Long term effects of digital education among healthcare professionals in paediatric dermatology: Opportunities for improving care

Aviël Ragamin¹,² | Renske Schappin¹,² | Willemijn C. A. M. Witkam² | Magda Spiering¹,² | Elodie Mendels¹,² | Marie L. A. Schuttelaar³ | Suzanne G. M. A. Pasmans¹,²

¹Department Dermatology, Center of Pediatric Dermatology, Erasmus MC University Medical Center-Sophia Children’s Hospital, Rotterdam, The Netherlands
²Department of Dermatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands
³Department of Dermatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Correspondence
Suzanne G. M. A. Pasmans, Department Dermatology, Center of Pediatric Dermatology, Erasmus MC University Medical Center-Sophia Children’s Hospital, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.
Email: s.pasmans@erasmusmc.nl

Abstract
Background: Topical corticosteroids (TCS) are the cornerstone of treatment for patients with atopic dermatitis (AD). Unfortunately, anxiety and misplaced beliefs on TCS, known as corticophobia, is common among health care professionals (HCPs) and could influence their practices, resulting in suboptimal patient care.

Objectives: To investigate the effects of digital education (DE) on the knowledge of TCS, practices and corticophobia among HCPs in paediatric dermatology.

Methods: HCPs registered for an interactive online masterclass on paediatric dermatology including the treatment of AD and TCS were invited to participate in a survey on knowledge of TCS, self-reported practices and corticophobia. Corticophobia was measured using the TOPICOP-P questionnaire (range: 0%–100%, with higher scores indicating more corticophobia). Participants received the survey before, directly after, and 6 months after DE.

Results: Of the 86 participants, 66 (77%) completed the survey before the masterclass, 76 (88%) directly after, and 34 (40%) 6 months after. Key components of knowledge on TCS and self-reported practices improved greatly after DE, such as correct prescription amount of TCS (45%, 91%, 88%) and application instructions (56%, 99%, 94%). Overall corticophobia decreased after DE with median scores dropping from 33% before DE to 25% after DE (p < 0.01) and remained 25% 6 months later.

Conclusion: Interactive DE for HCPs is an efficient tool to attain prolonged improvements of knowledge on TCS, practices, and corticophobia. All these factors are important for optimal care for patients. This study shows great opportunities for improving care by investing in HCPs.

1 | INTRODUCTION

Atopic dermatitis (AD), also known as atopic eczema, is a common chronic inflammatory disease of the skin.⁴ It is characterized by chronic inflammatory skin resulting in intense itch and red skin lesions. With a prevalence up to 20%, AD is common in children.⁵

Topical corticosteroids (TCSS) are the cornerstone of treatment for children with AD.⁶ Although safety and efficacy of TCS are well-studied, HCPs can experience
fear and anxiety for potential side effects caused by TCS, also known as corticophobia. Anxiety and misplaced beliefs among HCPs could influence prescription practices and patient education. Reluctance to treat AD with TCS could lead to greater disease burden, whereas unintentional risk messages about TCS during patient education could reduce treatment adherence. To improve adherence and disease control in AD, uniformity in prescription practices and education about TCS must be achieved among HCPs that interact with patients with AD.

In the Netherlands, most children with AD are treated with TCS by general practitioners and pediatricians. Additionally, youth health care physicians have an important role in primary detection of AD and education of caregivers to use emollients and to adhere to the TCS, as they perform regular developmental check-ups, see Appendix S1. Lastly, (district) nurses and nurse practitioners play an essential role in paediatric dermatology as they educate patients and in the case of nurse practitioners, prescribe treatment. Unfortunately, these groups receive limited dermatological education during training.

The short-term effects of additional education on TCS for pharmacists have been demonstrated before. However, the effects of digital educational interventions aimed at improving knowledge, practices and corticophobia among HCPs that prescribe, treat and educate patients with AD is still lacking. For other diseases, digital education seems to be a (cost)-effective tool to improve practices on the short term. However, improving practices in AD may be a greater challenge as non-dermatologists have more anxiety for TCS. Digital education, should therefore not only improve knowledge, but the anxiety as well. Furthermore, the long-term effects of digital education are still unclear.

