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A skin cancer prevention photoaging intervention for secondary schools in Brazil delivered by medical students: randomized controlled trial – study protocol

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ABSTRACT

Introduction

The incidence of melanoma is increasing faster than any other major cancer both in Brazil and worldwide. Especially the Southeast of Brazil has high incidences of melanoma and early detection is comparably low. A main risk factor for developing melanoma is exposure to UV radiation. To increase attractiveness is a major motivation for unhealthy tanning behavior in adolescents. A medical-student delivered intervention that harnesses the broad availability of mobile phones as well as adolescents' interest in their appearance may be a novel way to improve skin cancer prevention.

Methods and Analysis

We developed a free mobile app ("Sunface") which will be implemented in at least 30 secondary school classes with 21 subjects (at least 30 classes with 21 subjects for control) in February 2018 in the city of Itauna (Southeast Brazil) via a novel method called mirroring. In a 45 minutes classroom seminar, the students' altered three-dimensional selfies on tablets are "mirrored" via a projector in front of their whole class showing the effects of unprotected UV exposure on their own future faces. External block randomization via computer is performed on the class level with a 1:1 allocation. In addition to sociodemographic data, skin type, ancestry, UV protection behavior and its predictors are measured via a paper-pencil questionnaire before, three and six months post-intervention. The primary endpoint is the difference in the 30-day-prevelance of daily sunscreen use between both groups at six months follow-up. Secondary endpoints include the difference of daily sunscreen use at three months follow-up, if a self-skin exam in accordance with the ABCDE rule was

performed within the six months follow-up and other measures of sun protection behavior.

Ethics and dissemination: Ethical approval is obtained from the ethics committee of the University of Ituna. Results are disseminated at conferences and in peer-reviewed journals.

Trial Registration: #NCT03178240

Strengths and limitations of this study

- This is the first randomized controlled trial on school-based skin cancer prevention in Brazil.
- This is the first randomized controlled trial on a photoaging app in the field of skin cancer prevention.
- Sensitizing prospective physicians for the importance of skin cancer prevention is mandatory.
- For the reason that intervention and control classes are located in the same schools, cluster effects can not be excluded entirely.

Introduction

According to the World Health Organization, the incidence of melanoma is increasing faster than any other major cancer both in Brazil and worldwide. Melanoma is the most common cancer in young adults, posing a substantial health and economic burden [1].

About 90% of melanomas are associated with UV exposure, in particular with the frequency of severe sun burns, and are therefore eminently preventable [2]. Multiple studies were able to show that daily sunscreen use with a sun protection factor (SPF) above 30, as recommended by international dermatology guidelines, may prevent sunburns and skin cancer, including melanoma [3-6]. Interventions aiming at encouraging sun protection habits are important particurlaly among adolescents, as increased risk of skin cancer is associated with cumulative UV exposure and with sunburns early in life [7-9]. In line with this association, various recent experimental

studies designed to test these effects in young target groups aimed at promoting sunscreen use as an end point [10-13] and others used different UV protection behaviors (including avoiding sunbeds) or behavior scores [14-23]. Given the substantial amount of time children and adolescents spend in the school environment, addressing skin cancer prevention in this setting is crucial and provides a unique opportunity to propel skin cancer prevention programs [24].

Although Brazil has one of the highest UV indexes on earth, tanning is culturally established and Brazilians are used to unprotected overexposure to sun, especially in childhood and teenage years [25-29]. In a population-based survey with 1.604 participants in the south of Brazil from 2008, 48.7% reported at least one sunburn in the prior year [28]. In an attempt to mitigate the health damage caused by excessive UV-exposure, Brazil was the first country to forbid indoor tanning in 2009, albeit with limited success [27]. Especially the southeast of Brazil (the location of this study) is populated by citizens with a European ethnicity and therefore has high incidences of melanoma (up to 23.5/100,000 inhabitants) with a lack of early diagnosis and an overall survival below the worldwide rates [30-33].

Despite the effectiveness of daily sunscreen and its implementation in international dermatologic guidelines [34], a study conducted in Brazil among 398 medical students from the city of Curitiba showed that only 8.4% use sunscreen daily, 4.3% had already used tanning beds and 85.5% had already had sunburns in the past despite having undergone a clinical rotation in a Dermatology department [26]. The issue of a lack of exemplary behavior among prospective physicians regarding skin cancer prevention is known on a global scale [35-37]. The authors conclude that novel ways of engagement are needed to answer the increasing demand for skin cancer awareness among physicians.

The Sunface mirroring intervention aims at both: providing science-based skin cancer prevention to a large number of adolescents and by this means sensitizing prospective physicians for the importance of exemplary behavior [38, 39].

Current knowledge on school-based skin cancer prevention

A recent randomized trial with Australian high school students demonstrated that appearance-based videos on UV-induced premature aging were superior in encouraging sunscreen use to videos of the same length focussing on health aspects exclusively [10]. These findings are in line with international studies demonstrating the important influence of self-perceived attractiveness on self-esteem in adolescence [40, 41]. Furthermore, enhancing ones attractiveness is a main motivation for tanning in adolescents both in Brazil and worldwide [42-44]. In addition, the success of appearance-based photoaging interventions, in which an image is altered to predict future appearance in the fields of tobacco and adiposity prevention shows promise of these interventions in behavioral change settings [45-49].

In the setting of skin cancer prevention, a quasi-experimental study by Williams et al. demonstrated significant higher scores for predictors of sun protection behavior in young females from the UK (average age=23,7; SD=5,03; 70 participants in total) by means of a photoaging desktop program [50]. Furthermore, the photoaging software has been shown to be effective in changing young adults' sun-tanning intentions in both genders in a study with ten participants in total (7 female and 3 male) [51]. However, prior studies are limited by a small sample size and limitations of expanding the target population.

Introduction of the Sunface App

We harnessed the widespread availability of mobile phones and adolescents' interest in appearance to develop the free mobile phone app "Sunface" which lets the user take a selfie and then offers three categories: "daily sun protection", "no sun protection" and "weekly sunbed" showing the altered face 5-25 years in the future (1-4). All effects are based on the individual skin type the user can choose at the start of the app (Fig. 5). The app also shows the most common UV-induced skin cancers via extra buttons and calculates how the odds ratio is increased with different behaviors. In addition, the app gives advice on sun protection, explains the facial

<Figure 1-4 provided as additional files>

<Figure 5 provided as additional file>

Afterwards, the app offers many sharing options (animated video or photo) with family and friends. By this means, the social network of the user may also be informed about the various photoaging effects of excessive UV-exposure, potential health consequences, and learn about the app.

In order to produce realistic effects (Fig. 6) and to show the user realisitic odds ratios for the options they choose in the app for the three most strongly associated skin pathologies, an extensive review of the current literature on UV-induced skin-damage [52, 53] was conducted for each specific skin type. As no trials with 25 years of follow-up were available, we had to extrapolate the current evidence on UV-induced skin damage for the specific skin types.

<Figure 6 provided as additional file>

This randomized trial was designed to answer the following main questions:

Is the implementation of the app in secondary schools in southeastern Brazil effective in encouraging daily sunscreen use among adolescents? Is it equally effective for both genders? Is it effective for the most sensitive skin types? How does the app-intervention change the attitudes towards sun protection in accordance with the theory of planned behaviour [54]?

Methods and Analysis

Trial Design

The Sunface trial is designed as a randomised, controlled superiority trial with two parallel groups and our primary end point is the difference in daily sunscreen use (past 30 days) from baseline to six months follow-up compared between the two groups (Fig. 7). The planned study period is February 2018 to November 2018. The study groups will consist of randomized classes receiving the intervention and control classes within the same schools (no intervention). Randomization is externally and centrally performed at school level with a 1:1 allocation (control:intervention) via computer [12]. A total of at least 60 secondary school classes in Itauna, Brazil participate in the teacher-conducted baseline survey in February 2018. Immediately after the baseline survey, the intervention classes receive a 45 minutes lasting app-based intervention conducted by local volunteering medical students. Follow-up surveys are conducted 3 and 6 months post-intervention.

<Figure 7 provided as an additional file>

Intervention

The school-based intervention under evaluation consists of a 45-minute module in the classroom setting. It is presented by 2 medical students per classroom to about 21 students at a time. The goal is to initiate and guide the student evaluation process of skin cancer prevention with age-appropriate information that helps them to reframe positive opinions and views regarding sun protection habits in a gain-framed and interactive manner.

To integrate app-based photoaging interventions into the school-based setting, we previously developed and tested the mirroring approach in a pilot study [46]. Mirroring means that the students' altered three-dimensional selfies on smartphones or tablets are "mirrored" via a projector in front of the whole class. The mirroring approach is implemented by volunteering medical students from the University of Itauna who receive a standardized training in advance. To ensure the participation of all students within a certain class and to avoid contamination within schools, we implement the mirroring intervention via 10 Samsung Galaxy Tablets that are already set up and brought to the schools by the volunteers.

In the first 10-minute phase, the displayed face of one student volunteer is used to show the app's altering features in the three categories to the peer group, providing an incentive for the rest of the class to test the app. Students can interact with their own animated face via touch (sneezing, coughing, etc.; see Multimedia Appendix 1). In front of their peers, they could display their image as a non-/sun protection user/weekly tanning bed user 5, 10, 15, 20 and 25 years in the future (see Figures 1a and 2). Multiple device displays can be projected simultaneously, which are used to

consolidate the altering measures with graphics (eg, to explain wrinkle formation). We implement mirroring with Galaxy Tab A (Samsung) via Apple's proprietary AirPlay interface using the Android app "Mirroring360" (Splashtop Inc.).

<Multimedia Appendix 1 uploaded as an additional file>

In the second 15-minute phase, students are encouraged to try the app on one of the tablet computers. The number of provided tablet computers was calculated so the phase would take up to 12 minutes at the most, factoring in a utilization time of about 4 minutes per student. By this calculation, 25 minutes of the mirroring intervention and 10 provided tablets were sufficient to have every student within a class of 40 pupils successfully photoaged at least once.

In the following 15 minutes, the remaining functions of the app are discussed with the students: Facial changes, the ABCDE rule and the guidelines for sun protection are addressed in an interactive setting. At the end of the classroom seminar we ask for the students' final judgments on daily sunscreen use to create positive peer pressure and influence the students' subjective norm in accordance with the theory of planned behavior [54].

In the last 5 minutes, the perception of the intervention by the students is measured directly after the intervention via four items in an anonymous survey on 5-point-Likert scales (1) "The animation of my 3D-selfie motivates me to use daily sunscreen," (2) "I learned new benefits of sun protection", (3) "The intervention motivates me to check my skin with the ABCDE rule in the next six months" and (4) "The intervention was fun."

Participants

Eligibility criteria at baseline

Students from Itauna in southeast Brazil attending grades 6 to 12 in all types of regular secondary school are eligible.

Contaminated classes

All classes will be included in the final intention-to-treat analysis. However, app use will be assessed in both groups at six months follow-up to assess contamination of control classes and will be the basis for a secondary (sensitivity) analysis with the methods described in the Analysis section of this protocol.

Procedure

Data are collected via a paper-pencil questionnaire. In addition to sociodemographic data (age, gender and school type), the questionnaire captures the Fitzpatrick skin type, the ancestry of the school students [55] and the frequency of sunscreen use in the past 30 days as well as other sun protection behaviors. These items are based on the sun exposure and protection index (SEPI) questionnaire [56] and were either used in their original form or adapted to the specific circumstances of the present study. Since no Portuguese equivalents of the instruments were available, we used the Conceptual Method for translation described by the WHO/UNESCAP Project on Health and Disability Statistics[57]. Newly translated and/or modified items were extensively pretested and subjected to statistical analyses (internal consistency/Cronbach's α, exploratory and confirmatory factor analyses, which represented the basis for item selection).

Data Collection

Each data collector received training for data collection and was required to use an adapted standardised protocol for data collection, an optimized version of the one used in the Smokerface randomized trial [58].

Cluster-randomisation

In accordance with the guidelines for good epidemiologic practice (GEP guideline) classes within schools are externally and centrally randomly assigned to the control or intervention group via block-randomization in a ratio of 1:1 (control:intervention) via computer by a statistician at the University of Duisburg-Essen, Germany. Stratification will be performed per grade.

Outcomes

The primary endpoint is the difference in the 30-day-prevelance of daily sunscreen use between both groups at six months follow-up. Secondary endpoints include the difference of daily sunscreen use at three months follow-up, if a self-skin exam in accordance with the ABCDE rule was performed within the six months follow-up and other measures of sun protection behavior. For all end points, the number needed to treat (NNT) will be calculated in addition. A daily sunscreen user is defined as a pupil who claims to have used sunscreen daily in the 30 days preceding the survey.

Statistical considerations

Sample size calculation

We calculated sample sizes of 630 in the intervention group and 630 in the control group, which were obtained by sampling 30 classes with 21 students each in the intervention group and 30 classes with 21 students each in the control group to achieve 80% power to detect a prevalence difference between the groups of 5%. The daily sunscreen prevalence was assumed to be 6% under the null hypothesis and11% under the alternative hypothesis based on a small pilot survey with 150 students in Itauna. The test statistic used is the two-sided score test (Farrington & Manning). The significance level of the test is 0,05. Normal class size in Brazil is 35 pupils and thus, a loss-to-follow-up effect of 40% was taken into account.

Data entry

Data entry is supported by the current software version of Formic Fusion by the Xerox AG (Kloten, Switzerland) and recommended scanners.

Analysis

To examine baseline differences in pupils' characteristics in our experimental design, we will use χ^2 tests for the categorical variables and t-tests for continuous variables. To test for differences in baseline and follow-up smoking prevalence between groups, we will use a cluster-adjusted Mantel-Haenszel χ^2 test[59] at a significance level of 5% (two-sided). For the main analysis, HLM (hierarchical linear models) will be applied. HLM can handle the nested structure of the data and will be used to test for between-group differences in within-group changes in sun protection behaviour over time. HLM will also be used to investigate the influence of further covariates (such as gender, European ancestry and skin type) and time-dependent behaviour in secondary analyses. Statistical analyses will be performed using the newest version of SPSS Statistics (IBM Corporation, New York, USA).

The effect that missing data might have on results will be assessed via sensitivity analysis. Dropouts (essentially participants who withdraw consent for continued follow-up or who are missing in the classroom during the survey) will be included in the analysis by modern imputation methods for missing data and multiple imputation will be used to estimate treatment effect [60].

Discussion

This is the first cluster-randomized school-based trial on photoaging skin cancer prevention and the first trial on medical student-delivered school-based skin cancer prevention worldwide. While classic health educational school-based approaches in skin cancer prevention were evaluated as inferior to appearance-based approaches [10], there is a global lack of novel, innovative strategies that harness the available technology in the internet-age while taking widely accepted theories for behavioral change into account [54]. Although multiple studies were able to show that skin cancer risk is predominantly associated with sun exposure early in life, there is a lack of awareness in risk groups. In southeastern Brazil specifically, there is a high incidence of melanoma and the early detection is below the worldwide rates [31]. At the same time, there are no randomized trials on skin cancer prevention on PubMed that were implemented in Brazil.

