	Control	1 <sup>st</sup> tertile	3 <sup>rd</sup> tertile	Intervention	Control	1 <sup>st</sup> tertile	3 <sup>rd</sup> tertile
Mean	100.7	100.1	94.7	90.4	117.1	116.6	80.9	124.5
SD	121.9	105.7	150.1	56.6	49.2	93	32.2	48.4

min = minutes; SD = standard deviation.

Time spent reading learning modules and diagnosing training cases among the participants within both study groups (intervention, control) and performance groups (1<sup>st</sup> and 3<sup>rd</sup> tertile). The 1<sup>st</sup> and 3<sup>rd</sup> tertile groups consist of the 33% participants with the lowest and highest performance on the retention test.

group spent the same amount of time reading ( $t = 0.13$ ,  $df = 30.5$ ,  $P = 0.90$ ) and significantly more time diagnosing the training cases ( $t = -3.8$ ,  $df = 43.8$ ,  $P = <0.001$ ) compared to the low-performance group (Table 1). Participants spent 40% of their training time on the first 100 cases (mean: 93.8 min) and the remaining time on the last 500 cases (mean: 146.8 min).

## Conclusions

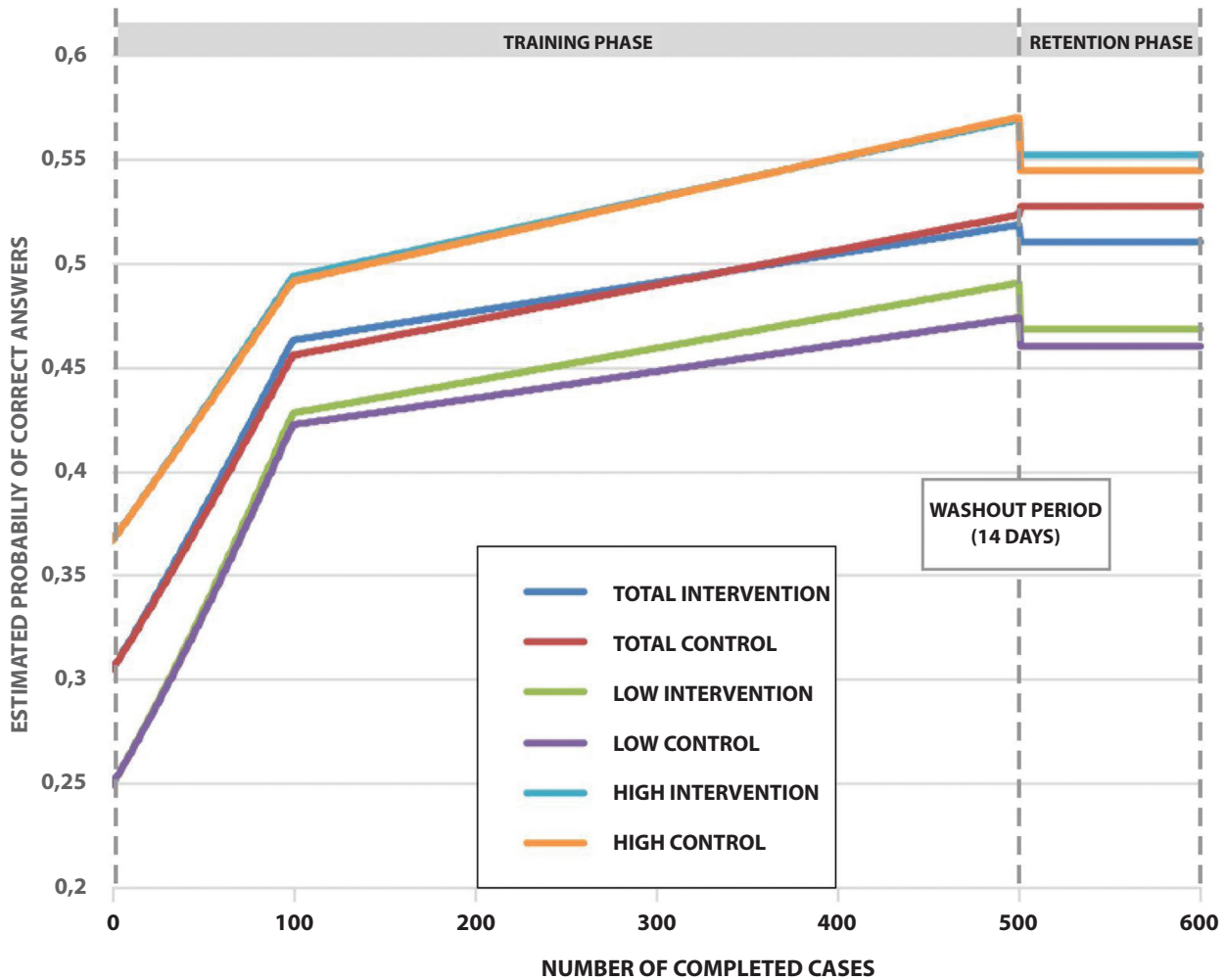
This study explored a novel approach towards digital training in skin cancer diagnostics. The vast majority of participants

(78%), irrespective of trial groups, passed a reliable test in skin cancer diagnostics, following a mean training time of 217 minutes. Access to explanations of the histopathological correlation for dermoscopic criteria did not affect participants learning curves or skill retention.

