UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

Colegio de Ciencias de la Salud

Validation and adaptation of a tool to estimate the risk of acne-induced scars in an Ecuadorian population: Protocol and Pilot Study

Proyecto de Investigación

.

Jorge Antonio Estrella Porter

Medicina

Trabajo de titulación presentado como requisito
para la obtención del título de
Médico

Quito, 03 de julio de 2019

UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

COLEGIO CIENCIAS DE LA SALUD

HOJA DE CALIFICACIÓN
DE TRABAJO DE TITULACIÓN

Validation and adaptation of a tool to estimate the risk of acne-induced scars in an Ecuadorian population: Protocol and Pilot Study

Jorge Antonio Estrella Porter

Calificación:

Nombre del profesor, Título académico — Jonathan Guillemot, MA, MSc, PhD(c)

Firma del profesor _____

Quito, 03 de julio de 2019

Derechos de Autor

Por medio del presente documento certifico que he leído todas las Políticas y Manuales de la Universidad San Francisco de Quito USFQ, incluyendo la Política de Propiedad Intelectual USFQ, y estoy de acuerdo con su contenido, por lo que los derechos de propiedad intelectual del presente trabajo quedan sujetos a lo dispuesto en esas Políticas.

Asimismo, autorizo a la USFQ para que realice la digitalización y publicación de este trabajo en el repositorio virtual, de conformidad a lo dispuesto en el Art. 144 de la Ley Orgánica de Educación Superior.

Firma del estudiante: _____

Nombres y apellidos: Jorge Antonio Estrella Porter

Código: 00110652

Cédula de Identidad: 1714399753

Lugar y fecha: Quito, 03 julio de 2019

DEDICATORIA

Este trabajo representa uno de los pasos finales que he recorrido en la dura carrera de medicina. Quiero usar este trabajo como una muestra de que los sueños se cumplen. Por eso, se lo dedico a todos aquellos quienes tienen un sueño, sobre todo el de ser médico, para que sepan que, si lo pueden soñar, seguro lo pueden tener. No hay límites para aquel que sueña y trabaja duro. ¡No desistan, porque si yo pude, ustedes también!

AGRADECIMIENTOS

A mis queridos padres, quienes son responsables de cada una de mis cualidades y virtudes. Gracias, porque sin ustedes yo no sería nadie. A mi querido hermano, por darme la mano cuando más lo he necesitado, y por nunca dejarme caer. A mi querido profesor Jonathan, quien ha sido un maestro y un gran amigo, y me ha enseñado lo importante de la investigación. A mis colegas, Isa Viteri y Mikaela Camacho, gracias por todo su apoyo en este trabajo; gracias a ustedes entiendo la importancia del trabajo en equipo. A mi querida Universidad, por haberme hecho un profesional íntegro e integral. A mi amiga Clara Cullen, quien en estos meses me ha apoyado como ninguna otra persona, y quien, desde lo lejos, ha sabido hacerme sentir escuchado, comprendido y apoyado. Y a mí, Jorge, porque, aunque fue difícil, nunca te rendiste.

RESUMEN

Antecedentes: El acné es una de las condiciones dermatológicas más prevalentes de nuestro tiempo, ya que se estima que 9,4% de la población mundial sufre de esta enfermedad. Los pacientes con acné tienen una calidad de vida considerablemente disminuida. Las cicatrices por acné, una de las consecuencias de esta enfermedad, también se asocian con una franca disminución de la calidad de vida, y pueden ser evitadas, en su mayoría, si los pacientes reciben un tratamiento adecuado y a tiempo. En 2017, una herramienta clínica fue desarrollada por Tan y colaboradores para clasificar a los pacientes con acné en dos grandes categorías: con riesgo más alto y riesgo más bajo de desarrollar cicatrices por acné. Los investigadores usaron una muestra poblacional de tres países diferentes para desarrollar esta herramienta dermatológica. Su aplicabilidad fuera de las poblaciones de estudio todavía no se ha determinado.

Objetivos: Este estudio busca presentar un protocolo, evaluado mediante un estudio piloto, que pueda usarse para validar y adaptar, de ser necesario, la herramienta mencionada para la predicción del riesgo de desarrollo de cicatrices por acné, en poblaciones diferentes a las utilizadas originalmente para su desarrollo.

Métodos: Un protocolo de estudio fue desarrollado, durante varios meses, para crear un proceso sistemático que permita validar y adaptar a diferentes poblaciones, en este caso Ecuador, la herramienta desarrollada por Tan y colaboradores, para predecir el riesgo de que un paciente con acné desarrolle cicatrices. Originalmente, esta herramienta fue diseñada usando una muestra de una población de tres países: Francia, Brasil y Estados Unidos; su uso fuera de estas poblaciones no está documentado. El protocolo desarrollado en el estudio fue probado con un estudio piloto, que usó una muestra de 10 pacientes ecuatorianos que tuvieron o tienen acné. La retroalimentación del estudio piloto fue utilizada para mejorar el protocolo de estudio que se usará en una fase ulterior, todavía pendiente, para una investigación con una muestra de más de 400 personas.

Resultados: En base a la retroalimentación de 11 dermatólogos, 7 ecuatorianos y 4 expertos internacionales, el protocolo probó ser viable pues permitió recabar datos suficientes para validar y adaptar la herramienta de Tan y colaboradores, de acuerdo con el análisis estadístico planteado. Las fotografías tomadas a los participantes fueron un recurso valioso para la evaluación dermatológica. La luz tangencial durante la toma de fotografías se mostró necesaria para que los dermatólogos puedan definir la presencia o ausencia de cicatrices por acné mediante el uso de fotografías. Para un paciente determinado, los resultados del estudio piloto demostraron que los dermatólogos coinciden completamente en su evaluación sobre presencia o ausencia de cicatrices por acné en una minoría de veces (30%), y que la percepción sobre la presencia de cicatrices por acné varía entre pacientes y dermatólogos.

Conclusiones: Considerando la morbilidad relacionada con el acné y las cicatrices asociadas, son necesarias herramientas que alerten a los pacientes con acné sobre su riesgo de desarrollar cicatrices, para que puedan recibir un pronto y adecuado tratamiento, orientado a la prevención de su desarrollo. El protocolo propuesto en este estudio muestra una forma viable de validar la herramienta de predicción de cicatrices por acné propuesta por Tan y

colaboradores, a diferentes poblaciones. Todavía se necesita aplicar este protocolo a una población ecuatoriana más grande, para resultados más definitivos.

Palabras Clave: Acné, Cicatrices de acné, factores de riesgo, validación, adaptación, prevención.

ABSTRACT

Background:
Acne is among the most prevalent dermatological conditions, as it is estimated that 9.4% of the general population has acne. Patients with acne have a considerably diminished quality of life. Acne scarring, one of the consequences of acne, is also associated with a similar burden and can be avoided if patients receive the appropriate and timely treatment. In 2017, a clinical tool was designed by Tan et Al. to classify patients with acne into lower-risk and higher-risk for acne scars development, by using a population from three countries to develop it. Its applicability outside the population used remains to be determined.

Objective:
This study presents a protocol, tested with a pilot study, that can be used to validate and adapt, if necessary, the proposed tool to a different population group from the one used to develop it.

Methods:
A study protocol was developed to create a systematic way of validating and adapting the tool created by Tan et Al. to different populations, Ecuador in this case, from the ones used for its validation -France, Brazil and United States-. The protocol was tested with a pilot study using a sample of 10 patients who currently have or have had acne. Feedback from the pilot study was used to improve the study protocol for the final investigation.

Results:
Protocol, based on feedback from 11 dermatologists -7 from Ecuador, and 4 international experts-, proved to be feasible as it provided enough data to validate and adapt the tool developed by Tan et. al, according to the proposed statistical analysis. Images taken to participants were a valuable resource for dermatological evaluation. Tangential light appeared to be necessary for evaluating the presence or absence of acne scars through photography. Results showed that dermatologists completely agreed on the presence or absence of acne scars in a particular patient in a minority of times (30%), and that perception of acne scarring differs between patients and dermatologists.