Thus, this trial provides the opportunity to evaluate an innovative, highly scalable, appearance-based intervention in a high risk population and provide data to estimate whether photoaging mobile apps have the potential to be broadly implemented in schools via the mirroring intervention but also via other vectors (i.e. posters [58] or smartphone based advertising campaigns in Appstore and Playstore) or could be a valuable addition to existing educational programs. Besides that, as it is medical-

student delivered, this trial also sensitizes future physicians to the importance of skin cancer prevention, highlighting their associated responsibilities within communities [35, 61].

According to the theory of planned behavior (TPB), the subjective norm and the expected self-efficacy of the participants play a substantial role in their resulting behavior: What do their peers think about tanning? Is the result of tanning regarded as attractive and does it therefore increase ones chances to find a boy-/girlfriend? How likely is it that own behavioral change can influence this reaction positively? The mirroring intervention triggers strong reactions of the peer-group of the individual participant towards their photoaged future self (=affecting subjective norm) but also illustrates the power of own behavioral change (and thereby increases ones expectation of self-efficacy, another predictor of the TPB) to influence this reaction by the peers [46].

Limitations

Since this study is conducted only in Brazil, results might not be generalisable to other cultural or national settings. However, the theoretical basis for this intervention, the theory of planned behavior has been proven to apply to most cultural contexts around the globe [54]. As this trial is enrolled in about 10 different public schools total it should be representable for most school types.

As we have to choose classes but not schools as a cluster due to sample size limitations, cluster-effects can not be excluded entirely. However, multiple steps are taken to limit contamination between control and intervention classes (i.e. the name of the App is not mentioned to the pupils by the trained medical students and the teachers of the control classes are strictly prohibited to talk about the intervention

with their students). Cluster-effects are also monitored in the endline questionnaire and provide basis for a sensitivity analysis.

Conclusion

In summary, we present a novel way of integrating photoaging in school-based skin cancer prevention in a population with high risk for developing skin cancer, which affects the students' peer group and considers the predictors of tanning in accordance with the theory of planned behavior. Our study is the first randomized controlled trial on skin cancer prevention in Brazil and the first randomized trial on a medical student-delivered app- and school-based skin cancer prevention strategy in general.

Dissemination

All legal and data protection issues were discussed with the responsible authorities, and participants are required to provide informed consent. All participant information will be stored in locked file cabinets in areas with limited access. Participants' study information will not be released outside of the study without the written permission of the participant. Results will be disseminated at national and international conferences and in peer-reviewed journals.

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Authors' Contributions

TJB initiated the study, invented, designed and organized the intervention, wrote the manuscript, drafted the design of the study and performs the statistical analyses. BBS participated in the conception of the study. JK, PJ, IS, BI, FB and DS contributed to the design of the study and analyses of data, and proofread the manuscript. BBS and OCL contributed to the design and logistics of the study, assisted with the translation of classroom materials, and reviewed the final version of the manuscript. BLF, OMF, HAL, ACCO conduct data entry and coordinate/conduct the intervention in Brazil, supported the translation of the classroom materials, and proofread the manuscript.

Conflicts of Interest

None declared.

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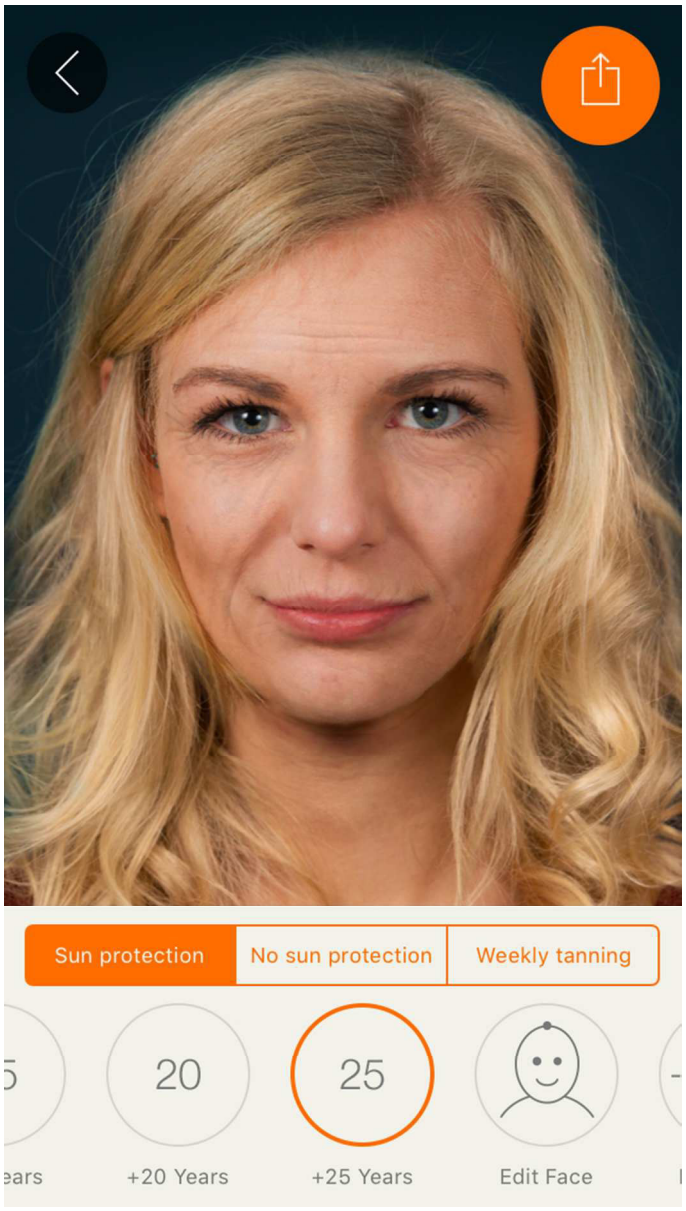

Figure 1: Effect view of the app with bottom bar indicating the effects shown on ones own face.

225x400mm (72 x 72 DPI)

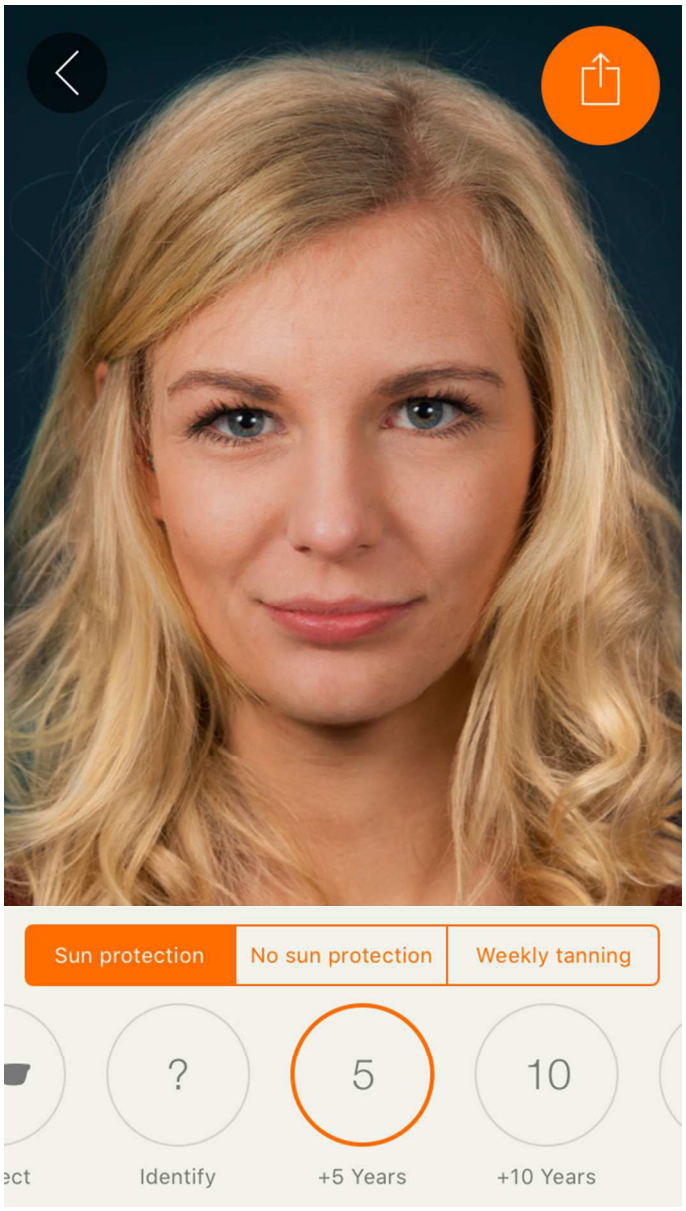

Figure 2: Effect view of the app with bottom bar indicating the effects shown on ones own face.

225x400mm (72 x 72 DPI)

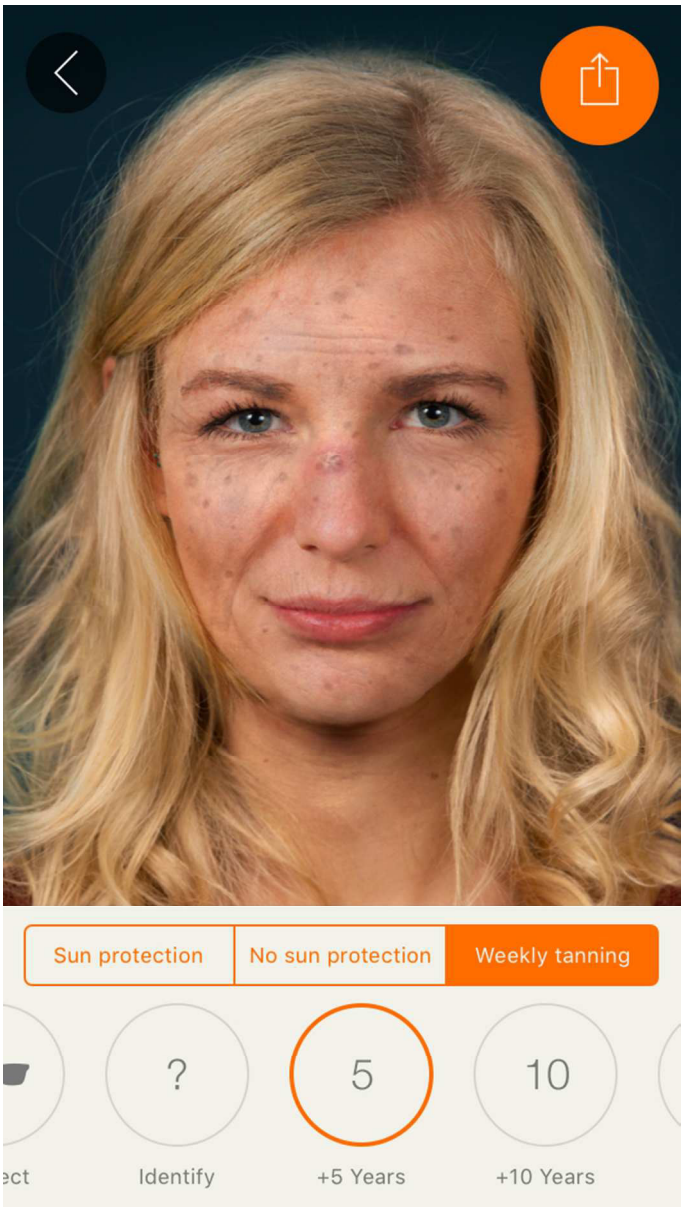

Figure 3: Effect view of the app with bottom bar indicating the effects shown on ones own face.

225x400mm (72 x 72 DPI)

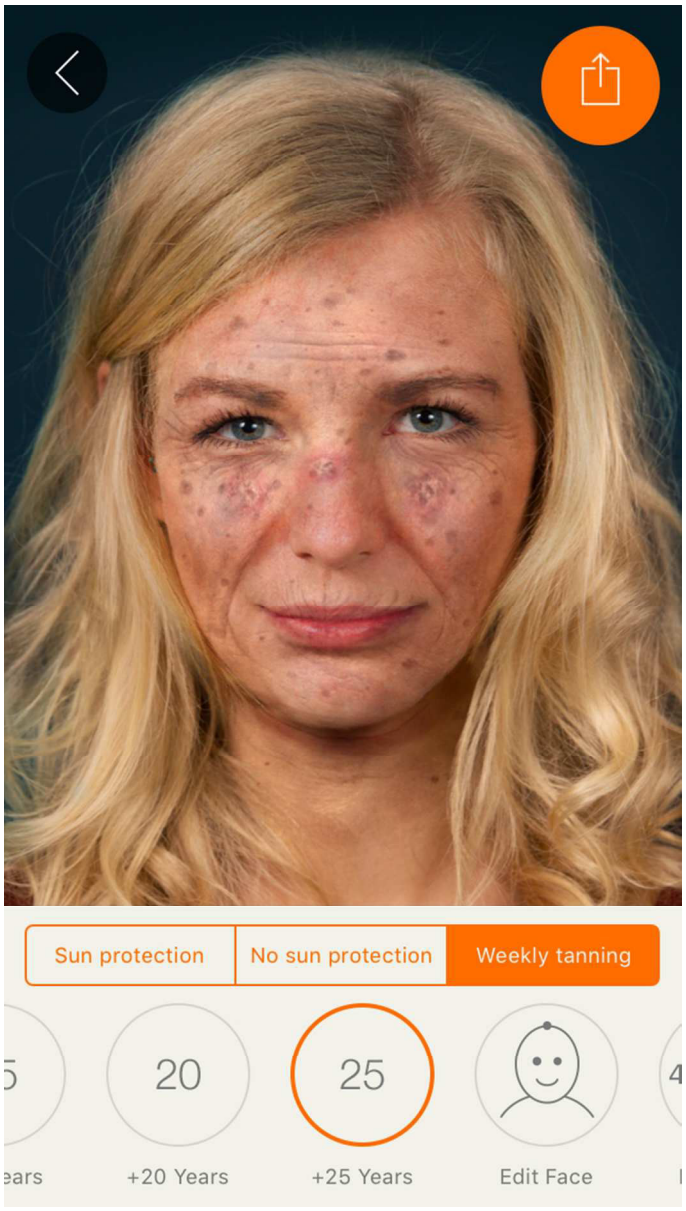

Figure 4: Effect view of the app with bottom bar indicating the effects shown on ones own face.