In this study, we therefore aim to investigate the effects of interactive digital education for professionals in paediatric dermatology by assessing key components of knowledge on TCS, practices, and corticophobia with regards to treatment of children with AD.

2 MATERIALS AND METHODS

2.1 Setting

Health care professionals registered for an interactive online masterclass on paediatric dermatology (Dutch: Kinderdermatologie: Masterclass voor zorgprofessionals in de Jeugdgezondheidszorg – SCEM – 2020) were asked to participate anonymously in a survey on atopic dermatitis in children in October 2020 in the Netherlands. During this masterclass, interactive digital education was provided by a team of paediatric dermatologists, a paediatric psychologist, and a nurse practitioner based on the National AD guidelines. One plenary session of 45 min specifically addressed treatment of AD. During this session participants received information on the aetiology of AD, emollients and TCS (including key aspects such as the fingertip unit (FTU), a rule for the amount of TCS that needs to be applied, tapering schedules, potency classes, and side effects of TCS). Participants were asked to complete a survey before, immediately after, and 6 months after the masterclass. Invitations for the survey were sent by email, the survey was designed in Google Forms.

2.2 Survey

The anonymous survey contained several topics, including socio-demographics, knowledge, self-reported practices and corticophobia. After 6 months, the survey contained additional questions to evaluate the effects of digital education, asking participants whether their beliefs and practices changed. Questions were asked in a specific order to reduce order effects.

Knowledge was assessed with questions covering important aspects of topical treatment such as the FTU, different potency classes of TCS, and tapering schedules. Practices were assessed with questions covering important application instructions and amount of TCS needed for treatment. Beliefs on TCS and corticophobia were investigated with the Topical Corticosteroid Phobia questionnaire for professionals (TOPICOP-P). This questionnaire was originally
developed for patients with AD, but has previously been modified for healthcare professionals. The questionnaire consists of 12 items with a 4-point scale that address two important dimensions “worries” (6 items) and “beliefs” (6 items) on TCS. Although, other studies report an additional subscale (fear) of the TOPICOP questionnaire, we followed the original and statistically substantiated calculation that divides the TOPICOP questionnaire into two subscales. A score ranging from 0% to 100% can be calculated for each dimension and for the total scale, with higher scores reflecting more severe corticophobia. An overview of the complete survey is provided in the Appendix S2.

2.3 Statistical analysis

Responses were analyzed using SPSS software (version 26; IBM Corp). Differences between pre-education, post-education and 6 months thereafter were analyzed with independent t-tests for normally distributed interval variables, Mann-Whitney U tests for not normally distributed variables, chi-square test for categorical variables with >2 variables and Fisher's exact test for dichotomous variables. Additionally, Spearman's coefficients (for Mann-Whitney U tests) and Cramer's V (for chi-square and Fisher's exact) were calculated to determine effect sizes. An effect size of 0.10 was considered a small effect, 0.30 a medium effect, and 0.50 a large effect, for Cramer's V effect size interpretation was adjusted when degrees of freedom >1. For subgroup analyses, participants were divided in three subgroups: Pediatricians (consisting of pediatricians and residents in paediatrics), youth health care physicians (consisting of physicians and residents in youth health care), and nurses (consisting of nurses and nurse practitioners). A two-sided p < 0.05 was considered statistically significant.