Conclusions:
Considering the morbidity related to acne and acne scars, tools designed as prevention elements that alert patients about their risk of developing scarring due to their acne process are necessary. The proposed protocol shows a feasible way of validating the tool proposed by Tan et al, to different populations. This protocol still needs to be applied to a larger Ecuadorian population, for more definitive results.

Keywords:
Acne, acne scars, risk factors, validation, adaptation, prevention.

TABLE OF CONTENTS

INDEX OF TABLES

INTRODUCTION

Acne is among the most common dermatological condition, as it is estimated that 9.4% of the general population has acne, thereby making it the eighth most prevalent condition worldwide[1]. Its prevalence among those aged 12 to 24 years can reach as high as 85%, with variations in different populations[2]. While acne is often perceived as a secondary condition due to its temporary characteristic, emotional and psychological burden is high[3]. Patients with acne have a considerably diminished quality of life[4], as they are more likely to suffer from depression, anxiety[5] and deficits in quality of life. The extent of these symptoms are comparable to that of patients with chronic disability associated with asthma, epilepsy, diabetes or arthritis[6,7].

Acne often leads to the development of scars, which can become permanent[8]. Acne scarring is associated with psychosocial burden similar to that associated with acne[9]. Scarring can however be avoided if patients receive appropriate and timely treatment[10]. Although risk factors for the development of acne scars are known, few tools exist to predict the risk of acne scarring to support treatment decision-making.

In 2017, Tan et al. described a tool which assesses risk for acne scarring in patients with acne based on four risk factors: “severity of acne”, “family history of acne scarring”, “squeezing and picking behaviors” and “duration of acne”. The tool provides a binary outcome on the risk of acne scarring by categorizing respondents as being at “lower risk” or “higher risk” of developing acne scars. The tool was calibrated and validated based on a pre-existing database containing a large sample of young adults from the United States, France and Brazil, and resulted in a sensitivity of 82% and specificity of 43%[11]. Its applicability to different populations remains unclear.

This study presents a protocol aiming to validate and adapt the tool created by Tan et al. to estimate the risk of acne-induced scarring in any population. The protocol was tested though a pilot study in the context of Quito, Ecuador.

MATERIALS AND METHODS

Approach.

This study consists of two phases: development of a study protocol, and application of the protocol to a real-world scenario through a pilot study. A third phase, still pending, consists in the application of the study protocol -with its corrections after the feedback from the pilot study- to a final investigation. The results from the third phase will be included in a different paper.

Protocol for the validation of the tool.

With the intention of facilitating its replication, we first provide a brief description of the study protocol and make the complete methodology available as supplementary material (see Additional Material Section). The protocol is designed to assess the validity and generate data to adapt the tool by Tan et al to any population. The protocol presented below is adapted to the context of Quito, Ecuador. To this end, the protocol is designed to provide the approach to:

1. Establish the validity of the studied tool in a different population by comparing its performance between the original study and the results in the population under study;
2. If necessary, modify and calibrate the tool to the population under study;

3. Determine the presence of acne-induced scars in an Ecuadorian population of young adults using professional dermatological evaluation as gold standard;
4. Determine the risk factors and its associated relative weight for acne-induced scars in the population under study.
5. Determine the difference in perception about the presence/absence of acne scars between self-assessment of patients and professional evaluation, and among dermatologists.

A convenience sample of young adult student population of Universidad San Francisco de Quito USFQ, Quito, Ecuador, will serve as Ecuadorian study population. For an external validation study of a predictive logistic regression model, it is usually recommended a minimum of 100 events and 100 nonevents[12]. Based on the literature, around 40% of people who visit the dermatologist have scars due to acne[13]. Therefore, we estimated a minimum number of participants for the final study at around 250 persons.

Eligibility criteria for the study population were developed and are presented in **Table 1**.

Table 1. Eligibility criteria for the participants in the study

Eligibility Criteria
• To be a person aged 18-25 at the time of participation. • To have suffered acne at any time point, including having active acne at the time of the study. • To be a student of Universidad San Francisco de Quito USFQ. • In case of using makeup during data collection, to be willing to remove it from the face to enable high quality photographs of the skin to be captured. • To accept signing the informed consent, including consent for photographs to be captured. • To have no beard and/or visible facial hair in men.

Eligible participants will be administered a survey as they would have done when their acne was at its worst. The survey will contain the questions included in the tool developed by Tan

et al, among others aiming to address the other study objectives. Based on their responses, respondents will be categorized as lower-risk or higher-risk patients for developing acne scars.

Upon administration of the survey, participants will immediately be taken three photographs (front, and right and left profile) and, based on those photographs, a team of three dermatologists will independently evaluate the presence or absence and severity of facial scars due to acne in each of the participants. Photographs will be taken in a photobooth with standardized camera settings, to avoid any type of bias.

To ensure that each picture is reviewed by more than one dermatologist, and to avoid fatigue from one single dermatologist reviewing the complete set of pictures, three professionals in the area will be chosen.

Eligibility criteria for the dermatologists were developed and are presented in **Table 2**.

Table 2. Eligibility criteria for the selection of the team of dermatologists:

Eligibility criteria
• To be a doctor with a specialty degree in dermatology. • To have at least five years of experience in seeing patients with acne. • To have provided medical attention to at least 35 acne patients per years over the last 5 years. • To consent to the project participation an accept the workload proposed.

For each possible risk stratification criteria, we will calculate the proportion of patients categorized as lower-risk and higher-risk, and determine the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV).

The performance of the tool in an Ecuadorean population will be assessed by evaluating calibration and discrimination measures[14]. Calibration, the agreement between the observed results and the predicted results (based on the tool), will be evaluated by using:

- Calibration plot (results will be plotted with predictions on the x-axis, and the outcome on the y-axis), alongside the calibration slope (which should be close to 1 if the tool performs well) and intercept ('calibration-in-the-large').
- Hosmer-Lemeshow goodness-of-fit test.

Discrimination, the ability to differentiate patients with the outcome from those without it, will be determined by using:

- Receiver Operating Characteristic (ROC) curve, which plots the true positive rate (sensitivity) against the false positive rate (1-specificity)
- Concordance statistic (c-statistic) -area under the ROC curve- will be calculated to determine the degree of discrimination (a value of 0.5 represents chance, and 1 represents perfect discrimination)

If both calibration and discrimination cannot be established with the required parameters, the tool will not be considered valid for an Ecuadorian population.

To adapt the model, if necessary, a logistic regression will be conducted based on the available variables. The odds ratio will be calculated for each of the possible risk factors evaluated in the survey using a logistic regression. Factors with a 95%-confidence interval greater than 1, will be considered as significant risk factors. A new receiver operating curve with the retained factors will be plotted, and the most appropriate threshold will be selected based on clinical relevance. This data will be transformed into a questionnaire.

A determination of the observed concordance between the self-perception of patients about acne scars, and the dermatological evaluation will also be done. To complete the analysis and adjust the effect of chance on the proportion of the calculated simple concordance, Cohen's Kappa concordance coefficient will be calculated, so it could be analyzed and interpreted.

Finally, to stablish the difference in perception about the presence/absence of acne scarring among the dermatological experts, the number of total cases in which all three dermatologists agree and disagree will be determined. Cohen's Kappa concordance coefficient will be calculated as well.

Approach to piloting the protocol.

The pilot study aimed to check the feasibility of the proposed study protocol, and to obtain valuable feedback from the process.

A survey with 25 questions -same survey that will be used for the final study- was designed to be applied to eligible participants, who fulfilled all the eligibility criteria. The survey included data related to the epidemiology of their acne, and the self-perception of related scars. Participants answered the survey one by one, and went immediately to a photobooth, where three photographs (front, right and left profile) were taken, with standardized camera settings and light. Appropriate measures were taken to guarantee the anonymity of the participants during the process (see Additional Material Section).