225x400mm (72 x 72 DPI)

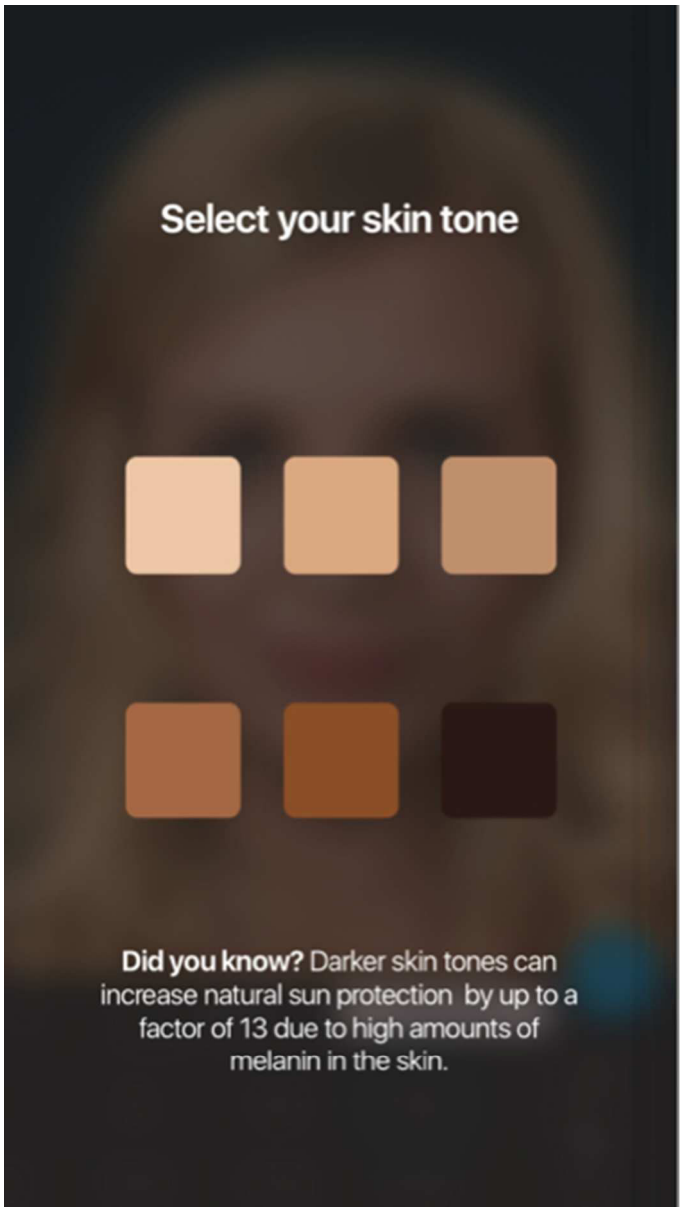

Figure 5: Fitzpatrick skin type picker at the start of the app.

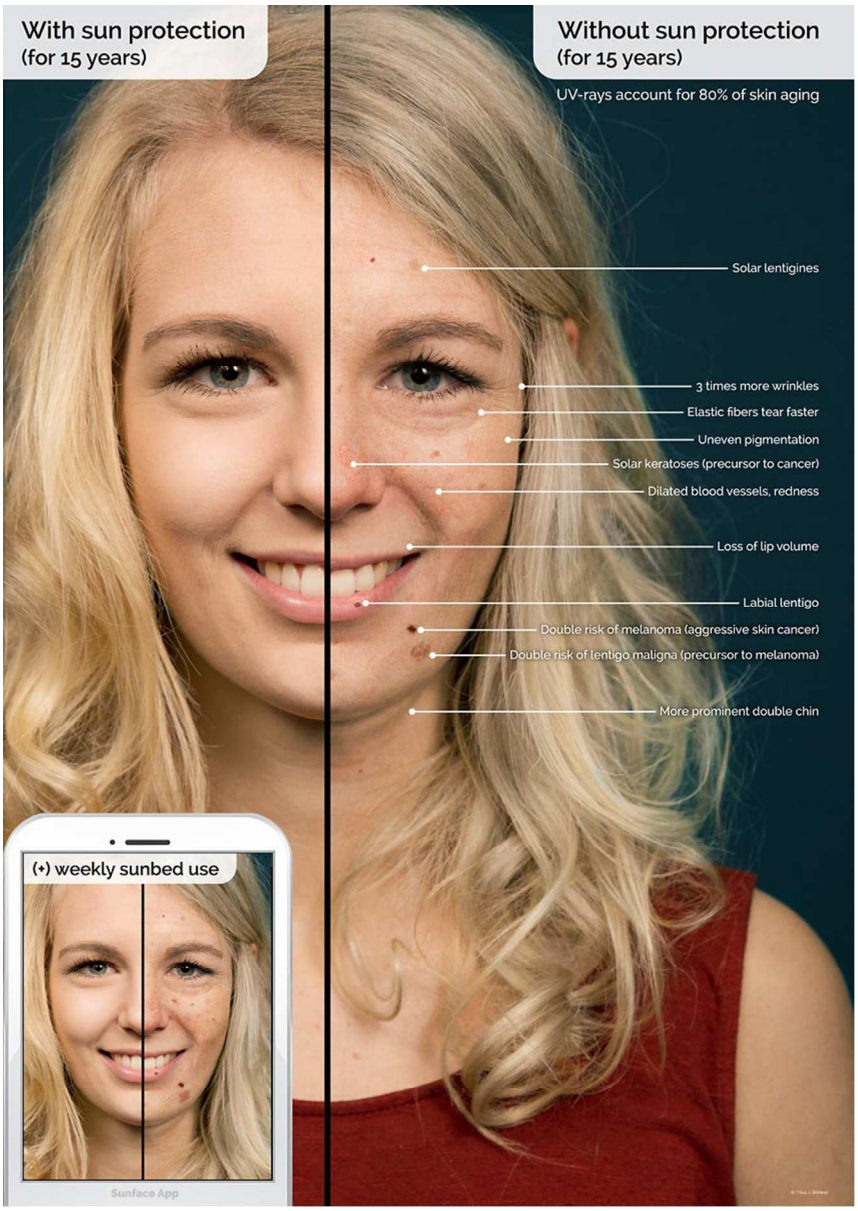

Figure 6: Explanation graphic of the effects seen provided as an infographic within the app.

299x423mm (72 x 72 DPI)

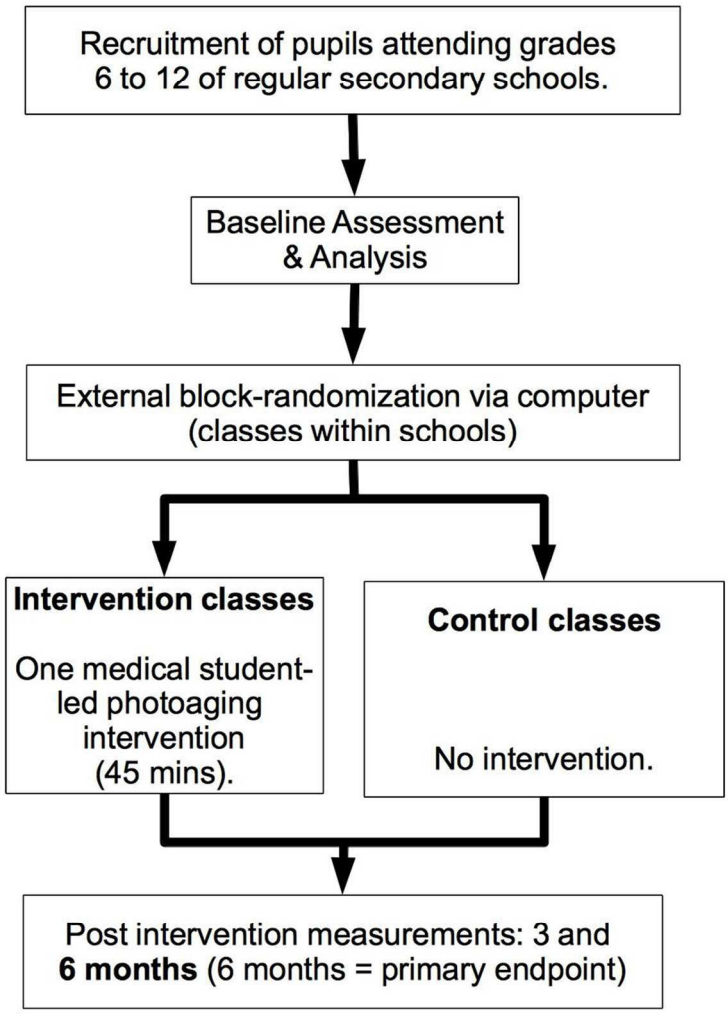

Figure 6
Study design.

Figure 7: Study Design

370x523mm (72 x 72 DPI)

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A skin cancer prevention photoaging intervention for secondary schools in Brazil delivered by medical students: protocol for a randomized controlled trial

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A skin cancer prevention photoaging intervention for secondary schools in Brazil delivered by medical students: protocol for a randomized controlled trial

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ABSTRACT

Introduction

The incidence of melanoma is increasing faster than any other major cancer both in Brazil and worldwide. The southeast of Brazil has especially high incidences of melanoma, and early detection is low. Exposure to UV radiation represents a primary risk factor for developing melanoma. Increasing attractiveness is a major motivation for adolescents for tanning. A medical student-delivered intervention that harnesses the broad availability of mobile phones as well as adolescents' interest in their appearance may represent a novel method to improve skin cancer prevention.

Methods and Analysis

We developed a free mobile app ("Sunface"), which will be implemented in at least 30 secondary school classes, each with 21 students (at least 30 classes with 21 students for control) in February 2018 in Southeast Brazil via a novel method called mirroring. In a 45-minute classroom seminar, the students' altered three-dimensional selfies on tablets are "mirrored" via a projector in front of their entire class, showing the effects of unprotected UV exposure on their future faces. External block randomization via computer is performed on the class level with a 1:1 allocation. Sociodemographic data, as well as skin type, ancestry, UV protection behavior and its predictors are measured via a paper-pencil questionnaire before as well as three and six months post-intervention. The primary endpoint is the group difference in the 30-day prevalence of daily sunscreen use at a six-month follow-up. Secondary endpoints include (1) the difference in daily sunscreen use at a three-month follow-up, (2) if a self-skin exam in accordance with the ABCDE rule was performed within the six-month follow-up and (3) the number of tanning sessions.

Ethics and dissemination: Ethical approval was obtained from the ethics committee of the University of Itauna. Results will be disseminated at conferences and in peer-reviewed journals.

Trial Registration: #NCT03178240

Strengths and limitations of this study

• This is the first study measuring the longitudinal effectiveness of a photoaging mobile app to change sun protection behavior.

• External randomization via computer and a relatively high number of clusters ensure good comparability between groups.

• Cluster effects cannot be excluded because the intervention and control classes are located in the same schools.

Introduction

According to the World Health Organization, the incidence of melanoma is increasing more rapidly than any other major cancer both in Brazil and worldwide. Melanoma is one of the most common cancers in young adults and poses substantial health and economic burdens [1].

Approximately 90% of melanomas are associated with UV exposure, in particular with the frequency of severe sunburns, and are therefore highly preventable [2]. Multiple studies showed that daily sunscreen use with a sun protection factor (SPF) above 30, as recommended by international dermatology guidelines, may prevent sunburns and skin cancer including melanoma [3-6].

Brazil has one of the highest UV indexes on earth; additionally, tanning is culturally established and Brazilians commonly experience unprotected overexposure to the sun, especially in their childhood and teenage years [7-11]. In a 2008 population-based survey with 1,604 participants in the south of Brazil, 48.7% reported at least one sunburn in the prior year [10]. In an attempt to mitigate the health damage caused by excessive UV exposure, Brazil was the first country to prohibit indoor

tanning in 2009, albeit with limited success [9]. The southeast of Brazil (the location of this study) is especially populated by citizens with a European ancestry and therefore has high incidences of melanoma (up to 23.5/100,000 inhabitants) with a lack of early diagnosis and an overall survival below worldwide rates [12-15].

Interventions encouraging sun protection habits are important, particularly among adolescents, as increased risk of skin cancer is associated with cumulative UV exposure and sunburns early in life [16-18]. In line with this association, various recent experimental studies to test these effects in young target groups aimed at promoting sunscreen use as an end point [19-22], and others used various UV protection behaviors (including avoiding sunbeds) or behavior scores [23-32]. Given the substantial amount of time that children and adolescents spend in the school environment, addressing skin cancer prevention in this setting is crucial and provides a unique opportunity to propel skin cancer prevention programs [33].

Despite the effectiveness of daily sunscreen and its implementation in international dermatologic guidelines [34], a study conducted in Brazil among 398 medical students from the city of Curitiba showed that only 8.4% use sunscreen daily, 4.3% had already used tanning beds and 85.5% had past sunburns despite having undergone a clinical rotation in a Dermatology department [8]. The lack of exemplary behavior among prospective physicians regarding skin cancer prevention is known on a global scale [35-37]. The authors of this study have concluded that novel engagement methods are needed to answer the increasing demand for skin cancer awareness among physicians.

The Sunface mirroring intervention aims to provide science-based skin cancer prevention to a large number of adolescents in an attempt to sensitize prospective physicians to the importance of exemplary behavior [38, 39].

Current knowledge on school-based skin cancer prevention

Unhealthy behavior in regards of UV exposure is mostly initiated in early adolescence [40], often with the idea that a tan increases attractiveness [41-43]; the problems related to melanoma and skin atrophy are too far in the future to fathom.

A recent randomized trial with Australian high school students demonstrated that appearance-based videos on UV-induced premature aging were superior in encouraging sunscreen use to videos of the same length focusing exclusively on health aspects [19]. These findings are in line with international studies demonstrating the important influence of self-perceived attractiveness on self-esteem in adolescence [44, 45]. Furthermore, enhancing one's attractiveness is a primary motivation for tanning in adolescents both in Brazil and worldwide [41, 46, 47]. In addition, the success of appearance-based photoaging interventions, in which an image is altered to predict future appearance in the fields of tobacco and adiposity prevention, shows promise for these interventions in behavioral change settings [48-53].

In the setting of skin cancer prevention, a quasi-experimental study by Williams et al. demonstrated significantly higher scores for predictors of sun protection behavior in young women from the UK (70 participants in total) using a photoaging desktop program [54]. Furthermore, the photoaging software 'showed promising reduction in young adults' tanning intentions in a study with ten participants in total (7 female and

3 male) [55]. However, prior studies are limited by their small sample size and limitations related to expanding the target population.

Introduction of the Sunface app

We harnessed the widespread availability of mobile phones and adolescents' interest in appearance to develop the free mobile phone app "Sunface," which enables the user take a selfie and then offers three categories: "daily sun protection", "no sun protection" and "weekly tanning," showing the altered face at 5 to 25 years in the future (Figure 1, Figure 2, Figure 3, Figure 4). All effects are based on the individual skin type that the user can choose at the start of the app (Figure 5). The app also shows the most common UV-induced skin cancers via extra buttons and calculates how the odds ratio is increased with different behaviors. In addition, the app gives advice on sun protection, explains the facial changes and encourages skin examinations using the ABCDE rule (assess border irregularity, color variety, diameter, and evolution [56]).

Afterwards, the app offers many sharing options (animated video or photo) with family and friends. By this means, the social network of the user may also be informed about the various photoaging effects of excessive UV exposure and potential health consequences, as well as potentially learning about the benefits of using the app [57].