3 RESULTS

3.1 Demographic characteristics

A total of 86 HCPs participated in the online masterclass. The questionnaire was completed 176 times: 66 times before, 76 times directly after, and 34 times 6 months after the online masterclass (Table 1). This resulted in a response rate of 77% before, 88% directly after, and 40% 6 months after the masterclass. The majority of the responders were females and the median age was approximately 45 years. Youth health care physicians formed the largest group of responders. Almost half of the responders prescribed TCS or gave instructions on TCS use on a daily or weekly basis. No significant differences in age, gender, profession, and prescription frequency were found between responders before and after the online masterclass. Medical guidelines were the most common source of information on TCS. The proportion of responders that reported masterclasses and conferences as an important source of information increased after the masterclass from 57% to 81% directly after the masterclass and increased further to 100% (p < 0.01) 6 months after the online masterclass.

3.2 Effects of digital education on knowledge and self-reported practices

Familiarity with all key aspects of TCS, such as the FTU, TCS potency classes, and tapering schemes all increased significantly after digital education (Table 2). These effects remained after 6 months. In addition, improvement of patient education concerning the application instructions and amount TCS improved had a large effect size directly after digital education. Professionals kept giving correct instructions after 6 months. A ceiling effect was detected for treatment duration, with already almost 100% of professionals providing correct information before digital education.

3.3 Effects on corticophobia

Overall corticophobia significantly decreased after digital education and this effect remained stable over the course of 6 months, Table 3. Further analysis shows a significant improvement in overall beliefs of physicians in public health and in nurses. No significant effects were found on the worries subscale among all professionals. However, the medium effect size suggests that these findings may not be significant due to a relative small sample size.

3.4 Effects of education after 6 months

After 6 months, the majority of responders (68%) reported that their practice patterns or patient education changed or felt empowered after digital education, see Appendix (Table S4). An increase in patient education on the use of TCS was reported by 39% of HCPs. Only a small portion (10%) of participating HCPs reported to refer less patients. Although, the response rate for the other statements was significantly lower (only 28%), the answers provide some relevant insights in the perceived effects of digital education. HCPs reported to make more use of tapering schedules (44%), prescribed more potent (22%) and more TCS (22%). Finally, almost all responders (89%) felt more competent with TCS treatment of AD.
### Overview of participant characteristics

| Item                              | Pre-education (n = 66) | Post-education (n = 76) | Follow-up after 6 months (n = 34) | Sig. (p value) |
|-----------------------------------|------------------------|-------------------------|-----------------------------------|----------------|
| Age, year (95% CI)                | 45 (43–48)             | 45 (43–47)              | 45 (42–48)                        | 0.98           |
| Female, no (%)                    | 57 (89)                | 70 (92)                 | 32 (97)                           | 0.54           |
| Profession, no (%)                |                        |                         |                                   | 0.92           |
| Pediatrics                        | 19 (30)                | 25 (33)                 | 6 (18)                            | 0.92           |
| Youth health care physicians      | 31 (48)                | 35 (46)                 | 19 (56)                           | 0.92           |
| Nurses\(^d\)                      | 14 (22)                | 16 (21)                 | 8 (24)                            | 0.92           |
| TCS prescription or education frequency, no (%) | | | | 0.90 |
| (Almost) never                    | 18 (29)                | 21 (28)                 | 11 (35)                           | 0.90           |
| Monthly                           | 16 (25)                | 23 (30)                 | 7 (23)                            | 0.90           |
| Weekly                            | 23 (37)                | 24 (32)                 | 8 (26)                            | 0.90           |
| Daily                             | 6 (10)                 | 8 (11)                  | 5 (16)                            | 0.90           |
| Source of information on TCS, no (%) | | | | 0.90 |
| Guidelines                        | 42 (70)                | 60 (81)                 | 26 (79)                           | 0.90           |
| Evidence based journals           | 14 (23)                | 22 (29)                 | 7 (21)                            | 0.90           |
| Own experience                    | 31 (52)                | 37 (50)                 | 10 (30)                           | 0.90           |
| Masterclasses, congresses, etc.   | 34 (57)                | 60 (81)                 | 33 (100)                          | 0.90           |
| Information pamphlets             | 9 (15)                 | 14 (9)                  | 2 (6)                             | 0.90           |
| Commercial material               | 0 (0)                  | 1 (1)                   | 1 (3)                             | 0.90           |

Note: Percentages and numbers may not add up because of missing values.