To ensure the best possible feedback from the process, a formal invitation to participate in the pilot study was extended to 13 dermatologists, of whom 11 replied. Inclusion and exclusion criteria were applied to them. The final dermatological team was composed by seven Ecuadorian dermatologists, and four international acne experts.

The images taken to the participants were uploaded to a platform that facilitated the presentation of data to dermatologists. Access to this data was permitted only to the dermatological team and the research team. Each set of pictures from each participant was then evaluated by the 11 dermatologists, to determine the presence/absence of acne scars. Their evaluation was considered the gold standard.

The statistical analysis was carried out with the same guidelines described on the study protocol.

The study protocol and pilot were approved by The Institutional Review Board of the USFQ (Comité de Ética de Investigación en Seres Humanos Universidad San Francisco de Quito) on September 25th 2018 under the code 2018-193IN.

RESULTS

The pilot study was carried out in October 2018. A sample of twelve possible participants was recruited from students of Universidad San Francisco de Quito USFQ, following the same process and inclusion and exclusion criteria that will be used for the final study. From the 12 interested participants, 10 met the inclusion criteria (six women and four men, aged 20-25, mean age: 23 years old).

Table 3 summarizes the evaluation of the 11 participating dermatologists, and the self-perception of the patients evaluated on the presence or absence of acne scars.

Table 3. Summary of the dermatological evaluation findings in the pilot study.

Patient	Patient's report on the presence or absence of scars due to acne *	Dermatological evaluation: Does the patient have acne scars?											
		D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	Summary from the dermatological evaluation
001-P	P	*p*	P	P	A	A	A	A	A	A	A	A	Scars are present: 27% Scars are absent: 73%
002-P	P	P	*p*	P	*p*	*p*	*p*	*p*	*p*	*p*	*p*	*p*	Scars are present: 100% Scars are absent: 0%
003-P	A	A	A	A	A	P	A	A	A	A	A	A	Scars are present: 9% Scars are absent: 91%
004-P	P	*p*	P	P	*p*	*p*	*p*	A	*p*	*p*	*p*	*p*	Scars are present: 91% Scars are absent: 9%
005-P	A	*p*	A	P	A	*p*	*p*	A	*p*	A	*p*	*p*	Scars are present: 64% Scars are absent: 36%
006-P	A	A	A	*p*	A	A	A	A	A	*p*	A	A	Scars are present: 18% Scars are absent: 82%
007-P	A	*p*	A	*p*	P	A	*p*	*p*	*p*	P	*p*	*p*	Scars are present: 82% Scars are absent: 18%
008-P	A	P	*p*	P	*p*	*p*	*P*	*p*	P	*p*	P	*p*	Scars are present: 100% Scars are absent: 0%
009-P	A	A	P	P	A	A	*p*	A	*p*	*p*	A	A	Scars are present: 45% Scars are absent: 55%
010-P	P	P	*p*	P	P	P	*p*	*p*	*p*	*p*	*p*	*p*	Scars are present: 100% Scars are absent: 0%

p: Scars are present, but mild P: Scars are present, more than mild A: Scars are absent

Green boxes: Ecuadorean dermatologists. Blue boxes: International Acne Experts

From the 10 participants evaluated, the dermatologists globally agreed on their evaluation in only three cases; in all of them there was always a minimal disagreement (that to say is some determined the presence of mild scars due to acne, while others determined more than mild scars, but all of them agreed with the presence of acne scars). In those three cases, the patients agreed on their self-assessment with the professional assessment in only two occasions; the third patient did not recognize the presence of acne scars even though 11 dermatologists did.

International acne experts agreed on their evaluation in seven out of 10 patients, from which five were major agreements (same answer about the presence of acne scars, and severity) and two were minor disagreements (difference in defining mild scars or more than mild scars, but presence of acne scars was the common answer). On the other hand, Ecuadorean dermatologists agreed on their evaluation in three out of 10 patients, from which all were minor disagreements. Ecuadorean dermatologists never had a major agreement on their evaluations.

Considering the simple majority as the final dermatological evaluation, patients agreed with it in six out of 10 cases; of these, only 50% of the time there was a major agreement between the patients and the absolute totality of dermatologists. Agreements between patients and the final dermatological evaluation occurred equally when determining absence and presence of scars, which means that there was not a clear predilection for the situation in which it was more common to find agreements among both groups.

Dermatologists were also asked for feedback on the whole process. **Table 4** summarizes the feedback.

Table 4. Feedback from dermatologists about the pilot study.

	Patient status for the picture	Photography Quality	Light Environment	Angle of the pictures	Data Presenting System
Agreements	8 (73%)	7 (64%)	7 (64%)	7 (64%)	10 (91%)
Disagreements (need improvement)	3 (27%)	4 (36%)	4 (36%)	4 (36%)	1 (9%)

Regarding the feedback, three dermatologists suggested the need of improvement in patient status for the picture, which was mostly related to guarantying that women were not using make up and men had none or almost no facial hair. Four dermatologists disagree with the

photography quality; all the four suggested that there was the need to zoom in and out the presented pictures. Light environment was also a matter of discussion, as 4 dermatologists suggested that additional -tangential- light was required. Regarding the angle of the pictures, four dermatologists suggested the need of improvement, standardizing positions in all participants. Finally, the data presenting system was almost a complete agreement; one dermatologist proposed that additional patient data -such as history of previous scars different to acne related- should be included.

DISCUSSION

Results of the pilot study suggest that self-perception of acne scars is not accurate in many cases, if dermatological evaluation is considered as gold standard. Sometimes, patients may underestimate their condition while sometimes they may overestimate it. This was already described in previous studies assessing subjective assessment scales for determining acne-scarring; self-assessment has been recognized as an untrustworthy approach for the assessment of severity in comparison to scales using dermatological evaluation[15]. It is necessary to improve the information provided to patients so that they can recognize the presence of acne scars more easily and go to their dermatologist for scar treatment.

When evaluating acne scars, four broad approaches can be used: (1) scar subtype counting, (2) subjective self-assessment, (3) global acne scar severity scoring and (4) multimodal imaging[16]. Even though these methods try to systematize the evaluation of acne scarring -by considering scar type and number of lesions [17], for example-, there is still not an objective way to guarantee that all acne scar lesions are included, or to guarantee that lesions that are not acne-related are not included for the different evaluation system. The results of the pilot

study show this. Objective measurements for objectively including acne-related scars to different evaluation tools are lacking.

Based on the feedback provided by dermatologists in the investigation, the proposed study shows to be feasible: the process of collection, processing and presentation of data proved to meet the objectives set and provided valuable data necessary for the statistical analysis plan. Some limitations, however, were identified. A sample for USFQ might not be the most representative sample of an Ecuadorean population aged 18-25, as this university is highly exclusive (which arises issues related to health status, access to medical evaluations….). Another limitation identified was the fact that photography of patients will never equal the quality of face-to-face evaluation, as bidimensional imaging does not allow volumetric assessment, a necessary element for determining the quality of a suspected scar[16]. Tangential light should be included in the final study, to guarantee a more three-dimensional image of patients.

CONCLUSION

Considering the great morbidity related to acne and acne scars, tools designed as prevention elements that alert patients about their risk of developing scarring due to their acne process are necessary. In 2017, Tan et al. proposed a tool which was proven valid via a cross-validation with the populations used to develop it. The validity of the tool outside the population has not been stablished. The proposed protocol and pilot study showed the feasibility of a systematized process to validate this tool in different populations, which in this case was a sample from an Ecuadorian population. The protocol and pilot study also showed to be valuable in obtaining extra information related to self-perception of acne scars, and dermatological evaluation, which is useful for understanding the situation of the condition in

the population studied. A study with a bigger sample is still necessary to achieve the objectives proposed in the protocol developed.