To produce realistic effects (Figure 6) and to show the user realistic odds ratios for the options they choose in the app for the three most strongly associated skin

pathologies, an extensive review of the current literature on UV-induced skin damage [58, 59] was conducted for each specific skin type. As no trials with 25 years of follow-up were available, we had to extrapolate the current evidence on UV-induced skin damage for the specific skin types. The evidence consists of more than 50 publications to create realistic effects from a clinician's standpoint (which may differ from what the average person perceives as realistic).

We recently implemented this app in 2 German secondary schools via a method called mirroring. We "mirrored" the students' altered 3-dimensional (3D) selfies on mobile phones or tablets via a projector in front of their entire grade. Using an anonymous questionnaire, we then measured sociodemographic data as well as risk factors for melanoma and the perceptions of the intervention on a 5-point Likert scale among 205 students of both sexes aged 13-19 years (median 15 years).

In our pilot study, we found more than 60% agreement in both items measuring motivation to reduce UV exposure and only 12.5% disagreement: 126 (63.0%) agreed or strongly agreed that their 3D selfie motivated them to avoid using a tanning bed, and 124 (61.7%) agreed or strongly agreed to increase use of sun protection; only 25 (12.5%) disagreed with both items. However, no effects on actual behavior could be measured due to the cross-sectional design of the study [60].

This randomized trial was designed to answer the following questions:

Is the implementation of the app in secondary schools in southeastern Brazil effective in encouraging daily sunscreen use among adolescents? Is it equally effective for both genders? Is it effective for the most sensitive skin types? How does the app

intervention change the attitudes towards sun protection in accordance with the theory of planned behavior [61]?

Methods and Analysis

Study Design

The Sunface trial is designed as a randomized controlled superiority trial with two parallel groups. Our primary end point is the difference between the two groups in daily sunscreen use (past 30 days) from baseline to six months follow-up (Figure 7). The planned study period is February 2018 to November 2018. The study groups will consist of randomized classes receiving the intervention and control classes within the same schools (no intervention). Randomization is externally and centrally performed at the school level with a 1:1 allocation (control:intervention) via computer [12]. A total of at least 60 secondary school classes in Itauna, Brazil will participate in the teacher-supervised baseline survey in February 2018, which is conducted by trained data collectors. One week after the baseline survey, the intervention classes receive a 45-minute app-based intervention conducted by local medical student volunteers. Follow-up surveys will be conducted 3 and 6 months post-intervention.

Figure 7

Intervention

The school-based intervention under evaluation consists of a 45-minute educational module in the classroom setting using a photoaging app. The intervention is presented by 2 medical students per classroom to approximately 21 students at a time. The goal is to initiate and guide the student evaluation process of skin cancer prevention with age-appropriate information that helps the students reframe positive

opinions and views regarding sun protection habits in a gain-framed and interactive manner.

To integrate app-based photoaging interventions into a school-based setting, we previously developed and tested the mirroring approach in a pilot study [49]. Mirroring means that the students' altered three-dimensional selfies on smartphones or tablets are "mirrored" via a projector in front of the entire class. The mirroring approach is implemented by medical student volunteers from the University of Itauna, who receive standardized training in advance. To ensure the participation of all students within a certain class and to avoid contamination within schools, we will implement the mirroring intervention via 10 Samsung Galaxy Tablets that are already set up and brought to the schools by the volunteers.

In the first 10-minute phase, the displayed face of one student volunteer is used to show the app's altered features in the three categories to the peer group, providing an incentive for the rest of the class to test the app. Students can interact with their own animated face via touch (sneezing, coughing, etc.; see Multimedia Appendix 1). In front of their peers, they will be able to display their image as a non-/sun protection user/weekly tanning bed user at 5, 10, 15, 20 and 25 years in the future (see Figure 1 and Figure 2). Multiple device displays can be projected simultaneously, which are used to consolidate the altered measures with graphics (e.g., to explain wrinkle formation). We implement mirroring with Galaxy Tab A (Samsung) via Apple's proprietary AirPlay interface using the Android app "Mirroring360" (Splashtop Inc.).

<Multimedia Appendix 1 uploaded as an additional file>

In the second 15-minute phase, students are encouraged to try the app on one of the tablet computers. The number of provided tablet computers was calculated so that the phase would take up to 12 minutes at the most after factoring in a utilization time of approximately 4 minutes per student. By this calculation, 25 minutes of the mirroring intervention and 10 provided tablets were sufficient to have every student within a class of 40 pupils successfully photoaged at least once.

In the following 15 minutes, the remaining functions of the app are discussed with the students: facial changes, the ABCDE rule and the guidelines for sun protection are addressed in an interactive setting. At the end of the classroom seminar, we ask for the students' final judgments on daily sunscreen use to create positive peer pressure and influence the students' subjective norm in accordance with the theory of planned behavior [61].

In the last 5 minutes, the perception of the intervention by the students is measured directly after the intervention in an anonymous survey on a 5-point Likert scale via four items: (1) “The animation of my 3D selfie motivates me to use daily sunscreen,” (2) “I learned new benefits of sun protection,” (3) "The intervention motivates me to check my skin with the ABCDE rule in the next six months," and (4) “The intervention was fun.”

Participants

Eligibility criteria at baseline

Students from Itauna in southeast Brazil attending grades 6 to 12 in all types of regular secondary school are eligible.

Contaminated classes

All classes will be included in the final intention-to-treat analysis. However, app use will be assessed in both groups at six months follow-up to assess contamination of control classes and will be the basis for a secondary (sensitivity) analysis with the methods described in the Analysis section of this protocol.

Procedure

The schools are recruited via E-mail, telephone and personal appointment (in most cases with the principal). Reasons for non-participation are not recorded. Data are collected via a paper-pencil questionnaire. In addition to sociodemographic data (age, gender and school type), the questionnaire captures the Fitzpatrick skin type, the ancestry of the school students [62] and the frequency of sunscreen use in the past 30 days as well as other sun protection behaviors. These items are based on the sun exposure and protection index questionnaire [63] and were either used in their original form or adapted to the specific circumstances of the present study. No Portuguese equivalents of the instruments were available; thus, we used the Conceptual Method for translation described by the WHO/UNESCAP Project on Health and Disability Statistics [64]. Newly translated and/or modified items were extensively pretested and subjected to statistical analyses (internal consistency/Cronbach's α and exploratory and confirmatory factor analyses, which represented the basis for item selection).

Data Collection

Each data collector received training for data collection and was required to use an adapted standardized protocol for data collection, an optimized version of that used in the Smokerface randomized trial [65].

Cluster randomization

In accordance with the guidelines for good epidemiologic practice, classes within schools are externally and centrally randomly assigned to the control or intervention group via block randomization in a 1:1 ratio (control:intervention) via computer by a statistician at the University of Duisburg-Essen, Germany. Stratification will be performed by grade.

Outcomes

The primary endpoint is the difference in the 30-day-prevalence of daily sunscreen use between both groups at six months follow-up. Secondary endpoints include the difference in daily sunscreen use at three months follow-up if a self-skin exam in accordance with the ABCDE rule [56] was performed within the six-month follow-up and the number of tanning sessions in the past 30 days. For all end points, the number needed to treat will also be calculated. A daily sunscreen user is defined as a pupil who claims to have used sunscreen daily in the 30 days preceding the survey.

Statistical considerations

Sample size calculation

We calculated sample sizes of 630 in the intervention group and 630 in the control group, which were obtained by sampling 30 classes with 21 students each in the intervention group and 30 classes with 21 students each in the control group to achieve 80% power to detect a prevalence difference between the groups of 5%. The daily sunscreen prevalence was assumed to be 6% under the null hypothesis and 11% under the alternative hypothesis based on a small pilot survey with 150 students in Itauna. The test statistic used is the two-sided score test (Farrington & Manning). The significance level of the test is 0.05. Normal class size in Brazil is 35 pupils; a lost to follow-up effect of 40% was taken into account.

Data entry

Data entry will be supported by the current software version of Formic Fusion by Xerox AG (Kloten, Switzerland) and the recommended scanners.

Analysis

To examine baseline differences in pupils' characteristics in our experimental design, we will use χ^2 tests for categorical variables and t-tests for continuous variables. To test for between-group differences in baseline and follow-up daily sunscreen use in the past 30 days, we will use a cluster-adjusted Mantel-Haenszel χ^2 test [66] with a significance level of 5% (two-sided). For the main analysis, HLM (hierarchical linear models) will be applied. HLM can handle the nested structure of the data and will be used to test for between-group differences in within-group changes in sun protection behavior over time. HLM will also be used to investigate the influence of further covariates (such as gender, European ancestry and skin type) and time-dependent behavior in secondary analyses. Statistical analyses will be performed using SPSS Statistics (IBM Corporation, New York, USA).

The effect that missing data may have on results will be assessed via sensitivity analysis. Dropouts (essentially participants who withdraw consent for continued follow-up or who are missing from the classroom during the survey) will be included in the analysis, and multiple imputation will be used to estimate the treatment effect [67].

Discussion

This is the first cluster-randomized school-based trial on photoaging skin cancer prevention and the first trial on medical student-delivered school-based skin cancer prevention worldwide. While classic health educational school-based approaches in skin cancer prevention were evaluated as inferior to appearance-based approaches [19], there is a global lack of novel, innovative strategies that harness current technology while taking widely accepted theories for behavioral change into account [61]. Although multiple studies have shown that skin cancer risk is predominantly associated with sun exposure early in life, there is a lack of awareness regarding risk groups.

Thus, this trial provides the opportunity to evaluate an innovative, highly scalable, appearance-based intervention in a high-risk population. It will also provide data to estimate whether photoaging mobile apps have the potential to be broadly implemented in schools via the mirroring intervention but also via other avenues (i.e., posters [65] or smartphone-based advertising campaigns in the App Store and Google Play Store) or could be a valuable addition to existing educational programs. Additionally, because it is delivered by medical students, this trial also sensitizes future physicians to the importance of skin cancer prevention, highlighting their associated responsibilities within communities [35, 68].

According to the theory of planned behavior (TPB), the subjective norm and the expected self-efficacy of the participants play a substantial role in their resulting behavior: What do their peers think about tanning? Is the result of tanning regarded as attractive and does it therefore increase one's chances of finding a boy/girlfriend? How likely is it that a behavioral change can positively influence this reaction? The mirroring intervention triggers strong reactions of the peer group of the individual participant towards their photoaged future self (=affecting subjective norm) but also illustrates the power of one's own behavioral change (and thereby increases one's expectation of self-efficacy, another predictor of the TPB) to influence this reaction by peers [49].

Limitations

Because this study is conducted only in Brazil, the results may not be generalizable to other cultural or national settings. However, the theoretical basis for this intervention (the theory of planned behavior) has been proven to apply to most cultural contexts around the globe [61]. As this trial enrolls approximately 10 different public schools, it should be representative for most school types.

We must choose classes and not schools as a cluster due to sample size limitations; thus, cluster effects cannot be entirely excluded. However, multiple steps are taken to limit contamination between the control and intervention classes (i.e., the name of the app is not mentioned to the pupils by the trained medical students, and the teachers of the control classes are strictly prohibited to talk about the intervention with their students). Cluster effects are also monitored in the endline questionnaire and provide a basis for a sensitivity analysis.

Some students may find the effects of the Sunface App unrealistic, as indicated in

our recently published pilot study. However, this does not appear to attenuate motivation to adhere to UV protection behavior [60].

In summary, we evaluate the long-term effects on behavior of a novel method that integrates photoaging in a school-based skin cancer prevention program in a population with a high risk for developing skin cancer. The program affects the students' peer group and also considers predictors for tanning. Our study is the first randomized controlled trial on skin cancer prevention in Brazil and the first randomized trial based on a medical student-delivered app and school skin cancer prevention strategy.

Ethics and Dissemination

Written informed consent will be obtained from both the participants themselves and their parents. All participant information will be stored in locked file cabinets in areas with limited access. The participants' study information will not be released outside the study without the written permission of the participant. Results will be disseminated at conferences, in peer-reviewed journals and on our websites.

Acknowledgements

The authors would like to thank all participating schools, students, volunteering medical students and teachers who helped organize the classroom visits in the city of Itauna.

Authors' Contributions

TJB initiated the study, invented, designed and organized the intervention, wrote the manuscript, drafted the design of the study and will perform the statistical analyses. BBS participated in the conception of the study. JK, PJ, IS, MG, FB and DS contributed to the design of the study and data analyses and proofread the manuscript. BBS and OCL contributed to the design and logistics of the study, assisted with the translation of classroom materials and reviewed the final version of the manuscript. BLF, OMF, HAL and ACCO will conduct data entry and coordinate/conduct the intervention in Brazil. They also supported the translation of the classroom materials and proofread the manuscript. All authors declare responsibility for the data and findings presented and have full access to the final trial dataset.

Conflicts of Interest

None declared.

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Figure Legends

Figure 1: Effect view: 25 years of skin aging with sun protection.
Figure 2: Effect view: 5 years of skin aging with sun protection.
Figure 3: Effect view: 5 years of weekly tanning without sun protection.
Figure 4: Start screen of the app prompts the user to pick his skin type.
Figure 5: Maximum effect view: 25 years of UV-damage due to weekly tanning.
Figure 6: Explanatory graphic of the effects within the app.
Figure 7: Study Design.

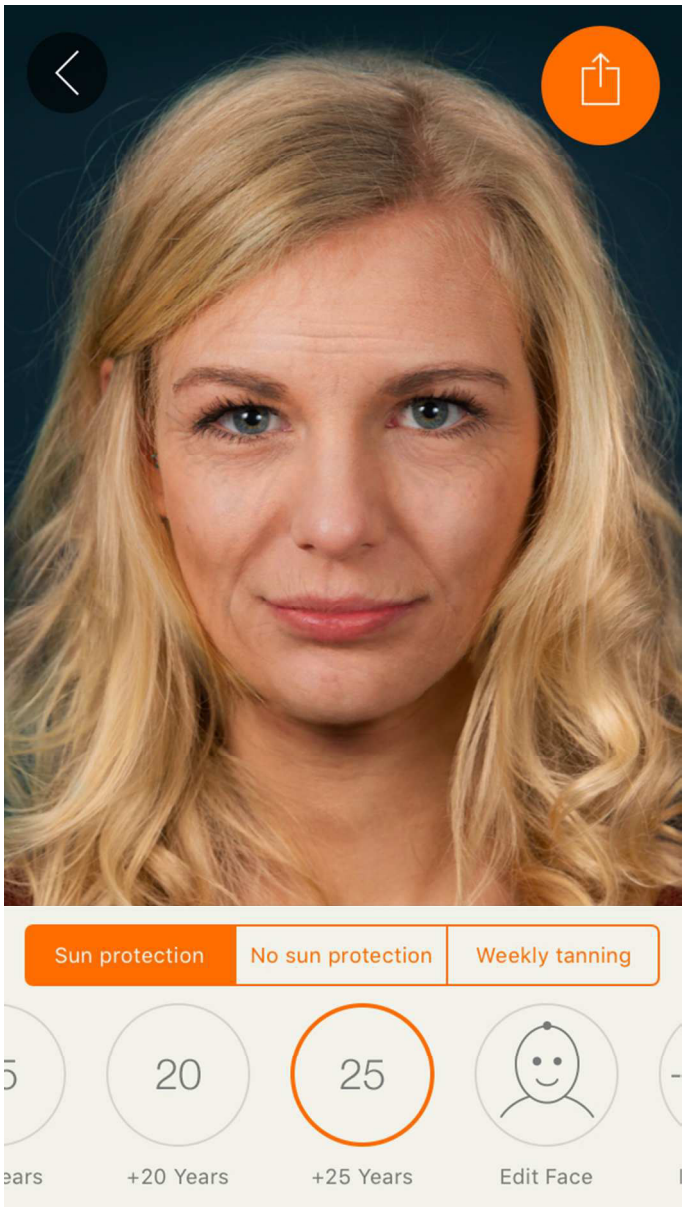


Figure 1: Effect view: 25 years of skin aging with sun protection.