Abbreviation: TCS, topical corticosteroids. Bold values indicate statistically significant outcomes (p ≤ 0.05)

\(^a\)Responses before digital education compared to responses directly after digital education.

\(^b\)Responses before digital education compared to responses 6 months after education.

\(^c\)Responses directly after digital education compared to responses 6 months after education.

\(^d\)Nurses consisted out of nurses and nurse practitioners (2 pre and post-education, 1 after 6 months of follow-up). An effect size of 0.10 is considered small, 0.30 medium, and 0.50 large.\(^26\)
| Item                                      | Pre-education N (%) | Post-education N (%) | Six months after education N (%) | Pre versus Post<sup>a</sup> | Pre versus Follow-up<sup>b</sup> | Post versus Follow-up<sup>c</sup> |
|------------------------------------------|---------------------|----------------------|----------------------------------|-----------------------------|-------------------------------|-------------------------------|
|                                          |                     |                      |                                  | Effect size ($\phi_c$) | $p$                           | Effect size ($\phi_c$) | $p$ | Effect size ($\phi_c$) | $p$ |                      |
| Familiarity with FTU                     | 43 (69)             | 76 (100)             | 33 (100)                         | 0.44                        | <0.01                         | 0.37                        | <0.01 | -                        | -              |
| Familiarity with classes of potency      | 48 (76)             | 75 (99)              | 31 (94)                          | 0.35                        | <0.01                         | 0.22                        | 0.05        | 0.13                      | 0.22          |
| Familiarity with tapering schemes        | 56 (88)             | 75 (99)              | 32 (97)                          | 0.23                        | 0.01                          | 0.16                        | 0.16        | 0.06                      | 0.50          |
| Duration of a tube TCS                   |                     |                      |                                  | 0.50                        | <0.01                         | 0.42                        | <0.01 | 0.04                      | 0.73          |
| 1–2 weeks<sup>d</sup>                    | 27 (45)             | 69 (91)              | 29 (88)                          |                             |                               |                             |             |                           |               |
| 1 month or longer                       | 33 (55)             | 7 (9)                | 4 (12)                           |                             |                               |                             |             |                           |               |
| Treatment duration of TCS                |                     |                      |                                  | 0.21                        | 0.03                          | 0.16                        | 0.29        | -                        | -              |
| Until patches are gone<sup>d</sup>       | 50 (93)             | 73 (100)             | 33 (100)                         |                             |                               |                             |             |                           |               |
| Maximum duration 2–4 weeks               | 2 (7)               | 0 (0)                | 0 (0)                            |                             |                               |                             |             |                           |               |
| Application instructions                 |                     |                      |                                  | 0.53                        | <0.01                         | 0.40                        | <0.01 | 0.13                      | 0.22          |
| No instructions                          | 15 (24)             | 1 (1)                | 2 (7)                            |                             |                               |                             |             |                           |               |
| Thin                                     | 13 (21)             | 0 (0)                | 0 (0)                            |                             |                               |                             |             |                           |               |
| According FTU                            | 35 (56)             | 75 (99)              | 31 (94)                          |                             |                               |                             |             |                           |               |
| Thick                                    | 0 (0)               | 0 (0)                | 0 (0)                            |                             |                               |                             |             |                           |               |

Note: Percentages and numbers may not add up because of missing values.

Abbreviation: TCS, topical corticosteroids. Bold values indicate statistically significant outcomes ($p \leq 0.05$)

<sup>a</sup>Responses before digital education compared to responses directly after digital education.

<sup>b</sup>Responses before digital education compared to responses 6 months after education.

<sup>c</sup>Responses directly after digital education compared to responses 6 months after education. An effect size of 0.10 is considered small, 0.30 medium, and 0.50 large.