REFERENCES OF THE STUDY

1. Tan, J. K. L. & Bhate, K. A global perspective on the epidemiology of acne. *Br. J. Dermatol.* **172 Suppl 1**, 3–12 (2015).
2. Asai, Y. *et al.* Management of acne: Canadian clinical practice guideline. *CMAJ Can. Med. Assoc. J.* **188**, 118–126 (2016).
3. Hazarika, N. & Archana, M. The Psychosocial Impact of Acne Vulgaris. *Indian J. Dermatol.* **61**, 515–520 (2016).
4. Zauli, S. *et al.* Which factors influence quality of life in acne patients? *J. Eur. Acad. Dermatol. Venereol. JEADV* **28**, 46–50 (2014).
5. Barnes, L. E., Levender, M. M., Fleischer, A. B. & Feldman, S. R. Quality of Life Measures for Acne Patients. *Dermatol. Clin.* **30**, 293–300 (2012).
6. Tasoula, E. *et al.* The impact of acne vulgaris on quality of life and psychic health in young adolescents in Greece. Results of a population survey. *An. Bras. Dermatol.* **87**, 862–869 (2012).
7. Mallon, E. *et al.* The quality of life in acne: a comparison with general medical conditions using generic questionnaires. *Br. J. Dermatol.* **140**, 672–676 (1999).
8. Dréno, B. *et al.* How People with Facial Acne Scars are Perceived in Society: an Online Survey. *Dermatol. Ther.* **6**, 207–218 (2016).
9. Chuah, S. Y. & Goh, C. L. The Impact of Post-Acne Scars on the Quality of Life Among Young Adults in Singapore. *J. Cutan. Aesthetic Surg.* **8**, 153–158 (2015).

10. Madden, W. S. *et al.* Treatment of acne vulgaris and prevention of acne scarring: canadian consensus guidelines. *J. Cutan. Med. Surg.* **4 Suppl 1**, S2-13 (2000).
11. Tan, J. *et al.* Development of an atrophic acne scar risk assessment tool. *J. Eur. Acad. Dermatol. Venereol. JEADV* **31**, 1547–1554 (2017).
12. Substantial effective sample sizes were required for external validation studies of predictive logistic regression models. - PubMed - NCBI. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15845334. (Accessed: 4th March 2019)
13. Md, J. T., Md, <sup>a/sup> Sewon Kang & MD[c], <sup>b/sup> and James Leyden. Prevalence and Risk Factors of Acne Scarring Among Patients Consulting Dermatologists in the USA. *J Drugs Dermatol* (1485790771). Available at: http://jddonline.com/articles/dermatology/S1545961617P0097X. (Accessed: 29th May 2018)
14. Steyerberg, E. W. *et al.* Assessing the Performance of Prediction Models: A Framework for Traditional and Novel Measures. *Epidemiology* **21**, 128–138 (2010).
15. Almeida, H. de, Cecconi, J., Duquia, R. P., Souza, P. R. & Breunig, J. Sensitivity and specificity of self-reported acne in 18-year-old adolescent males. *Int. J. Dermatol.* **52**, 946–948 (2013).
16. Clark, A. K., Saric, S. & Sivamani, R. K. Acne Scars: How Do We Grade Them? *Am. J. Clin. Dermatol.* **19**, 139–144 (2018).
17. Dreno, B. *et al.* ECCA grading scale: an original validated acne scar grading scale for clinical practice in dermatology. *Dermatol. Basel Switz.* **214**, 46–51 (2007).

ADDITIONAL MATERIAL: STUDY PROTOCOL

Study abstract.

Acne is among the most common prevalent dermatological condition, as it is estimated that 9.4% of the general population has acne, thereby making it the eighth most prevalent condition worldwide. While acne is often perceived as a secondary condition due to its temporary characteristic, emotional and psychological burden is high. Patients with acne have a considerably diminished quality of life. Acne scarring, one of the consequences of acne, is also associated with a similar burden and can be avoided if patients receive the appropriate and timely treatment. Although there are descriptions of risk factors for the development of acne scars in the literature, few tools exist to predict the risk of acne scarring, nor can they be applied to clinical and non-clinical settings as primary prevention instruments. In 2017, Tan et al. described a tool which assesses risk for acne scarring in patients with acne based on four risk factors. While the tool was calibrated based on a large sample of populations from the United States, France and Brazil, its applicability to different populations is unclear. The present study aims to test and, if necessary, adapt the tool proposed by Tan et al. to an Ecuadorian population, so it can be used by doctors and patients as a tool to encourage timely acne treatment and therefore improve the prevention of acne scars. This study also aims to determine the specific risk factors for developing acne scars, and their individual weight, in an Ecuadorian population, as well as the difference in perception of the presence/absence of acne scarring between patients and dermatologist, and the difference in perception of the presence/absence of acne scarring among a group of dermatologists.

Introduction.

General overview of acne and acne scars.

Acne is a chronic dermatologic condition that affects around 9.4% of the general population, making acne the eighth most prevalent condition in the world[1]. Its prevalence among those aged 12 to 24 years is estimated to be as high as 85%, with variations in different populations[2]. Acne predominantly affects teenagers and young adults from the age of 11, with a peak at 16 years[18], and with persistence in the twenties and thirties[19]. Acne is associated with considerable psychosocial morbidity. Evidence supports that patients with acne are more likely to present depression, anxiety[5], and deficits in quality of life, in proportions comparable to patients with chronic disability due to asthma, epilepsy, diabetes or arthritis[6,7]. Several treatment options have been described, including topical compounds such as antibiotics, retinoids and benzoyl peroxide, which can be used in monotherapy or in combination with systemic compounds such as isotreonin, antiandrogens or antibiotics [11,20,21,22].

Acne is often associated with the development of scars, which can be of three types: atrophic, keloidal or hypertrophic, with atrophic scars being the most common type. Up to 43% of people who visit the dermatologist have scars due to acne[23]; anyway, the prevalence and severity of acne scars have not been well studied. The prevalence of acne scarring varies within different countries: for example, a study showed that among people with acne, the prevalence of scaring was 44% in Brazil, 37% in France, and 43% in USA[24]. The presence or absence of scars can be considered subjective and may vary from points of view.

Regarding self-perception of acne scars, few studies assess this issue. In a study conducted in six countries and in a population of 4618 people, 33% of respondents reported to have facial acne scars[8]. Additionally, an investigation conducted in the south of Ecuador determined that 18,11% of adolescents have the perception of suffering from acne scars[25]. None of these

studies compare these results to a professional dermatological assessment, suggesting that there could be a gap between acne scarring self- and professional-assessment.

According to a small sample used by Tan el al. 5 out of 10 interviewees have a self-perception of having acne scars; dermatologists determined the presence of acne scars in three of those 5 patients. This suggests that self-perception of having acne scars might not be accurate. There are few studies regarding the topic, even when acne scars can cause serious problems in patients´ daily life[26]

Since patients with acne and acne scars are not affected in terms of their general health condition, mobility, or lifespan, the burden of the two conditions is often underestimated. It is not uncommon for acne and its consequential scaring to be qualified as a "merely cosmetic" condition[27]. Therefore, the psychosocial effect of acne scarring has not been fully appreciated. However, as early as 1948, the psychosocial effect of acne was already acknowledged, when it was recognized that "there is not a single disease that causes more psychic problems, trauma, more mismatch between parents and children, more insecurity and general feelings of inferiority, and greater amounts of psychic suffering than acne vulgaris"[28]. For this reason, the early identification of patients at risk of developing scars due to acne is essential, as timely treatment can be a valuable resource to avoid the development of scars, and consequently, to prevent the morbidity (including the psychic effects) that are related to the pathology[10].

There are several known risk factors associated with the development of acne scars, although their individual weight is not yet fully categorized. Literature has long described the relationship between acne scars and the sun, giving special importance to avoid exposure in patients who receive certain types of treatments for correction[29]. Acne lesions, particularly the inflammatory ones, can cause permanent scarring[30]. Evidence suggests that the severity

of scaring is related to the delay in the start of acne treatment[31]. Literature generally correlates severity of acne to severity of acne scarring[32].