54x96mm (300 x 300 DPI)

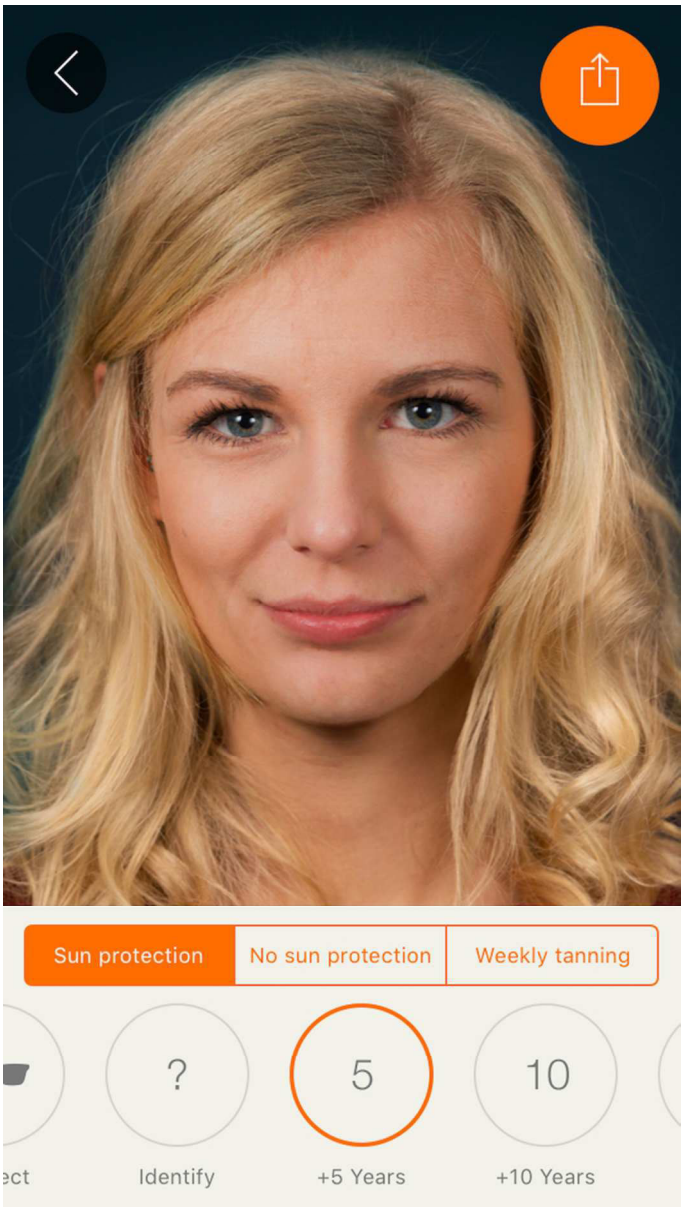


Figure 2: Effect view: 5 years of skin aging with sun protection.

67x120mm (300 x 300 DPI)

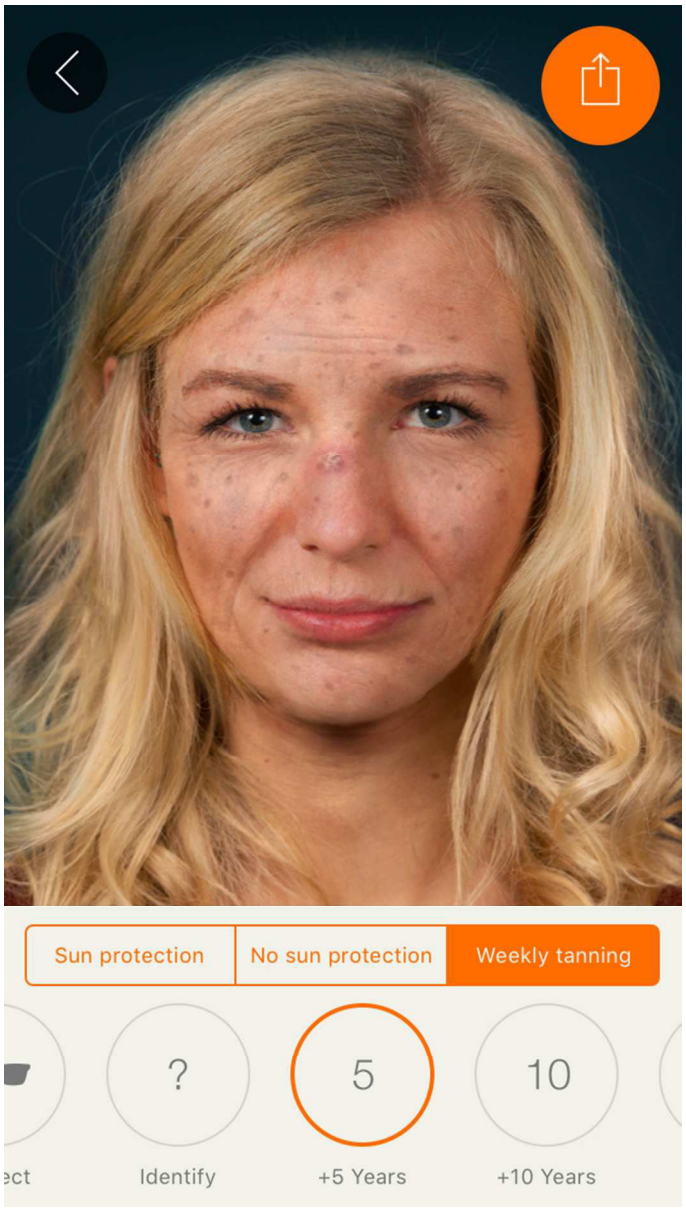


Figure 3: Effect view: 5 years of weekly tanning without sun protection.

54x96mm (300 x 300 DPI)

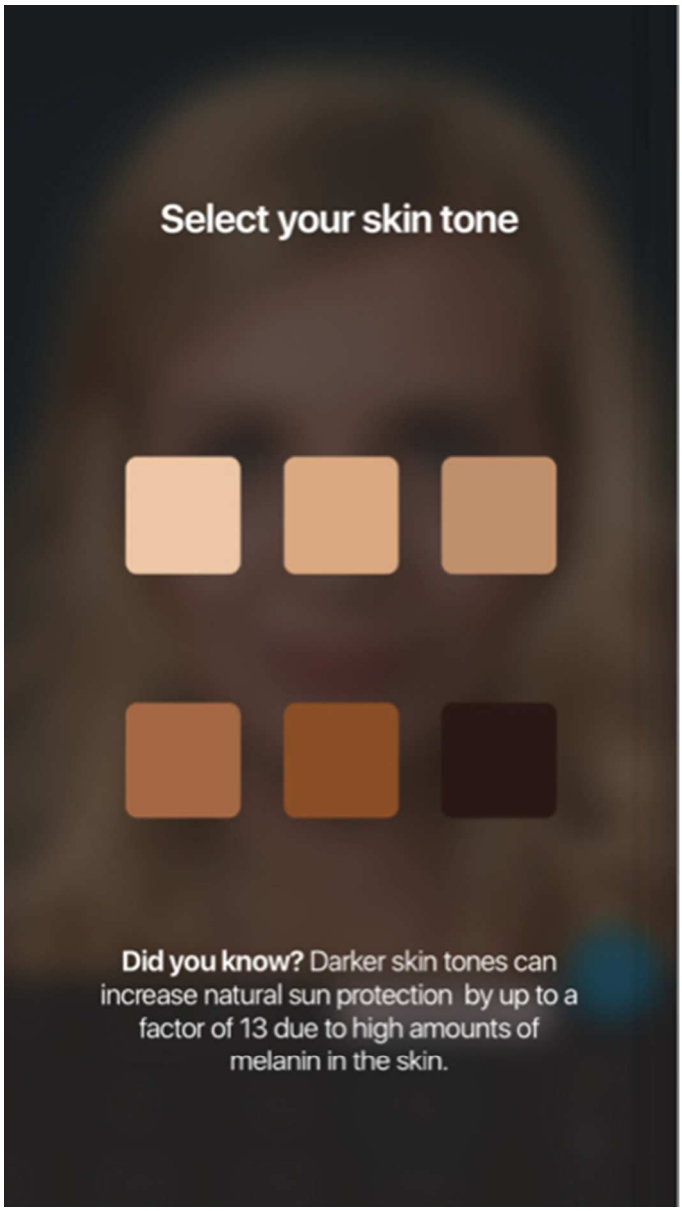
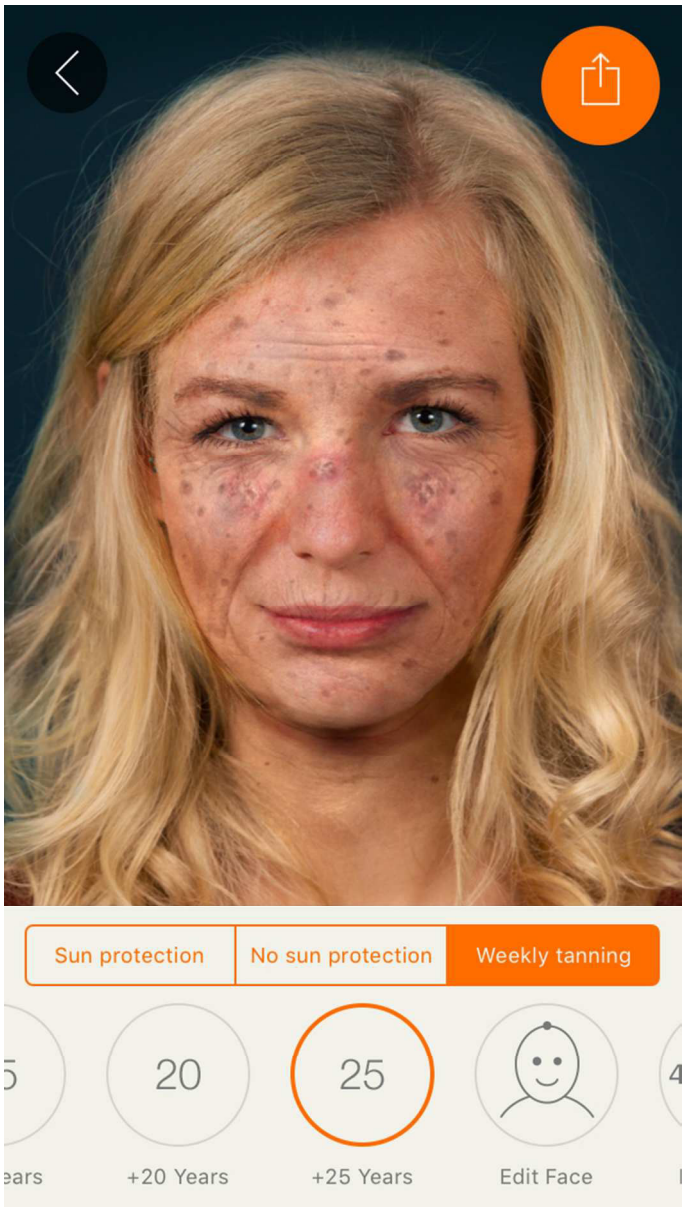


Figure 4: Start screen of the app prompts the user to pick his skin type.

30x54mm (300 x 300 DPI)



Maximum effect view: 25 years of UV-damage due to weekly tanning.

54x96mm (300 x 300 DPI)

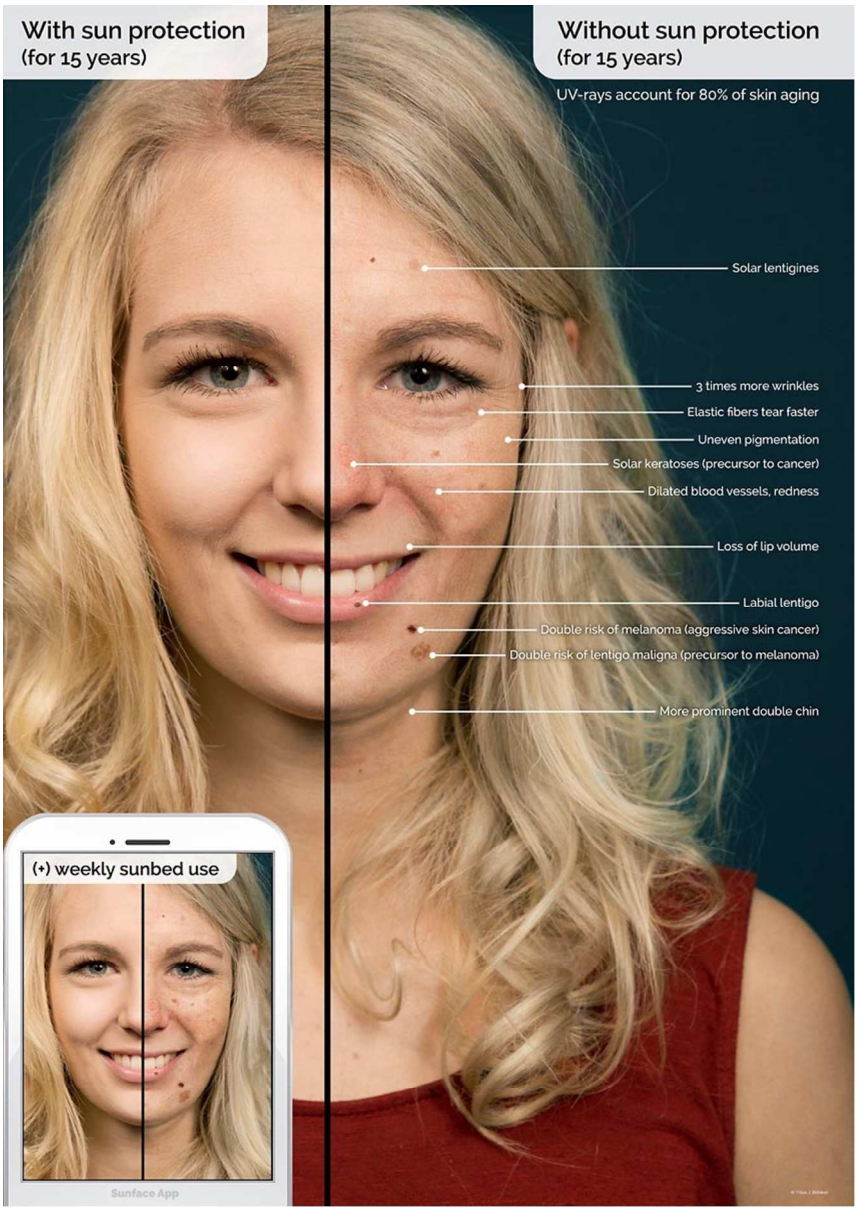


Figure 6: Explanatory graphic of the effects within the app.