<sup>d</sup>Correct response.
### TABLE 3 Effects of digital education on corticophobia

| Corticophobia | Pre-education | Post-education | Six months after education | Pre versus Post<sup>a</sup> | Pre versus Follow-up<sup>b</sup> | Post versus Follow-up<sup>c</sup> |
|---------------|---------------|---------------|---------------------------|----------------------------|-------------------------------|-------------------------------|
|               | N  | Median % (IQR) | N  | Median % (IQR) | N  | Median % (IQR) | Effect size (r) | p | Effect size (r) | p | Effect size (r) | p |
| Total corticophobia | | | | | | | | | | | | |
| Overall       | 57 | 33 (28–36) | 70 | 25 (19–33) | 32 | 25 (17–33) | 0.34 | <0.01 | 0.31 | <0.01 | 0.01 | 0.91 |
| Pediatrics    | 18 | 33 (25–38) | 24 | 24 (17–31) | 6  | 17 (14–28) | 0.38 | 0.09 | 0.55 | 0.01 | 0.30 | 0.67 |
| YH Physicians | 26 | 31 (26–36) | 32 | 25 (17–33) | 18 | 25 (17–33) | 0.22 | 0.02 | 0.15 | 0.33 | 0.06 | 0.12 |
| Nurses        | 13 | 39 (31–46) | 14 | 24 (19–30) | 8  | 28 (19–35) | 0.50 | 0.03 | 0.36 | 0.10 | 0.19 | 0.40 |
| ‘Beliefs’     | | | | | | | | | | | | |
| Overall       | 63 | 33 (22–39) | 76 | 28 (11–33) | 32 | 28 (11–33) | 0.24 | <0.01 | 0.27 | <0.01 | 0.03 | 0.78 |
| Pediatrics    | 18 | 33 (22–39) | 24 | 28 (11–33) | 6  | 11 (4–33)  | 0.31 | 0.35 | 0.49 | 0.14 | 0.20 | 0.86 |
| YH Physicians | 26 | 28 (17–39) | 32 | 28 (11–39) | 18 | 31 (11–33) | 0.12 | 0.04 | 0.06 | 0.65 | 0.02 | 0.29 |
| Nurses<sup>d</sup> | 13 | 42 (33–50) | 14 | 28 (11–39) | 8  | 33 (15–33) | 0.45 | 0.05 | 0.56 | 0.01 | 0.01 | 0.97 |
| ‘Worries’     | | | | | | | | | | | | |
| Overall       | 58 | 33 (22–44) | 70 | 28 (17–33) | 33 | 28 (22–33) | 0.26 | <0.01 | 0.21 | 0.05 | 0.05 | 0.58 |
| Pediatrics    | 18 | 31 (22–46) | 24 | 28 (18–33) | 6  | 22 (17–29) | 0.28 | 0.09 | 0.37 | 0.08 | 0.17 | 0.61 |
| YH Physicians | 27 | 33 (22–39) | 32 | 28 (22–33) | 18 | 28 (22–35) | 0.22 | 0.07 | 0.16 | 0.27 | 0.07 | 0.40 |
| Nurses<sup>d</sup> | 13 | 33 (22–50) | 14 | 22 (15–33) | 8  | 25 (22–33) | 0.35 | 0.09 | 0.13 | 0.60 | 0.23 | 0.30 |

Note: Percentages may not add up because of missing values.
Abbreviation: YH, Youth health care. Bold values indicate statistically significant outcomes (p ≤0.05).
<sup>a</sup>Responses before digital education compared to responses directly after digital education.
<sup>b</sup>Responses before digital education compared to responses 6 months after education.
<sup>c</sup>Responses directly after digital education compared to responses 6 months after education. The Mann–Whitney U test was used for all the analyses.
<sup>d</sup>Nurses consisted out of nurses and nurse practitioners (2 pre and post-education, 1 after 6 months of follow-up). TO·PICOP-P scores and subscores can range from 0 to 100. Higher scores imply more corticophobia. An effect size of 0.10 is considered small, 0.30 medium, and 0.50 large.
4 | DISCUSSION

In this study, we investigated the effects of interactive digital education on knowledge of TCS, self-reported practices, and corticophobia among HCPs involved in care for children with AD. After education, HCPs showed prolonged improvements in knowledge on TCS and practices, and less corticophobia. Participating HCPs underlined the added value of the interactive digital education. Our data suggest that interactive digital education for HCPs is an efficient tool to attain prolonged improvements among HCPs.