The rapid diagnostic improvement observed in this study resonates with former studies on case-based pattern recognition training for skin cancer diagnostics [9,10]. This proposed model for teaching complex visual diagnostics could potentially democratize skin cancer diagnostics. Primary care providers, nurses, and medical students can be educated in mass, improving access to high-quality skin cancer triage



## LEARNING CURVES



**Figure 5.** Learning curves during the training and retention phases.

The diagram depicts the learning curves for the entire group (intervention: dark blue, control: red), the high-performance group (intervention: light blue, control: orange), and the low-performance group (intervention: green, control: purple).

and reducing some of the current inequality in melanoma mortality [17,18]. Improved competencies could also pave the way for clinical implementation diagnostic artificial intelligence, providing a human safeguard against the algorithms erroneous predictions and inherent biases [19].

According to the “deliberate practice framework” for teaching diagnostics, novice learners need assistance from a domain expert, as they lack the competencies needed to identify and address their knowledge gaps [20]. A synthetic algorithm-driven domain expert could, in theory, be developed and integrated as a digital mentor within learning interventions such as the one used in this study. A digital mentor could be taught how to identify a student's learning pattern, weaknesses, and strengths based on prior student training data. The identified patterns could then be used to select and present the instructional material (cases, modules) most likely to increase the student competencies at any given time. Such individualized approaches could potentially reduce the observed difference between low- and high-performers and

postpone the deceleration of learning curves, further discussed below.

During post hoc analyses, we found that high-performers were more accurate than the low-performers throughout the study. High-performers were more accurate than low-performers already at the beginning of the trial, despite all participants being supposedly equally inexperienced. These findings suggest that some participants were dishonest about their expertise during inclusion or possessed a superior innate diagnostic accuracy. Regardless of the difference in diagnostic accuracy, both groups maintained parallel learning curves throughout the trial. In theory, the accuracy of low-performers should have increased faster than it did for the high-performers. It is significantly more challenging to increase one's diagnostic accuracy when it is high compared to low [21]. High-performers likely had a more efficient and intentional learning strategy throughout the trial. This hypothesis is supported by the fact that high-performers spent 35% more time diagnosing training

cases than low-performers. Learning curves decelerated following the first 100 training cases, possibly due to a faltering engagement, poor clinical contextualization, or a plateau in the trainees ability to recognize and mitigate their diagnostic errors. On average, each participant spent almost the same amount of time (40% of total time) diagnosing and reviewing the first 100 training cases as they did on the remaining 500 cases. This indicates that they shifted from a slow but actively engaged learning strategy towards a faster trial-and-error strategy that yielded a significantly worse outcome [22,23]. Educational engagement is strongly associated with internal and external motivation [24]. The academic curiosity, which was the sole motivation of the trial participants, may have faltered following 100 training cases, resulting in the learning curve deceleration. Adopting new clinical skills and knowledge becomes easier if the trainee has former clinical experience within the given domain, possibly because it is easier to conceptualize the clinical relevance of the skills being taught [22,25]. Participants in this trial had no former clinical experience, potentially impeding their ability to contextualize and acquire complex skills in visual diagnostics. Finally, the deceleration may have been caused by a plateau in the participants ability to analyze and address their knowledge gaps, ie failure of metacognition [26]. Additional studies, such as think-aloud verbal protocol studies, are needed to further our understanding of the low-versus high-performers learning strategies [27,28]. During think-aloud verbal protocol studies, participants are asked to perform a task and “think aloud” while being recorded. The thought processes are later deconstructed by a trained observer and converted into standardized code blocks prior to statistical analyses.

Our study has several limitations. First, we did not collect data on which subsections of the learning modules participants had read during the trial, limiting our ability to perform sub-analyses on the effect of the histopathological explanations. Secondly, the retention test is a proxy rather than an accurate measure of clinical skills. Finally, it is unclear whether our results can be reproduced among clinicians. Thirdly, domain experience generally increases a student ability to contextualize knowledge, and we theorize that our results would have been more pronounced among clinicians compared to medical students. Finally, several factors such as the participants general interest, motivation, and social or cultural status may have introduced biases in our results.

This study describes an efficient and scalable approach towards teaching pattern recognition in skin cancer diagnostics. We investigated the learning curves of medical students and found a deceleration following approximately 100 training cases and a continuous and stable superiority among the upper compared to lower tertile. Access to histopathological

explanations for dermoscopic criteria did not affect the students knowledge acquisition and retention.

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