71x101mm (300 x 300 DPI)

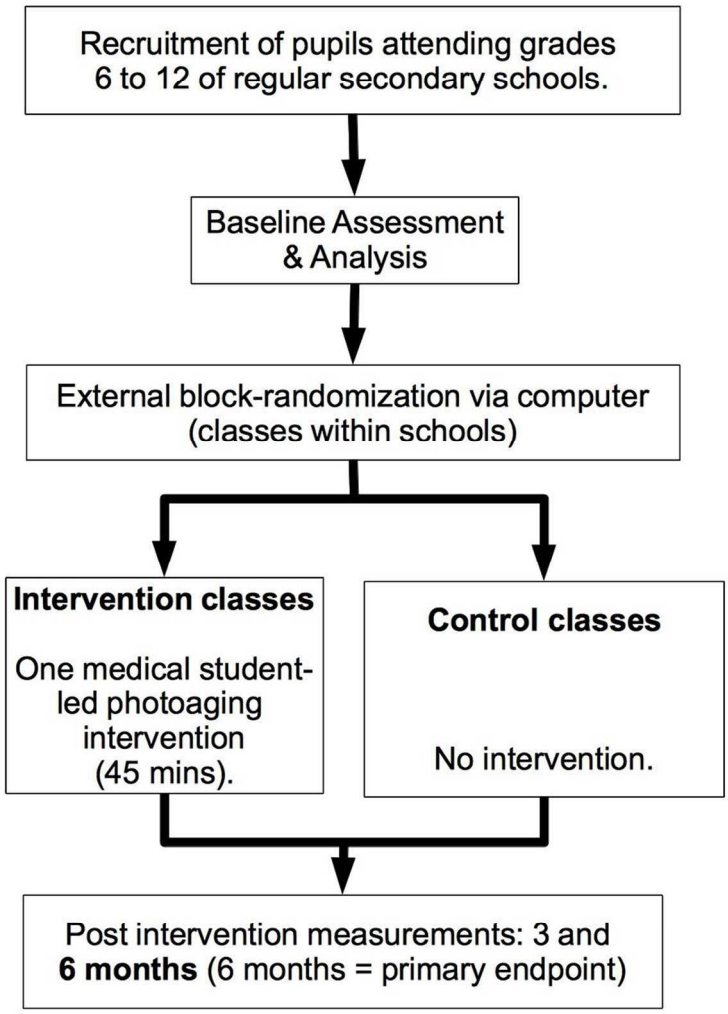


Figure 6
Study design.

Figure 7: Study Design.

88x125mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym **p. 1**
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry **p. 4**
	2b	All items from the World Health Organization Trial Registration Data Set **p. 4**
Protocol version	3	Date and version identifier **p. 2**
Funding	4	Sources and types of financial, material, and other support **p. 19**
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors **p. 1-2 and 19**
	5b	Name and contact information for the trial sponsor **p. 19**
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities **p. 19**
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) **n/a**
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention **p. 5-10**
	6b	Explanation for choice of comparators **p. 10**
Objectives	7	Specific objectives or hypotheses **p. 10**
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) **p. 10**

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained **p. 10 and 13**
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) **p. 13**
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered **p. 10-12**
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) **p. 16**
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) **p. 10**
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial **n/a**
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended **p. 14**
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) **p. 10**
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations **p. 14-15**
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size **p. 14-15**

Methods: Assignment of interventions (for controlled trials)

Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions **p. 14-16**

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned **p. 14**
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions **p. 14**
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how **p. 14**
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial **n/a**
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol **p. 13-16**
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols **p. 16**
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol **p. 13-16**
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol **p. 15**
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) **p. 15-16**
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) **p. 15-16**
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed **n/a (there are no treatment side effects; all authors declare responsibility for the collected data); p. 18**

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial **n/a**
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct **no treatment side effects**
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor **n/a**

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval **p. 4 and 18**
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) **if substantial changes are made, those are introduced in the published research paper**
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) **p. 18**
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable **p. 4 and 18**
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial **p. 18**
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site **p. 19**
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators **p. 19**
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation **n/a**
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions **p. 18**
	31b	Authorship eligibility guidelines and any intended use of professional writers **p. 19**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code

This manuscript/protocol is under consideration for publication in BMJ Open; p. 18-19.

Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates only available in Portuguese
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable **n/a**

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

A skin cancer prevention photoaging intervention for secondary schools in Brazil delivered by medical students: protocol for a randomized controlled trial

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A skin cancer prevention photoaging intervention for secondary schools in Brazil delivered by medical students: protocol for a randomized controlled trial

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ABSTRACT

Introduction

The incidence of melanoma is increasing faster than any other major cancer both in Brazil and worldwide. The southeast of Brazil has especially high incidences of melanoma, and early detection is low. Exposure to UV radiation represents a primary risk factor for developing melanoma. Increasing attractiveness is a major motivation for adolescents for tanning. A medical student-delivered intervention that harnesses the broad availability of mobile phones as well as adolescents' interest in their appearance may represent a novel method to improve skin cancer prevention.

Methods and Analysis

We developed a free mobile app ("Sunface"), which will be implemented in at least 30 secondary school classes, each with 21 students (at least 30 classes with 21 students for control) in February 2018 in Southeast Brazil via a novel method called mirroring. In a 45-minute classroom seminar, the students' altered three-dimensional selfies on tablets are "mirrored" via a projector in front of their entire class, showing the effects of unprotected UV exposure on their future faces. External block

randomization via computer is performed on the class level with a 1:1 allocation. Sociodemographic data, as well as skin type, ancestry, UV protection behavior and its predictors are measured via a paper-pencil questionnaire before as well as three and six months post-intervention. The primary endpoint is the group difference in the 30-day prevalence of daily sunscreen use at a six-month follow-up. Secondary endpoints include (1) the difference in daily sunscreen use at a three-month follow-up, (2) if a self-skin exam in accordance with the ABCDE rule was performed within the six-month follow-up and (3) the number of tanning sessions.

Ethics and dissemination: Ethical approval was obtained from the ethics committee of the University of Itauna. Results will be disseminated at conferences and in peer-reviewed journals.

Trial Registration: #NCT03178240

Strengths and limitations of this study

• This is the first study measuring the longitudinal effectiveness of a photoaging mobile app to change sun protection behavior.

• External randomization via computer and a relatively high number of clusters ensure good comparability between groups.

• Cluster effects cannot be excluded because the intervention and control classes are located in the same schools.

Introduction

According to the World Health Organization, the incidence of melanoma is increasing more rapidly than any other major cancer both in Brazil and worldwide. Melanoma is one of the most common cancers in young adults and poses substantial health and economic burdens [1].

Approximately 90% of melanomas are associated with UV exposure, in particular with the frequency of severe sunburns, and are therefore highly preventable [2]. Multiple studies showed that daily sunscreen use with a sun protection factor (SPF)

above 30, as recommended by international dermatology guidelines, may prevent sunburns and skin cancer including melanoma [3-6].

Brazil has one of the highest UV indexes on earth; additionally, tanning is culturally established and Brazilians commonly experience unprotected overexposure to the sun, especially in their childhood and teenage years [7-11]. In a 2008 population-based survey with 1,604 participants in the south of Brazil, 48.7% reported at least one sunburn in the prior year [10]. In an attempt to mitigate the health damage caused by excessive UV exposure, Brazil was the first country to prohibit indoor tanning in 2009, albeit with limited success [9]. The southeast of Brazil (the location of this study) is especially populated by citizens with a European ancestry and therefore has high incidences of melanoma (up to 23.5/100,000 inhabitants) with a lack of early diagnosis and an overall survival below worldwide rates [12-15].

Interventions encouraging sun protection habits are important, particularly among adolescents, as increased risk of skin cancer is associated with cumulative UV exposure and sunburns early in life [16-18]. In line with this association, various recent experimental studies to test these effects in young target groups aimed at promoting sunscreen use as an end point [19-22], and others used various UV protection behaviors (including avoiding sunbeds) or behavior scores [23-32]. Given the substantial amount of time that children and adolescents spend in the school environment, addressing skin cancer prevention in this setting is crucial and provides a unique opportunity to propel skin cancer prevention programs [33].

Despite the effectiveness of daily sunscreen and its implementation in international dermatologic guidelines [34], a study conducted in Brazil among 398 medical

students from the city of Curitiba showed that only 8.4% use sunscreen daily, 4.3% had already used tanning beds and 85.5% had past sunburns despite having undergone a clinical rotation in a Dermatology department [8]. The lack of exemplary behavior among prospective physicians regarding skin cancer prevention is known on a global scale [35-37]. The authors of this study have concluded that novel engagement methods are needed to answer the increasing demand for skin cancer awareness among physicians.

The Sunface mirroring intervention aims to provide science-based skin cancer prevention to a large number of adolescents in an attempt to sensitize prospective physicians to the importance of exemplary behavior [38, 39].

Current knowledge on school-based skin cancer prevention

Unhealthy behavior with respect to UV exposure is mostly initiated in early adolescence [40], commonly with the belief that a tan increases attractiveness [41-43] and the problems related to melanoma as well as skin atrophy are too far in the future to fathom.

A recent randomized trial with Australian high school students demonstrated that appearance-based videos on UV-induced premature aging were superior in encouraging sunscreen use to videos of the same length focusing exclusively on health aspects [19]. These findings are in line with international studies demonstrating the important influence of self-perceived attractiveness on self-esteem in adolescence [44, 45]. Furthermore, enhancing one's attractiveness is a primary motivation for tanning in adolescents both in Brazil and worldwide [41, 46, 47]. In addition, the success of appearance-based photoaging intervention mobile apps, in

which an image is altered to predict future appearance in the fields of tobacco and adiposity prevention, shows promise for these interventions in behavioral change settings [48-53].

In the setting of skin cancer prevention, a quasi-experimental study by Williams et al. demonstrated significantly higher scores for predictors of sun protection behavior in young women from the UK (70 participants in total) using a photoaging desktop program [54]. Furthermore, the photoaging software 'showed promising reduction in young adults' tanning intentions in a study with ten participants in total (7 female and 3 male) [55]. However, prior studies are limited by their small sample size and limitations related to expanding the target population.

Introduction of the Sunface app

We harnessed the widespread availability of mobile phones and adolescents' interest in appearance to develop the free mobile phone app "Sunface," which enables the user take a selfie and then offers three categories: "daily sun protection", "no sun protection" and "weekly tanning," showing the altered face at 5 to 25 years in the future (Figure 1, Figure 2, Figure 3, Figure 4). All effects are based on the individual skin type that the user can choose at the start of the app (Figure 5). The app also shows the most common UV-induced skin cancers via extra buttons and calculates how the odds ratio is increased with different behaviors. In addition, the app gives advice on sun protection, explains the facial changes and encourages skin examinations using the ABCDE rule (assess border irregularity, color variety, diameter, and evolution [56]).

Afterwards, the app offers many sharing options (animated video or photo) with family and friends. By this means, the social network of the user may also be informed about the various photoaging effects of excessive UV exposure and potential health consequences, as well as potentially learning about the benefits of using the app [57].

To produce realistic effects (Figure 6) and to show the user realistic odds ratios for the options they choose in the app for the three most strongly associated skin pathologies, an extensive review of the current literature on UV-induced skin damage [58, 59] was conducted for each specific skin type. As no trials with 25 years of follow-up were available, we had to extrapolate the current evidence on UV-induced skin damage for the specific skin types. The evidence consists of more than 50 publications to create realistic effects from a clinician's standpoint (which may differ from what the average person perceives as realistic).

We recently implemented this app in 2 German secondary schools via a method called mirroring. We "mirrored" the students' altered 3-dimensional (3D) selfies on mobile phones or tablets via a projector in front of their entire grade. Using an anonymous questionnaire, we then measured sociodemographic data as well as risk factors for melanoma and the perceptions of the intervention on a 5-point Likert scale among 205 students of both sexes aged 13-19 years (median 15 years).

In our pilot study, we found more than 60% agreement in both items measuring motivation to reduce UV exposure and only 12.5% disagreement: 126 (63.0%) agreed or strongly agreed that their 3D selfie motivated them to avoid using a tanning bed, and 124 (61.7%) agreed or strongly agreed to increase use of sun

protection; only 25 (12.5%) disagreed with both items. However, no effects on actual behavior could be measured due to the cross-sectional design of the study [60].

This randomized trial was designed to answer the following questions:

Is the implementation of the app in secondary schools in southeastern Brazil effective in encouraging daily sunscreen use among adolescents? Is it equally effective for both genders? Is it effective for the most sensitive skin types? How does the app intervention change the attitudes towards sun protection in accordance with the theory of planned behavior [61]?

Methods and Analysis

Study Design

The Sunface trial is designed as a randomized controlled superiority trial with two parallel groups. Our primary end point is the difference between the two groups in daily sunscreen use (past 30 days) from baseline to six months follow-up (Figure 7). The planned study period is February 2018 to November 2018. The study groups will consist of randomized classes receiving the intervention and control classes within the same schools (no intervention). Randomization is externally and centrally performed at the school level with a 1:1 allocation (control:intervention) via computer [12]. A total of at least 60 secondary school classes in Itauna, Brazil will participate in the teacher-supervised baseline survey in February 2018, which is conducted by trained data collectors. One week after the baseline survey, the intervention classes receive a 45-minute app-based intervention conducted by local medical student volunteers. Follow-up surveys will be conducted 3 and 6 months post-intervention.

Figure 7

Intervention

The school-based intervention under evaluation consists of a 45-minute educational module in the classroom setting using a photoaging app. The intervention is presented by 2 medical students per classroom to approximately 21 students at a time. The goal is to initiate and guide the student evaluation process of skin cancer prevention with age-appropriate information that helps the students reframe positive opinions and views regarding sun protection habits in a gain-framed and interactive manner.

To integrate app-based photoaging interventions into a school-based setting, we previously developed and tested the mirroring approach in a pilot study [49]. Mirroring means that the students' altered three-dimensional selfies on smartphones or tablets are "mirrored" via a projector in front of the entire class. The mirroring approach is implemented by medical student volunteers from the University of Itauna, who receive standardized training in advance. To ensure the participation of all students within a certain class and to avoid contamination within schools, we will implement the mirroring intervention via 10 Samsung Galaxy Tablets that are already set up and brought to the schools by the volunteers.