4.1 | Effects of digital education

Digital education is an effective tool to improve knowledge on TCS, practices, and corticophobia among HCPs involved in care for children with AD and in general.

First of all, we found significant and large improvements in knowledge on TCS and self-reported practices. These findings are in line with previous research investigating prescription behaviour of antibiotics for respiratory infections in primary care.\(^\text{19,27}\) Additionally, digital education improved beliefs of HCPs. Prior education, we found similar beliefs and anxiety for TCS, expressed as corticophobia scores, as compared to previous research among nurses and pediatricians.\(^\text{8,9}\) After education, we found approximately 20% decrease in corticophobia, leading beliefs to be comparable to dermatologists, which can be seen as the gold standard.\(^\text{9}\) The size of this improvement is similar to a personalized face-to-face intervention targeted at pharmacists, adding support to the case for digital education as an efficient tool.\(^\text{28}\)

Furthermore, almost all responders felt more competent with treatment of AD after digital interactive education. Finally, we report lasting effects of digital education on knowledge of TCS, practices, and corticophobia of HCPs. Although, other research on the long-term effects of digital education is lacking, our results suggest prolonged effects of digital education. More research will be needed to help fill the gap concerning the long-term effects of digital education, preferably based on patient outcomes in clinical trials. For now, digital interactive education seems to be an efficient tool to improve knowledge, practices and corticophobia among HCPs involved in care for atopic dermatitis and in general.

4.2 | Opportunity to improve care for atopic dermatitis

Guideline adherence among HCPs in paediatric dermatology should be improved to improve care for children with AD. In our study, we investigated adherence to key guideline recommendations for AD. Prior to digital education, only half of HCPs used TCS as recommended by clinical guidelines. Additionally, a large proportion of HCPs were unfamiliar with key aspects of treatment such as the existence of different TC potency classes. Other studies investigating guideline adherence among HCPs in paediatric dermatology are lacking. However, studies investigating anxiety with regards to TCS show great differences between dermatologist and non-dermatologist, suggesting similar findings.\(^\text{6}\) Keeping in mind that most HCPs treat AD or provide instructions on a weekly basis, improving care at this level may be a necessity to improve care. Several barriers may prevent HCPs from adhering to guidelines.\(^\text{29}\) In particular anxiety and negative beliefs on TCS, corticophobia, may contribute to less guideline adherence.\(^\text{8}\) However, more research is needed to identify barriers to guideline adherence and treatment differences across HCPs involved in order to improve care for AD.

Fortunately, after digital education almost all HCPs adopted guideline recommendations and familiarity with all key aspects increased. This suggests that adherence to AD guidelines can be improved. Ultimately, improving care at this level is needed for more adequately treatment of AD and improve treatment adherence among children and their caretakers. Investing in HCPs could lower health care consumption and cost as less referrals and follow-up visits may be needed. Improving guideline adherence among HCPs may be one of the most efficient tools to improve care.