Following a systematic review and Delphi panel of worldwide acne experts Tan et al. suggests that, six factors are the most relevant for determining risk of acne scarring: severity of acne, inflammation of acne lesions, duration of acne, family history of acne scaring, squeezing/picking behaviors and patient history of acne scarring[11]. The same authors state that there are several other "possibly relevant risk factors" for acne scarring (patient compliance to treatment, history of relapse after treatment, location of acne lesions, skin preparation -comedone/cyst removal-, patient history of scarring not related to acne, and treatment type), as well as "less relevant risk factors" (seborrheic skin type, ethnicity, gender, smoking, geographical location and body mass index).. Although these risk factors might be the same for different populations[23], their individual weight could be different.

Considering the psychosocial impact of acne scars, tools to predict the risk of developing scars due acne are a needed. In 2017, Tan et al. described the first tool that classifies the risk of acne scarring in patients with acne, based on four risk factors – severity of acne, family history of acne scaring, duration of acne and picking behaviors – at lower-risk or higher-risk of developing scars due to acne[11]. The tool claims to appropriately categorize almost two thirds of the study population, with a sensitivity of 82% and a specificity of 43%[11]. The study population used for the evaluation included patients from the United States, France and Brazil. Its applicability outside the populations studied is yet to be determined.

Situation in Ecuador.

Ecuador is an attractive country for the study of the physiopathology of acne and its relationship with the development of scars. Its variety of climates and geographic regions,

and its equatorial position with respect to the sun generate a diversity of conditions that other countries in which acne is studied do not display. Additionally, Ecuador displays a wide ethnic variety, which also makes the study of acne particular, considering that the literature describes a different prevalence for the development of this disease, and for its consequences (as scars), depending on the ethnic group [33,34,35].

Only few and rather low-quality studies investigated the issue of acne and acne scarring in Ecuador (a large majority are thesis work of students from careers in life sciences and health). Hence, establishing the epidemiology and psychosocial consequences for Ecuador are a challenge. The Ecuadorian Ministry of Public Health states, in the acne guidelines prepared by the institution, that scars are present in 1-12% of the population[36]; anyway, it is not stated if this data is related to the Ecuadorian population, or to the general population worldwide.

A study conducted in the Ecuadorian city of Cuenca identified the presence of anxiety and depression in 14.6% and 44.3 % of patients with some degree of acne, respectively[37]. There is no consensual record of the general prevalence of acne in the Ecuadorian population. The Ecuadorian Ministry of Public Health recently issued a *Guide to Clinical Practice in the Management and Treatment of Acne*. It suggests that up to 2,5% of patients with acne have concomitant depressive symptoms[36]. This data strongly clashes with that of the acne study conducted in Cuenca. There are no official records regarding the use of this guide is in clinical practice.

Despite the existence of literature describing the risk factors for developing acne scars in the world, there is no data regarding its applicability to the Ecuadorian context. Due to the limited information regarding risk factors associated to acne scarring in Ecuador, studying different risk factors can prove useful for the construction of future public health interventions related to the prevention of the burden related to acne scarring.

Rationale.

Testing and adjusting the tool developed by Tan et al., to an Ecuadorean population will help identify patients at increased risk of developing scars due to acne. Once made available to general practitioners and dermatologists, as well as to the population for self-assessment may facilitate the patient's decision to go to the specialist for timely and adequate acne treatment. The availability of this tool will improve the quality and evidence of decision making of adolescents and families in relation to pharmaceutical and non-pharmaceutical treatments for acne.

Eventually, this study might contribute to the reduction of the incidence of acne scars, thus mitigating the loss of quality of life and the psychosocial burden associated with the condition. First, this study aims determining the risk factors associated with acne scarring in Ecuador. Second, this study aims at determining the level of concordance between self- and professional assessment of acne scars in an Ecuadorian population. Finally, based on the findings from the previous aims, this study aims to test and adjust Tan et al.'s tool for the assessment of acne scarring risk to the Ecuadorian population.

Aims and objectives.

The study aims to determine the risk factors, and respective weight, associated with the development of scars due to acne in an Ecuadorian population, by using dermatological evaluation as the gold standard. More specifically, this study aims:

- To assess potential risk factors and their statistical weight in a sample that represents an Ecuadorian population.
- To identify those risk factors for acne scarring development that are unique to an Ecuadorian population.

- To identify those risk factors that, despite of being relevant for other populations, are not applicable for predicting acne scarring development to an Ecuadorian population.

Secondly, this study aims to determine the level of concordance between self- and professional assessment (as well as between professionals) of acne scars in an Ecuadorian population. More specifically, this study aims:

- To determine the prevalence of self-reported acne scarring, by asking participants whether they consider having acne scars or not, and if yes, their severity.
- To determine the prevalence of acne scarring from the perspective of dermatologists (professional assessment), by requiring three dermatologists to analyze participants photographs, and determine whether they consider that the participant has acne scars or not, and if yes, the severity.
- To assess the degree of concordance and discordance between self- and professional assessment and between professionals in terms of presence or absence of acne scars and severity.

Finally, this study aims to test and adjust the acne scarring prediction tool created by Tan et al. to an Ecuadorian population. More specifically, this aim entails:

- To validate the tool of Tan et al. within an Ecuadorian population, by determining the calibration and discrimination of the tool in a sample, and by using dermatologists' assessment as the gold standard method for determining the presence or absence of acne scarring.
- To adapt the tool of Tan et al., if necessary, to the reality of an Ecuadorian population, by determining those risk factors that are unique to Ecuadorians for

predicting acne scar formation and transforming them into a questionnaire.

- To develop a systematic way of validating the tool proposed by Tan et al. to different populations.

Study design.

Overview.

A sample of young adults, recruited from the student population of Universidad San Francisco de Quito USFQ, Quito, Ecuador which had (or currently has) acne, will be administered a survey. They will be asked to answer as they would have done when their acne was at its worst. The survey will include the questions included in the tool developed by Tan et al. It will also contain questions regarding age, sex, ethnic origin, acne management history, manipulation of acne lesions, and self-perception of the presence and severity of acne scars, among other variables (see appendix to see the survey proposed for this study).

Upon administration of the survey, participants will be photographed and, based on those photographs, a team of three dermatologists will evaluate the presence or absence and severity of facial scars due to acne in each of the participants. Considering the dermatological evaluation as the standard for the determination of the presence of acne scars, the data of true positives, false positives, true negatives and false negatives will be computed. Calibration and discrimination of the tool will be determined as well, in order to validate it.

Risk factors for acne scarring will also be determined, and their individual weight will be calculated. At the same time, researcher will carry out an evaluation on the perception of acne scarring in patients suffering from acne, comparing it with the perception of the team of dermatologists, to determine the degree of existing concordance/discordance. The degree

of concordance/discordance within the team of dermatologists on the presence of scars due to acne in the group of patients studied will also be evaluated.

Type of Study.

The study in question is an epidemiological cross-sectional observational study. It is a cross-sectional study as data will be collected from a sample at a single time point to examine the relationship between disease (or other health related state) and other variables of interest. It is an observational study, as no intervention will be applied to the population. The independent variable will not be controlled by any of the researchers in any time in the course of the study.

Universe.

For the implementation of the study, a sample of students from Universidad San Francisco de Quito USFQ between 18-25 years old will be recruited, as a representation of an Ecuadorian population of that age. The participants will answer the survey as they would have answered when their acne was at its worst.

Even though the Universidad San Francisco de Quito USFQ's student population is not completely a representative sample of the Ecuadorian population between 18-25 years old (mainly due to socioeconomical reasons, as this university is by far the most expensive and exclusive one in Ecuador), it will be used as a proxy for it. This is because the study wants to prove, among other things, that the tool developed by Tan et al. can be used in different populations than the ones that were considered for developing it.

Once validated and adapted, if necessary, the tool by Tan et al. will focus on benefitting Ecuadorean adolescents and preadolescents, more specifically, children aged 10-14 years who do not yet have scars but who do have acne. The idea is that Ecuadorian doctors can use

the adjusted tool as an instrument of prevention to determine the degree of risk (higher or lower) of developing acne scars in each individual before they develop scars, so they can provide timely treatment. Similarly, individuals from this target population can also use the proposed tool, for its ease and simplicity, to be able to determine the necessity for timely treatment.