In the first 10-minute phase, the displayed face of one student volunteer is used to show the app's altered features in the three categories to the peer group, providing an incentive for the rest of the class to test the app. Students can interact with their own animated face via touch (see Multimedia Appendix 1). In front of their peers, they will be able to display their image as a non-/sun protection user/weekly tanning bed user at 5, 10, 15, 20 and 25 years in the future (see Figure 1 and Figure 2).

Multiple device displays can be projected simultaneously, which are used to consolidate the altered measures with graphics (e.g., to explain wrinkle formation). We implement mirroring with Galaxy Tab A (Samsung) via Apple's proprietary AirPlay interface using the Android app "Mirroring360" (Splashtop Inc.).

<Multimedia Appendix 1 uploaded as an additional file>

In the second 15-minute phase, students are encouraged to try the app on one of the tablet computers. The number of provided tablet computers was calculated so that the phase would take up to 12 minutes at the most after factoring in a utilization time of approximately 4 minutes per student. By this calculation, 25 minutes of the mirroring intervention and 10 provided tablets were sufficient to have every student within a class of 40 pupils successfully photoaged at least once.

In the following 15 minutes, the remaining functions of the app are discussed with the students: facial changes, the ABCDE rule and the guidelines for sun protection are addressed in an interactive setting. At the end of the classroom seminar, we ask for the students' final judgments on daily sunscreen use to create positive peer pressure and influence the students' subjective norm in accordance with the theory of planned behavior [61].

In the last 5 minutes, the perception of the intervention by the students is measured directly after the intervention in an anonymous survey on a 5-point Likert scale via four items: (1) "The animation of my 3D selfie motivates me to use daily sunscreen," (2) "I learned new benefits of sun protection," (3) "The intervention motivates me to check my skin with the ABCDE rule in the next six months," and (4) "The intervention was fun."

Participants

Eligibility criteria at baseline

Students from Itauna in southeast Brazil attending grades 6 to 12 in all types of regular secondary school are eligible.

Contaminated classes

All classes will be included in the final intention-to-treat analysis. However, app use will be assessed in both groups at six months follow-up to assess contamination of control classes and will be the basis for a secondary (sensitivity) analysis with the methods described in the Analysis section of this protocol.

Procedure

The schools are recruited via E-mail, telephone and personal appointment (in most cases with the principal). Reasons for non-participation are not recorded. Data are collected via a paper-pencil questionnaire. In addition to sociodemographic data (age, gender and school type), the questionnaire captures the Fitzpatrick skin type, the ancestry of the school students [62] and the frequency of sunscreen use in the past 30 days as well as other sun protection behaviors. These items are based on the sun exposure and protection index questionnaire [63] and were either used in their original form or adapted to the specific circumstances of the present study. No Portuguese equivalents of the instruments were available; thus, we used the Conceptual Method for translation described by the WHO/UNESCAP Project on Health and Disability Statistics [64]. Newly translated and/or modified items were extensively pretested and subjected to statistical analyses (internal consistency/Cronbach's α and exploratory and confirmatory factor analyses, which represented the basis for item selection).

Data Collection

Each data collector received training for data collection and was required to use an adapted standardized protocol for data collection, an optimized version of that used in the Smokerface randomized trial [65].

Cluster randomization

In accordance with the guidelines for good epidemiologic practice, classes within schools are externally and centrally randomly assigned to the control or intervention group via block randomization in a 1:1 ratio (control:intervention) via computer by a statistician at the University of Duisburg-Essen, Germany. Stratification will be performed by grade.

Outcomes

The primary endpoint is the difference in the 30-day-prevalence of daily sunscreen use between both groups at six months follow-up. Secondary endpoints include the difference in daily sunscreen use at three months follow-up if a self-skin exam in accordance with the ABCDE rule [56] was performed within the six-month follow-up and the number of tanning sessions in the past 30 days. For all end points, the number needed to treat will also be calculated. A daily sunscreen user is defined as a pupil who claims to have used sunscreen daily in the 30 days preceding the survey.

Statistical considerations

Sample size calculation

We calculated sample sizes of 630 in the intervention group and 630 in the control group, which were obtained by sampling 30 classes with 21 students each in the intervention group and 30 classes with 21 students each in the control group to achieve 80% power to detect a prevalence difference between the groups of 5%. The daily sunscreen prevalence was assumed to be 6% under the null hypothesis and 11% under the alternative hypothesis based on a small pilot survey with 150 students in Itauna. The test statistic used is the two-sided score test (Farrington & Manning). The significance level of the test is 0.05. Normal class size in Brazil is 35 pupils; a lost to follow-up effect of 40% was taken into account.

Data entry

Data entry will be supported by the current software version of Formic Fusion by Xerox AG (Kloten, Switzerland) and the recommended scanners.

Analysis

To examine baseline differences in pupils' characteristics in our experimental design, we will use χ^2 tests for categorical variables and t-tests for continuous variables. To test for between-group differences in baseline and follow-up daily sunscreen use in the past 30 days, we will use a cluster-adjusted Mantel-Haenszel χ^2 test [66] with a significance level of 5% (two-sided). For the main analysis, HLM (hierarchical linear models) will be applied. HLM can handle the nested structure of the data and will be used to test for between-group differences in within-group changes in sun protection behavior over time. HLM will also be used to investigate the influence of further covariates (such as gender, European ancestry and skin type) and time-dependent behavior in secondary analyses. Statistical analyses will be performed using SPSS Statistics (IBM Corporation, New York, USA).

The effect that missing data may have on results will be assessed via sensitivity analysis. Dropouts (essentially participants who withdraw consent for continued follow-up or who are missing from the classroom during the survey) will be included in the analysis, and multiple imputation will be used to estimate the treatment effect [67].

Discussion

This is the first cluster-randomized school-based trial on photoaging skin cancer prevention and the first trial on medical student-delivered school-based skin cancer prevention worldwide. While classic health educational school-based approaches in skin cancer prevention were evaluated as inferior to appearance-based approaches [19], there is a global lack of novel, innovative strategies that harness current technology while taking widely accepted theories for behavioral change into account [61]. Although multiple studies have shown that skin cancer risk is predominantly associated with sun exposure early in life, there is often a lack of awareness in risk groups.

Thus, this trial provides the opportunity to evaluate an innovative, highly scalable, appearance-based intervention in a high-risk population. It will also provide data to estimate whether photoaging mobile apps have the potential to be broadly implemented in schools via the mirroring intervention but also via other avenues (i.e., posters [65] or smartphone-based advertising campaigns in the App Store and Google Play Store) or could be a valuable addition to existing educational programs. Additionally, because it is delivered by medical students, this trial also sensitizes future physicians to the importance of skin cancer prevention, highlighting their associated responsibilities within communities [35, 68].

According to the theory of planned behavior (TPB), the subjective norm and the expected self-efficacy of the participants play a substantial role in their resulting behavior. For example: What do their peers think about tanning? Is the result of tanning regarded as attractive and does it therefore increase one's chances of finding a boy/girlfriend? How likely is it that a behavioral change can positively influence this reaction? The mirroring intervention triggers strong reactions of the peer group of the individual participant towards their photoaged future self (=affecting subjective norm) but also illustrates the power of one's own behavioral change (and thereby increases one's expectation of self-efficacy, another predictor of the TPB) to influence this reaction by peers [49].

Limitations

Because this study is conducted only in Brazil, the results may not be generalizable to other cultural or national settings. However, the theoretical basis for this intervention (the theory of planned behavior) has been proven to apply to most cultural contexts around the globe [61]. As this trial enrolls approximately 10 different public schools, it should be representative for most school types.

We must choose classes and not schools as a cluster due to sample size limitations; thus, cluster effects cannot be entirely excluded. However, multiple steps are taken to limit contamination between the control and intervention classes (i.e., the name of the app is not mentioned to the pupils by the trained medical students, and the teachers of the control classes are strictly prohibited to talk about the intervention with their students). Cluster effects are also monitored in the endline questionnaire and provide a basis for a sensitivity analysis.

Some students may find the effects of the Sunface App unrealistic, as indicated in

our recently published pilot study. However, this does not appear to attenuate motivation to adhere to UV protection behavior [60].

(Tracked Change: We removed the paragraph on this being the first RCT on photoaging mobile apps for melanoma prevention as this was already stated in the Strengths and Limitations section.)

In summary, we evaluate the long-term effects on behavior of a novel method that integrates photoaging in a school-based skin cancer prevention program in a population with a high risk for developing skin cancer. The program affects the students' peer group and also considers predictors for tanning.

Ethics and Dissemination

Participation is voluntary and oral consent is sufficient. The ethics committee of the University of Itauna waived the necessity for informed written consent. All participant information will be stored in locked file cabinets in areas with limited access. The participants' study information will not be released outside the study without the written permission of the participant. Results will be disseminated at conferences, in peer-reviewed journals and on our websites.

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Authors' Contributions

TJB initiated the study, invented, designed and organized the intervention, wrote the manuscript, drafted the design of the study and will perform the statistical analyses. BBS participated in the conception of the study. MVH, MCK, YN, MG, FB and DS contributed to the design of the study and data analyses and proofread the manuscript. BBS and OCL contributed to the design and logistics of the study, assisted with the translation of classroom materials and reviewed the final version of the manuscript. BLF, OMF, HAL and ACCO will conduct data entry and coordinate/conduct the intervention in Brazil. They also supported the translation of the classroom materials and proofread the manuscript. All authors declare responsibility for the data and findings presented and have full access to the final trial dataset.

Conflicts of Interest

None declared.

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Figure Legends

Figure 1: Effect view: 25 years of skin aging with sun protection.
Figure 2: Effect view: 5 years of skin aging with sun protection.
Figure 3: Effect view: 5 years of weekly tanning without sun protection.
Figure 4: Start screen of the app prompts the user to pick his skin type.
Figure 5: Maximum effect view: 25 years of UV-damage due to weekly tanning.
Figure 6: Explanatory graphic of the effects within the app.
Figure 7: Study Design.

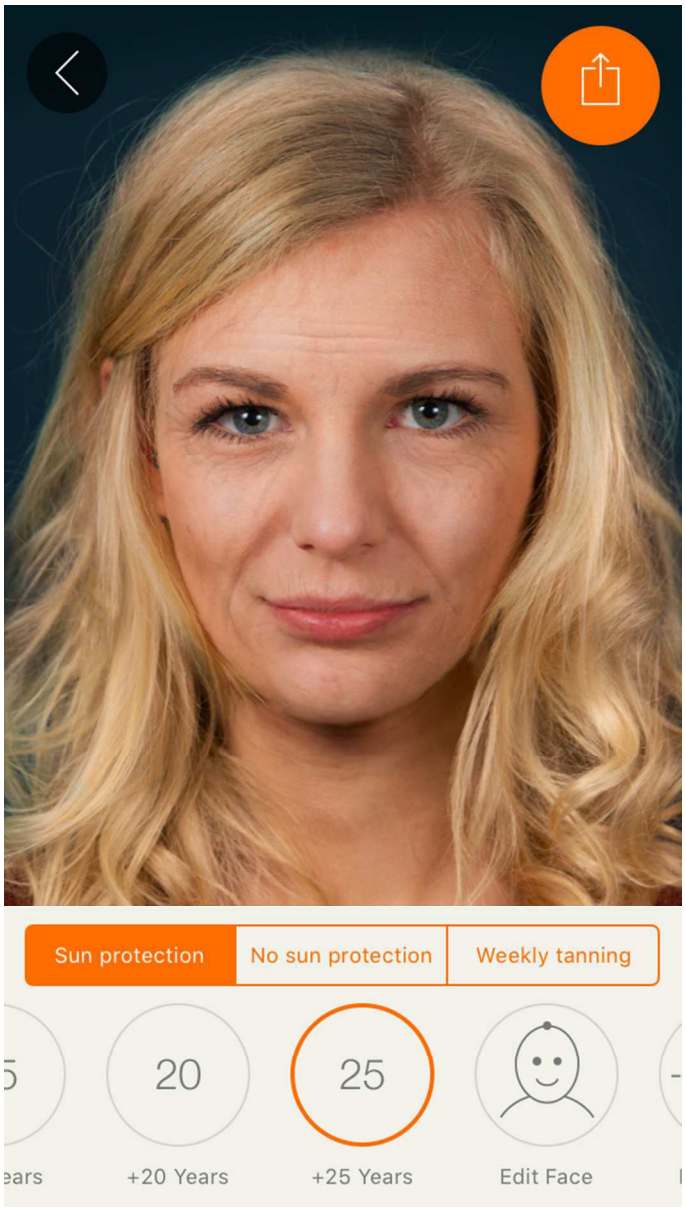


Figure 1: Effect view: 25 years of skin aging with sun protection.

54x96mm (300 x 300 DPI)

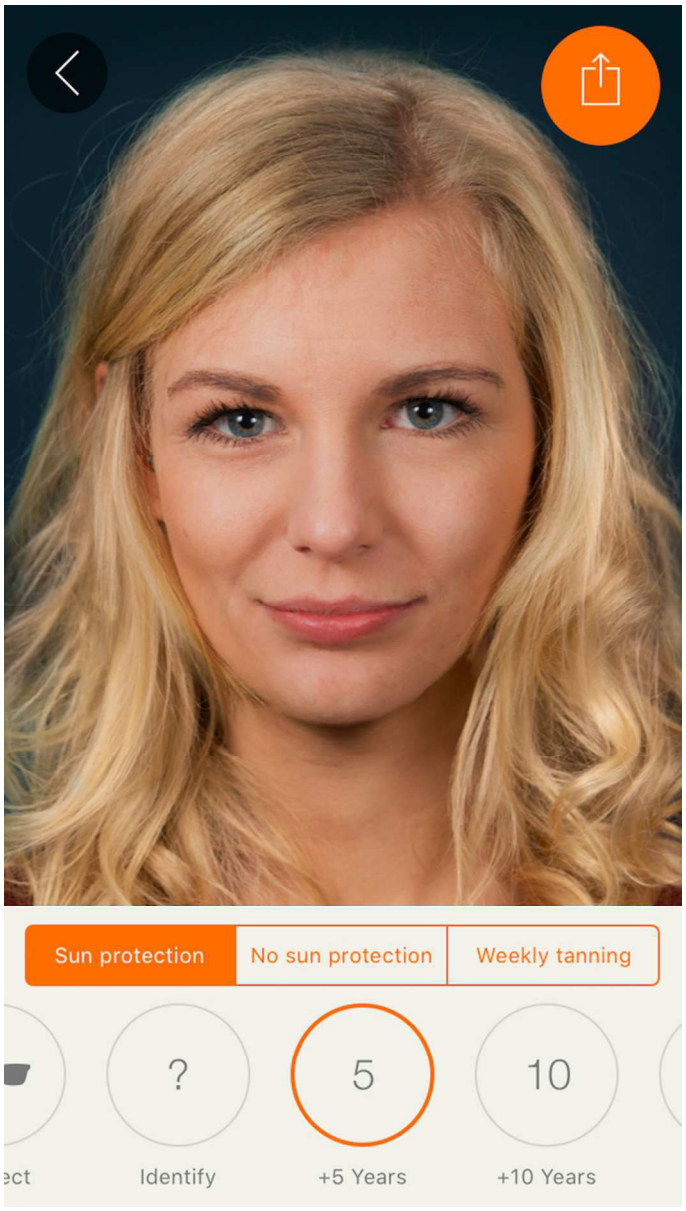


Figure 2: Effect view: 5 years of skin aging with sun protection.