4.3 | Limitations

Some limitations of this study need to be addressed. First, this is a questionnaire-based study and hence, real-life practices were not assessed. Differences in self-reported practices and real-life practices may exist. Professional desirability bias may have occurred. Second, selection bias may have occurred as HCPs with a specific interest in paediatric dermatology may have participated in the master class. Subsequently, practices among professionals in general may even deviate further from clinical guidelines and corticophobia scores may be underestimated in this study. Thirdly, due to a relative low response rate 6 months after the master class, we cannot exclude if selection bias may have occurred and if only HCPs already familiar with all guideline recommendations participated. However, the majority of participants reported a change in practices or felt empowered after 6 months, suggesting that participants were previously unfamiliar guideline recommendations. Finally, a relative small sample size was included and this study lacked participation of general practitioners. Due to the interactive nature and specific aim of the digital master class a larger sample was not feasible.
4.4 | Implications

Our study provides novel insights in the effects of interactive digital education for HCPs. In particular, this study shows that long lasting changes in knowledge of TCS, practices and corticophobia can be achieved, expecting to result in better care. HCPs themselves have a strong preference for interactive educational meetings to improve guideline adherence.30,31 Policy makers, medical associations, and specialists may use these findings to develop strategies for better implementation of evidence based clinical guidelines.

In addition, our results emphasize the opportunity of improving guideline adaptation. HCPs and policy makers should realize that the vast majority of patients with (mild) AD are treated by general practitioners, pediatricians, nurses, or physicians in primary health care. In these settings, TCS are most important part of treatment.3 For patients with moderate to severe AD also new therapies (i.e. biologicals or JAK inhibitors) will benefit individual patients. However, at a national level, patients with AD may benefit more from improving knowledge on existing treatments with TCS.32 Non-dermatologists provide a crucial role in patient education and can have a major impact on attitude towards TCS.7,33 In addition, education may lower healthcare costs, as fewer referrals may be needed. The results of this study imply a call to invest in additional training of HCPs in (paediatric) dermatology.

5 | CONCLUSION

This study demonstrates the long-term positive effects of digital education for HCPs. After digital education almost all HCPs reported to follow key recommendations of clinical guidelines. In addition, beliefs on TCS improved and corticophobia reduced to levels similar to dermatologists. These effects remained stable over the course of 6 months. This study emphasizes the necessity and opportunity to improve care for patients with AD by investing in interactive digital education to empower HCPs.

AUTHOR CONTRIBUTIONS
Aviel Ragamin: Conceptualization (equal); Data curation (lead); Formal analysis (equal); Methodology (equal); Writing – original draft (lead); Writing – review & editing (lead). Renske Schappin: Formal analysis (equal); Supervision (equal); Writing – original draft (supporting); Writing – review & editing (supporting). Willemijn C. A. M. Witkam: Formal analysis (supporting); Writing – original draft (supporting); Writing – review & editing (supporting). Magda Spierings: Writing – original draft (supporting); Writing – review & editing (supporting). Elodie Mendels: Writing – original draft (supporting); Writing – review & editing (supporting). Marie L. A. Schuttelaar: Supervision (supporting); Writing – original draft (supporting); Writing – review & editing (supporting). Suzanne G. M. A. Pasmans: Conceptualization (equal); Methodology (equal); Supervision (equal); Writing – review & editing (supporting).

ACKNOWLEDGEMENTS

The authors thank Lieke Szovan from SCEM for providing us with the opportunity to conduct this investigation during the educational conference.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not publicly available but are available from Suzanne G. M. A. Pasmans (s.pasmans@erasmusmc.nl) upon reasonable request.

ETHICS STATEMENT

This study was exempt from the Dutch Medical Research Involving Human Subjects Act according to the institutional review board of Erasmus MC (MEC-2020-0697).

ORCID

Avièl Ragamin https://orcid.org/0000-0003-3120-6653
Marie L. A. Schuttelaar https://orcid.org/0000-0002-0766-4382
Suzanne G. M. A. Pasmans https://orcid.org/0000-0003-1018-4475

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How to cite this article: Ragamin A, Schappin R, Witkam WCAM, Spiering M, Mendels E, Schutteelaar MLA, et al. Long term effects of digital education among healthcare professionals in paediatric dermatology: opportunities for improving care. Skin Health Dis. 2022;2(3):e143. https://doi.org/10.1002/ski2.143