Time Length of the Study.

The study is designed to last 12 to 14 months. This amount includes data collection, data processing, as well as the report and manuscript writing. For more information, related to the specific activities of the study and their schedule, refer to **Table 6¡Error! No se encuentra el origen de la referencia.**.

Methodology.

Sampling strategy.

Elegibility Criteria for participants.

For an external validation study of a predictive logistic regression model, it is usually recommended a minimum of 100 events and 100 nonevents[12]. Based on the literature, around 40% of people who visit the dermatologist have scars due to acne[23]. Therefore, we estimated a minimum number of participants for the study at around 250 persons. Anyway, and considering that the study also includes investigation on the difference on perception about dermatological and self-assessment of the presence/absence of acne scars, and among dermatological evaluation as well, twice the minimum number of participants will be recruited.

As stated before, the sample used in this study will be helpful to validate and adapt, if necessary, the tool by Tan et al, as it will represent people who have already been exposed to acne and might or might not have developed scars. Anyway, the sample is not the same as the population that, once validated and adapted, will be targeted by the tool (which are pre-adolescents and adolescents who still don't develop scars due to acne, and who are able to use the tool as a preventive resource).

for the study population were developed and are presented in **Table 1.** describes eligibility criteria for the study sample. Eligibility will be based on self-reported information and researchers will rely on this information. No administrative verification regarding student status and age will be performed.

Table 1. Eligibility criteria for the participants in the study

Eligibility Criteria
• To be a person aged 18-25 at the time of participation. • To have suffered acne at any time point, including having active acne at the time of the study. • To be a student of Universidad San Francisco de Quito USFQ. • In case of using makeup during data collection, to be willing to remove it from the face to enable high quality photographs of the skin to be captured. • To accept signing the informed consent, including consent for photographs to be captured. • To have no beard and/or visible facial hair in men.

Recruitment process.

Participants will be recruited within the Universidad San Francisco de Quito USFQ. The recruitment process will begin with an information campaign one week before initiation of data collection. The information campaign will include:

- Dissemination of the event via Facebook™, with the support of one of several student associations social networks, and via the university's official student e-mail

service. These communications will explain the study and encourage students to be part of it.

- Visit to classes on both the Cumbayá campus and the Hospital de Los Valles medical campus, in which students will receive an explanation about the project to be carried out, and they will be invited to be part of it. For this, teachers will be previously contacted for researchers to be granted access to the classrooms. Preferably, the classes that are visited will have at least 50 students.

Invitation to students for project participation.

One week before the start of the project, an advertising campaign to facilitate the recruitment of participants will be initiated. It is planned to visit at least 8 classes of 50 students or more each. It is expected that at least one of the 3 main students taking part as researcher of the study will attend each visit in the classrooms. To systematize the process, a standardized message will be used.

Posters for the recruitment of participants.

To facilitate the recruitment of volunteers, social media will be used. If possible, Facebook™ pages from students' associations will provide the podium for diffusion. To guarantee a good explanation a tentative poster was created, that will be share with a specific invitation message.

Incentive for the participants.

To facilitate the interest of students to participate in the project, an incentive of 10 USD per participant in the form of a university cafeteria certificate of consumption will be given to students who complete both the survey and photograph requirements.

Data collection tools & dermatology expert eligibility.

Survey development.

A survey will be used to collect data regarding all three study aims. For this reason, the survey will not only include the questions used in the Tan et al. tool, but also other data that will enable the establishment of correlations with the risk of developing acne scars. The study by Tan et al. proposed that there are at least 18 risk factors related with acne scarring, with different weight each. They should be considered as possible risk factors for the Ecuadorian population, among others, until proven the opposite. For this reason, the survey will include 25 questions related to the following items:

- Severity of acne
- Duration of acne
- Family History of acne scarring
- Squeezing/picking behaviours
- Patient history of acne scarring
- Patient compliance on treatment.
- History of relapse after treatment
- Location of acne lesions
- Skin preparation (comedone/cyst removal)
- Patient history of scarring (not related to acne)
- Treatment type
- Seborrheic skin type
- Ethnicity
- Gender

- Smoking
- Geographical location
- Overweight vs Normal Weight.
- Emotional Stress
- Nutrition
- Age

Construction of a Photobooth.

The photobooth is an indispensable element in the research process, as it guarantees the quality and systematization of the photographs, including lighting intensity, color and angle as well as distance and angles between the participant and the camera. The photobooth will include an adjustable height stool, to ensure standard head position; the bench will allow the participant to look directly at the camera and present his/her right and left profile. Specific markings will be created for the photographers to determine if the height of the participant's head position is correct, and to tell participants where to look.

The background of the photobooth will be homogeneous black, as it is the most appropriate to avoid shadows of the flash, and without any type of relief or brightness, to guarantee the quality of the photograph. The photobooth will be constructed using wood tubes as the skeleton, and it will be completely covered with black curtains, even in the roof, so that the minimum of light from the surroundings will enter. With this, light can be standardized to all participants.

The camera will be held to one of the walls of the photobooth, at a standardized distance of 75 cm, so researchers do not need to enter to the structure, which would compromise the quality of the light. If modifications in the distance between patients and the camera have to

be made to ensure maximum quality of the picture, optical zoom will be used. Photographs will be first evaluated in a pilot study, to ensure that dermatologists can decipher the presence of absence of scars based on the photographs provided.

Eligibility of expert dermatologists and incentive.

To ensure that each picture is reviewed by at least two dermatologists, and to avoid fatigue from one single dermatologist reviewing the complete set of pictures, three professionals in the area will be chosen. Their evaluation about the presence/absence about acne scarring will be considered the standard diagnostic method.

To encourage and reward the contribution of dermatology experts, an incentive in the form of a dinner for two to the USFQ Restaurant MARCUS will be offered to each of the three participating dermatologists.

To define which three dermatologists will participate, the following eligibility criteria will be used (Table 2). The eligibility criteria will be assessed based on self-reported information. No administrative verification will be performed to ensure that dermatologists fulfil all requirements.

Table 2. Eligibility criteria for the selection of the team of dermatologists:

Eligibility criteria
• To be a doctor with a specialty degree in dermatology. • To have at least five years of experience in seeing patients with acne. • To have provided medical attention to at least 35 acne patients per years over the last 5 years. • To consent to the project participation an accept the workload proposed.

In the case that more than 3 dermatologists enter the inclusion criteria, the 3 with the highest number of publications related to acne will be selected. All inclusion criteria must be met.

Data collection.

Survey implementation.

The collection data from the survey and photos will be obtained, ideally, over a course of six days (but it can be extended for as long as it will take to collect data), divided into 2 weeks in a row (3 days per week). Each day will be organized with a 4-hour working period, 2 hours in the morning (10h00-12h00) and 2 hours in the afternoon (between 14h00-16h00), to ensure greater possibility of recruiting participants.

A stand will be placed near the university's coliseum, with a table, where the participants will be able to answer the survey, and then, they will go to the photo booth located next to the table, to take their respective photo.

For the permission of the stand, one month prior to the beginning of the data collection the authorization of Alexandra Polanco, who coordinates the use of public spaces in university, will be requested. Additionally, and 3 weeks in advance (having already obtained the permission of Alexandra Polanco), we will speak with *Planta Física*, the department in charge of storage, to request their support in saving the photo booth after each of the 6 working days.

The study protocol and implementation will respect the USFQ honor code, as well as the guidelines of the university's bioethics committee.

Photo shooting.

For the photograph shooting process, there are some requirements for the patient presentation. The patient hair must be tied or pushed back, so the facial features can be seen clearly. Strands of hair must be tucked away, which is why there will be available disposable hair clips to accomplish this. It is ideal that the patient is photographed make-up free or with minimal make-up (not overdone or distracting). Additionally, any extra accessories, jewelry or garments must be removed in order to appreciate the whole face with uniformity.