67x120mm (300 x 300 DPI)

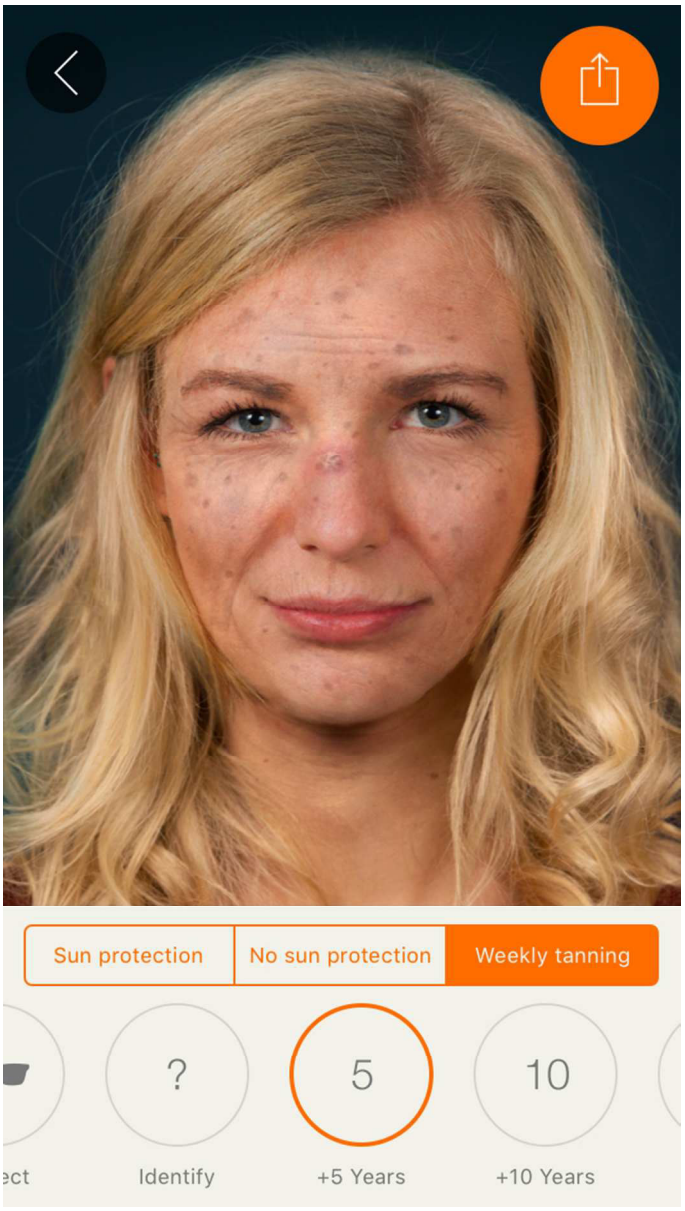


Figure 3: Effect view: 5 years of weekly tanning without sun protection.

54x96mm (300 x 300 DPI)

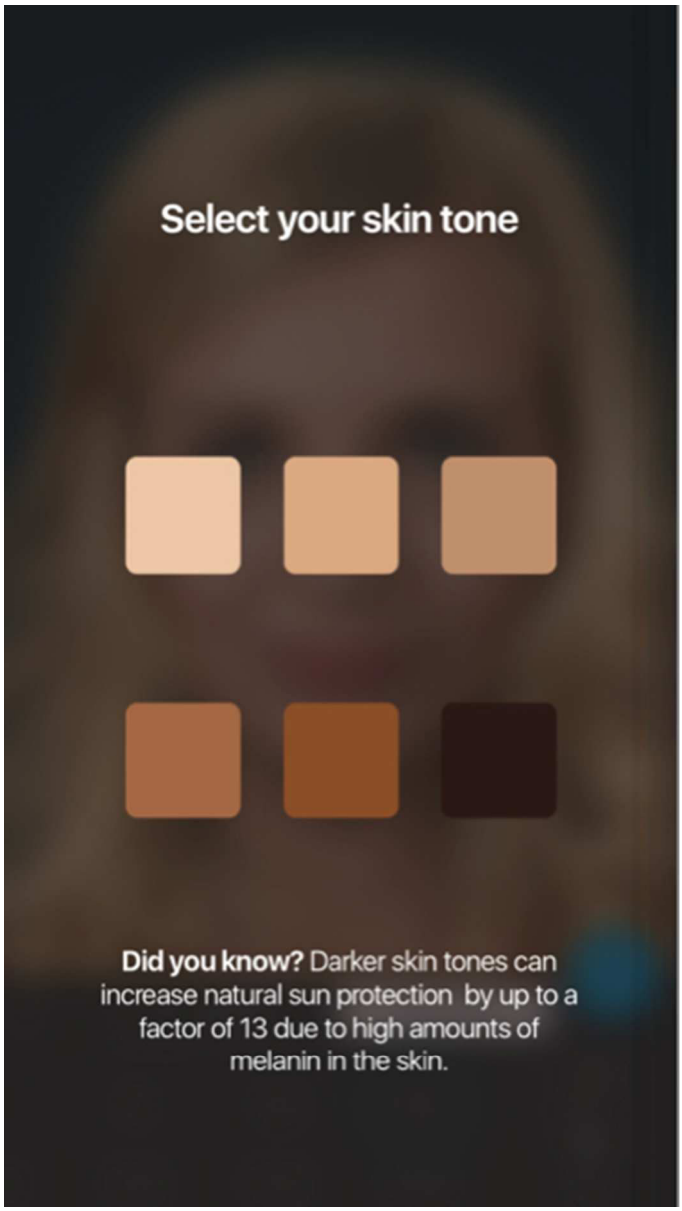
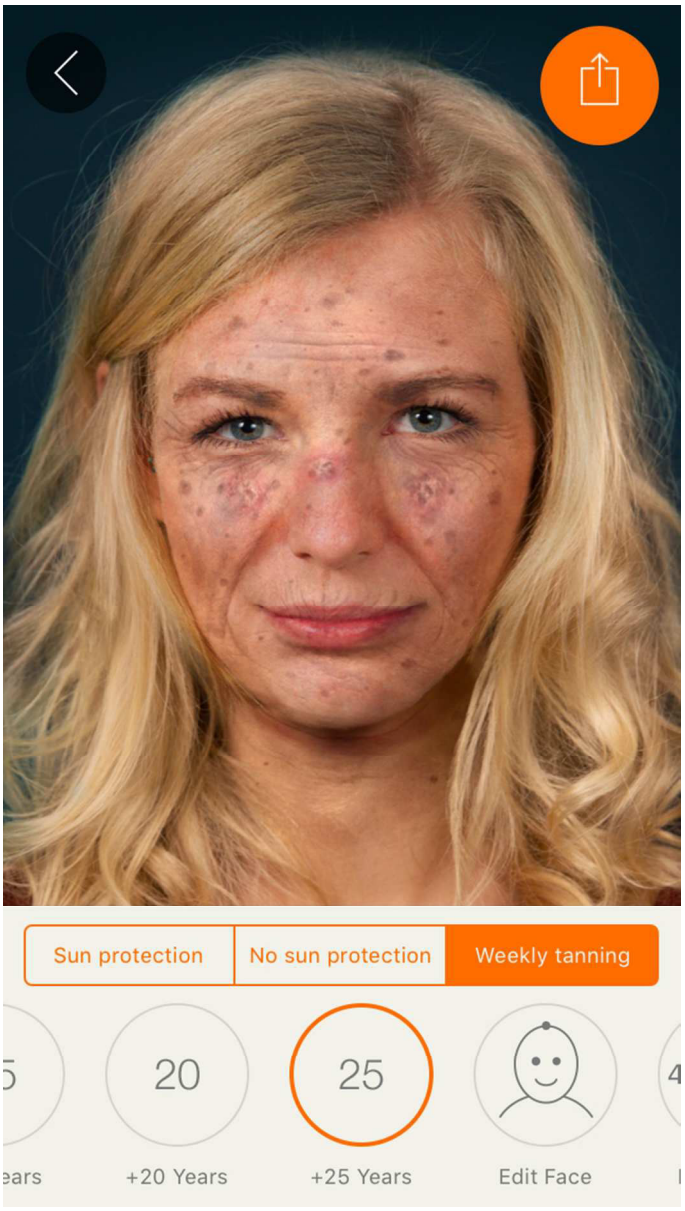


Figure 4: Start screen of the app prompts the user to pick his skin type.

30x54mm (300 x 300 DPI)



Maximum effect view: 25 years of UV-damage due to weekly tanning.

54x96mm (300 x 300 DPI)

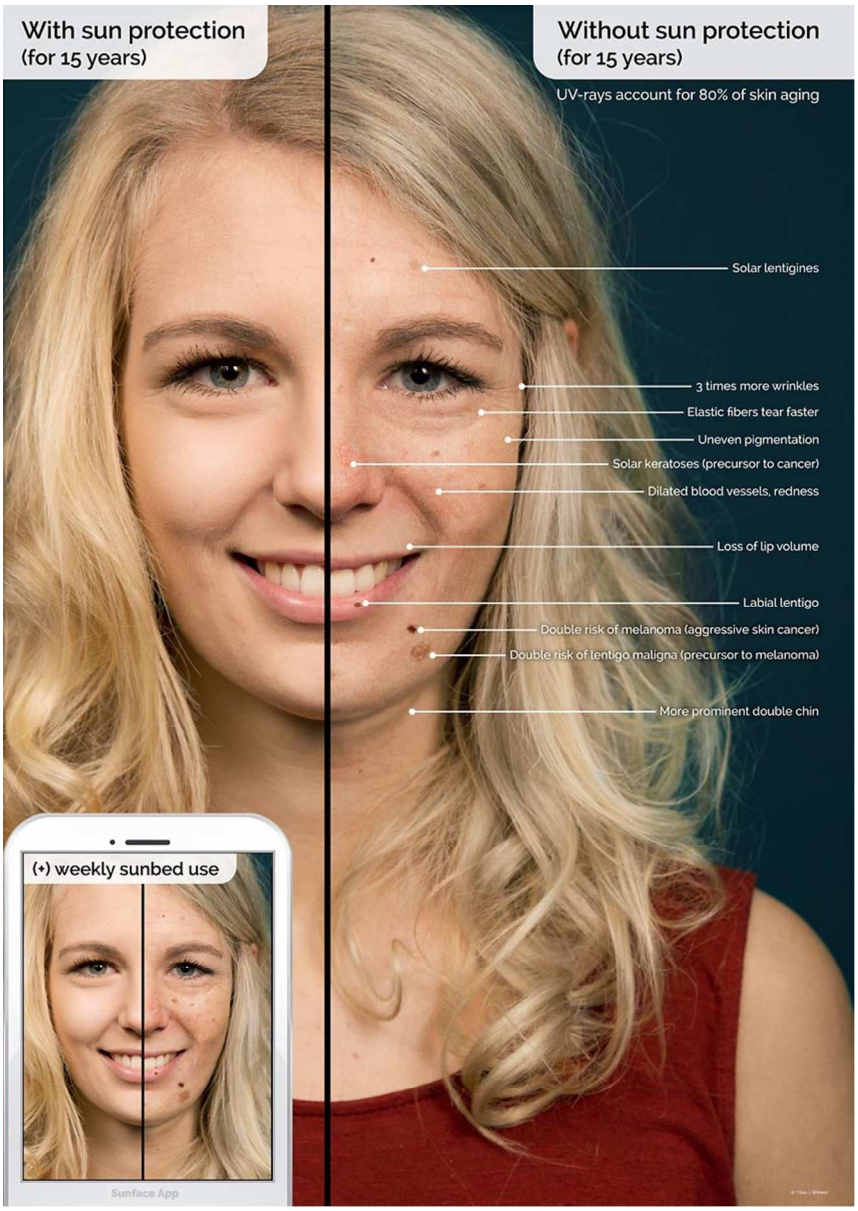


Figure 6: Explanatory graphic of the effects within the app.

71x101mm (300 x 300 DPI)

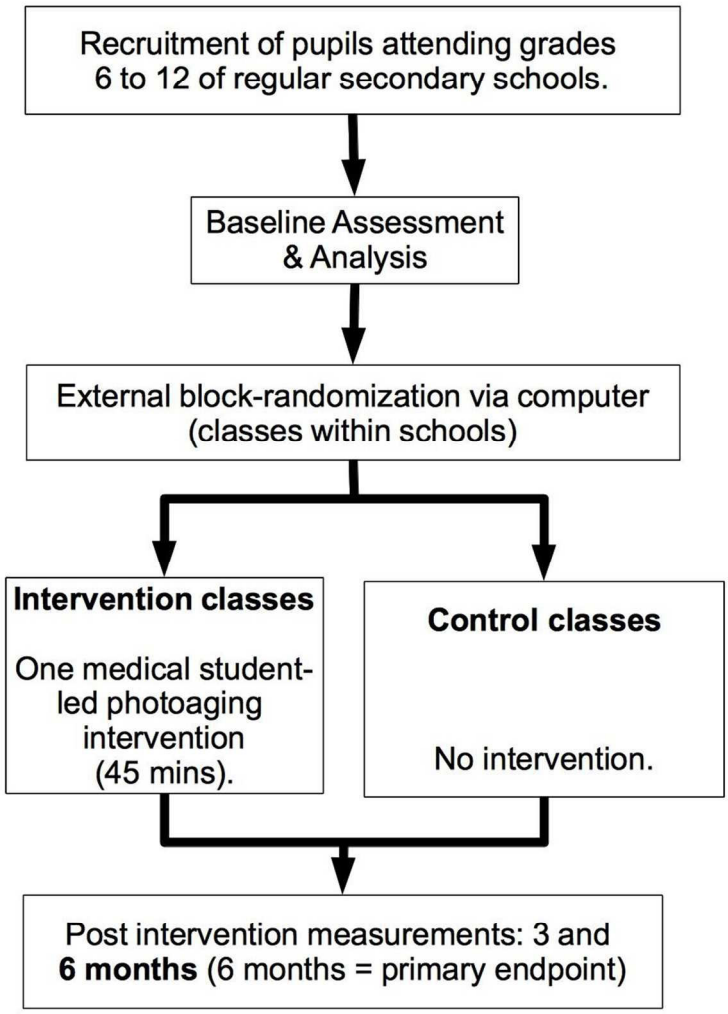


Figure 6
Study design.

Figure 7: Study Design.

88x125mm (300 x 300 DPI)