The three photograph that will be taken for each participant will include the following characteristics, which are recommended within dermatological iconography courses[38]:

- ISO low (80-100).
- Closed diaphragm for taking photos (AV mode f8.0 in compact cameras, AV mode f16.0 in reflex cameras)
- Use of flash, to guarantee the depth of field.
- Maximum resolution and minimum compression.
- Macro mode
- Automatic white balance.
- Average TV
- Frontal plane of the face and left and right profile.
- The face must be framed in its entirety within the photo, that is, the entire face and head must be included within each of the 3 planes in which the photos will be taken.
- Digital storage of the photograph, in JPEG or RAW format.

Matching between surveys and photographs.

To guarantee a good processing of the data, it is essential to guarantee that the surveys can be associated later with the respective photos of the participant. For this reason, it has been decided to follow the following system of taking surveys and photographs:

- Each study participant will answer the survey first; each survey will have an identification number.
- To guarantee that the survey can be associated with the photographs, and confidentially, each participant will immediately go to the photo booth.
- The 3 photographs will include the number of the survey, in the bottom (participants will hold the survey while being taken the pictures).

Three photos of each participant will be taken in a specific order, to avoid confusion (first in left profile, then in front, and finally in right profile). If any photo is blurred or for any reason there is the need to repeat it, the photograph that will be replaced will be deleted, to guarantee that there are always only 3 photos per participant (this will avoid confusion when processing data)**.**

Maintenance of the confidentiality process.

Confidentiality is essential in the research process, for this reason, the following considerations will be taken:

- Before conducting the survey, the patient will receive the informed consent form, and a small explanation on the part of the researchers about their rights as a participant.

- No participants will be requested to give their personal data at any time of the study, except for the epidemiological one required within the resolution of the survey (age, sex ...).
- During the photograph, each participant will use thin black glasses, designed by the research team, which will allow them to cover their eyes. This will ensure partial anonymity to the dermatologists and research team. While covering the eyes is an insufficient anonymity measure, the limited dispersal of the photograph (dermatologists and research team), eye covering is estimated enough.
- The photographs will be stored in the cloud, and only the team's principal investigators and dermatologists (under the supervision of team members) will have access to them; they will be password protected.
- The photographs will be erased 1 year after being taken.
- Photographs taken as part of the study will not be used for any academic or non-academic communication
- Only the research team will have access to the data set

Evaluation of the patients by the team of dermatologists

Due to logistics, three selected doctors will evaluate online the photos of the patients taken by the research team. To send the photos, a google drive document will be created where each photo will be labeled and classified according to the patient's number. Additionally, each doctor will receive a document where they can classify the evaluated patient as having or not acne scarring. In this document, each doctor will fill in with his professional opinion about the presence or absence of scars due to acne, and its severity. Each doctor will have his/her own document, so that his/her opinion is not influenced by the opinion of other colleagues

Pilot Study.

To guarantee the feasibility of the project, 6 weeks before starting the process of data collection with surveys and photographs, a small simulation will be carried out with a sample of 10 people. The pilot study aims to check the feasibility of the proposed study protocol, and to obtain valuable feedback from the process.

A survey with 25 questions -same survey that will be used for the final study- will be applied to eligible participants, who fulfilled all the eligibility criteria. The survey includes data related to the epidemiology of their acne, and the self-perception of related scars. Participants will answer the survey one by one, and will immediately go to a photobooth, where three photographs (front, right and left profile) will be taken, with standardized camera settings and light.

To ensure the best possible feedback from the process, a formal invitation to participate in the pilot study will be extended to at least 10 dermatologists. Inclusion and exclusion criteria will be applied to them. A final dermatological team containing both Ecuadorian dermatologists and at least 3 international acne experts is expected.

The images taken to the participants will be uploaded to the same proposed platform to facilitate the presentation of data to dermatologists. The statistical analysis will be carried out with the same guidelines described on the study protocol.

Safety Considerations.

None of the participants are exposed to a danger as such, as they will only fill out a brief survey and allow 3 photographs to be taken. However, the maintenance of confidentiality is essential in the process of patient safety and integrity. To achieve this, the research team has taken some measures of confidentiality.

Dissemination of Results & Publication Policy.

The information collected in this study will be shared through two major strategies. The first one is as a degree work for each of the 3 medicine students involved in the study, who will publish a final paper on the methods, results, analysis and discussion of the process as part of the requirements for graduation in the medical career from USFQ. There will be a total of 3 theses, which will be published within a period of 1 year from the data collection.

The second publication strategy consists of developing three scientific articles, one for each research question. The research articles will be prepared in parallel during the writing process of the theses works and will be oriented for publication in journals specialized in dermatology. The scientific papers will be published within a period of 2 years from the data collection.

Problems Anticipated.

Three main problems can be anticipated in this project. Researchers have planned the following solutions for them:

P1: Students agree to take the survey but then they deny being taken the pictures.

S1: Students will be told, before taking the survey, the necessity of also being taken the pictures. Students that present an initial deny, won't be consider. At the same time, pictures will be immediately taken after the survey.

P2: Dermatologist won't be willing to help as they might consider the work is too heavy and long.

S2: To solve this, we have decided to talk with the dermatologists before recruiting them for our team. At the same time, they will be offered to appear in the collaborators section of the published papers. A dinner at Marcus, the university fancy restaurant, will be offered as an incentive.

P3: The pictures get lost because there is a technical issue in the camera.

S3: To solve this, every 25 pictures taken, a security copy of the pictures will be made immediately and saved into a computer and into a USB drive.

Ethics.

Ethical Considerations.

Ethic is a key part of our study. We have proposed the following ethical considerations:

- Participants will be able to get out of the study whenever they want to. This means that even if they have signed an informed consent, they can request the investigators to erase their data and to not be considered for the study.
- The pictures won't be published in our thesis projects nor in the scientific papers.
- The photographs will be stored in the cloud, and only the team's main researchers and dermatologists (under supervision) will have access to them.
- The photographs will be destroyed after 1 year of being taken.
- After the study is finished, a general summary for the community will be published, so participants can have access to a document in which conclusions of the experiment can be shared in a comprehensible way.

Informed Consent.

An informed consent will be given to the students before they decide to fill the survey. The informed consent is written in Spanish, and it follows the structured required by the university.

Data management and statistical analysis.

Descriptive statistics.

Baseline characteristics (e.g., demographics, prognostic factors) will be described with

- Counts and proportions for categorical variables.
- Means ± standard deviations, median, interquartile range, minimum and maximum for continuous data.

Handling of missing data.

Multiple imputation will be conducted to impute missing data, as it is the preferred method for clinical prediction models when a predictor value is missing[39,40]. Briefly, multiple values of the missing predictor will be estimated using regression models and based on the observed predictors or patient's characteristics. Missing data are then replaced by the simulated value randomly selected from their predicted distribution. The MICE (Multivariate Imputation by Chained Equations) method will be used to create 20 imputed datasets.

Tool performance measure.

For each risk stratification criteria, we will calculate the proportion of patients categorized as low risk and determined the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV).

The performance of the tool will be assessed by evaluating calibration and discrimination measures[14].

Calibration corresponds to the agreement between the observed results and the predicted results (based on the tool). The following measures will be evaluated:

- Calibration plot (results will be plotted with predictions on the x-axis, and the outcome on the y-axis), alongside the calibration slope (which should be close to 1 if the tool performs well) and intercept ('calibration-in-the-large')
- Hosmer-Lemeshow goodness-of-fit test

Discrimination corresponds to the ability to differentiate patients with the outcome from those without it. To evaluate it, the following measures will be used:

- Receiver Operating Characteristic (ROC) curve, which plots the true positive rate (sensitivity) against the false positive rate (1-specificity)
- Concordance statistic (c-statistic) -area under the ROC curve- will be calculated to determine the degree of discrimination (a value of 0.5 represents chance, and 1 represents perfect discrimination)

If both calibration and discrimination cannot be established with the required parameters, the tool will not be considered valid for an Ecuadorian population.

Model adaptation

A logistic regression will be conducted based on the available variables.

To adapt the tool, the odds ratio will be calculated for each of the possible risk factors evaluated in the survey using a logistic regression. Factors with a 95%-confidence interval greater than 1, will be considered as significant risk factors. A new receiver operating curve with the retained factors will be plotted, and the most appropriate threshold will be selected based on clinical relevance. This data will be transformed into a questionnaire.

The performance of the new tool will be assessed by evaluating calibration and discrimination measures.

Level of concordance and discordance about acne scars.

A determination of the observed concordance between the self-perception of patients about acne scars, and the dermatological evaluation will also be done. To complete the analysis and adjust the effect of chance on the proportion of the calculated simple concordance, Cohen's Kappa concordance coefficient will be calculated, so it could be analyzed and interpreted.

To stablish the difference in perception about the presence/absence of acne scarring among the dermatological experts, the number of total cases in which all three dermatologists agree and disagree will be determined. Cohen's Kappa concordance coefficient will be calculated.

Other information related to the project.

Budget.

A 5000 USD grant was given to the Research Team to work on the present study by the Grant Program for Research of Universidad San Francisco de Quito USFQ, and by SIME (Sistemas Médicos USFQ). A big majority of the money will be used for the participants' incentive, as recruiting them is of huge importance for guaranteeing the success of the investigation. A more detailed explanation about the budget can be found in the following **Table 5**, and the schedule of activities is detailed in **Table 6**.

Table 5. General Budget for the project

General Budget		
Item	**Value**	**Justification**
Document Printing	100 USD	Each questionnaire will have at least three pages. The questionnaire will be supported with reusable documents to support the respondent. This amount is a conservative estimate (1000 pages in black and white ($ 0.05 / unit), 50 pages in color ($ 0.5 / unit)
Recruitment advertising	200 USD	The recruitment of participants will require an advertising campaign of the USFQ, including posters, Facebook ads, etc.
Data collection stand	800 USD	The data collection stand will include an area for participants to answer the questionnaire and a photo booth, including professional lighting and dark shading to ensure quality images
Incentive for participants	3,100 USD	Based on an expected sample of 310 students and an incentive of $ 10 per participant for consumption in the university cafeteria
Incentive for dermatologist	200 USD	Based on an expected group of 3 dermatologist; a two- people dinner at Marcus will be offered for them.

Investigation Assistant	600 USD	4 hours per week for 12 months; the assistant will support the organization and administration of the Project. It will include technical and administrative tasks, including technical support for the data collection post, data anonymization, etc.
TOTAL	5,000 USD	

Table 6. General Schedule of activities

SCHEDULE	**YEAR**							
Description of the activity	**DATE**							
		1	**2**	**3**	**4**	**5**	**6**	**7**
First protocol draft	30/01/2018	X						
Second protocol draft	22/02/2018	X						
Third protocol draft	20/04/2018	X						
Fourth protocol draft	30/05/2018	X						
Fifth protocol draft	20/06/2018	X						
Final protocol	26/08/2018	X						
Document submission for the bioethics committee	31/08/2018	X						
Construction of the photobooth	01/09/2018	X						
Dermatologists recruitment	15/09/2018	X						
Acquisition of incentives for the participants.	15/10/2018	X						

Photography test	15/11/2018 until 24/ 12/2018	X						
Adaptation of the photo booth based on photography tests	05/01/2019 until 05/ 02/2019		X					
Pilot Study	February, 2019		X					
Project diffusion for recruiting participants	First week of March, 2019		X					
Data collection	March and April, 2018		X					
Data processing	May, 2019		X					
Writing of the publications	March to June, 2019		X					
Final publications ready for dermatology journal submission (to be defined)	01/08/2019		X					

References of the study protocol.

1. Tan, J. K. L. & Bhate, K. A global perspective on the epidemiology of acne. *Br. J. Dermatol.* **172 Suppl 1**, 3–12 (2015).

2. Asai, Y. *et al.* Management of acne: Canadian clinical practice guideline. *CMAJ Can. Med. Assoc. J.* **188**, 118–126 (2016).
3. Hazarika, N. & Archana, M. The Psychosocial Impact of Acne Vulgaris. *Indian J. Dermatol.* **61**, 515–520 (2016).
4. Zauli, S. *et al.* Which factors influence quality of life in acne patients? *J. Eur. Acad. Dermatol. Venereol. JEADV* **28**, 46–50 (2014).
5. Barnes, L. E., Levender, M. M., Fleischer, A. B. & Feldman, S. R. Quality of Life Measures for Acne Patients. *Dermatol. Clin.* **30**, 293–300 (2012).
6. Tasoula, E. *et al.* The impact of acne vulgaris on quality of life and psychic health in young adolescents in Greece. Results of a population survey. *An. Bras. Dermatol.* **87**, 862–869 (2012).
7. Mallon, E. *et al.* The quality of life in acne: a comparison with general medical conditions using generic questionnaires. *Br. J. Dermatol.* **140**, 672–676 (1999).
8. Dréno, B. *et al.* How People with Facial Acne Scars are Perceived in Society: an Online Survey. *Dermatol. Ther.* **6**, 207–218 (2016).
9. Chuah, S. Y. & Goh, C. L. The Impact of Post-Acne Scars on the Quality of Life Among Young Adults in Singapore. *J. Cutan. Aesthetic Surg.* **8**, 153–158 (2015).
10. Madden, W. S. *et al.* Treatment of acne vulgaris and prevention of acne scarring: canadian consensus guidelines. *J. Cutan. Med. Surg.* **4 Suppl 1**, S2-13 (2000).
11. Tan, J. *et al.* Development of an atrophic acne scar risk assessment tool. *J. Eur. Acad. Dermatol. Venereol. JEADV* **31**, 1547–1554 (2017).
12. Substantial effective sample sizes were required for external validation studies of predictive logistic regression models. - PubMed - NCBI. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15845334. (Accessed: 4th March 2019)

13. Md, J. T., Md, <sup>a/sup> Sewon Kang & MD[c], <sup>b/sup> and James Leyden. Prevalence and Risk Factors of Acne Scarring Among Patients Consulting Dermatologists in the USA. *J Drugs Dermatol* (1485790771). Available at: http://jddonline.com/articles/dermatology/S1545961617P0097X. (Accessed: 29th May 2018)
14. Steyerberg, E. W. *et al.* Assessing the Performance of Prediction Models: A Framework for Traditional and Novel Measures. *Epidemiology* **21**, 128–138 (2010).
15. Almeida, H. de, Cecconi, J., Duquia, R. P., Souza, P. R. & Breunig, J. Sensitivity and specificity of self-reported acne in 18-year-old adolescent males. *Int. J. Dermatol.* **52**, 946–948 (2013).
16. Clark, A. K., Saric, S. & Sivamani, R. K. Acne Scars: How Do We Grade Them? *Am. J. Clin. Dermatol.* **19**, 139–144 (2018).
17. Dreno, B. *et al.* ECCA grading scale: an original validated acne scar grading scale for clinical practice in dermatology. *Dermatol. Basel Switz.* **214**, 46–51 (2007).
18. Dreno, B. & Poli, F. Epidemiology of acne. *Dermatol. Basel Switz.* **206**, 7–10 (2003).
19. Bhate, K. & Williams, H. C. Epidemiology of acne vulgaris. *Br. J. Dermatol.* **168**, 474–485 (2013).
20. Thiboutot, D. *et al.* New insights into the management of acne: an update from the Global Alliance to Improve Outcomes in Acne group. *J. Am. Acad. Dermatol.* **60**, S1-50 (2009).
21. Gollnick, H. P. *et al.* A consensus-based practical and daily guide for the treatment of acne patients. *J. Eur. Acad. Dermatol. Venereol. JEADV* **30**, 1480–1490 (2016).
22. Zaenglein, A. L. *et al.* Guidelines of care for the management of acne vulgaris. *J. Am. Acad. Dermatol.* **74**, 945-973.e33 (2016).

23. Tan, J., Kang, S. & Leyden, J. Prevalence and Risk Factors of Acne Scarring Among Patients Consulting Dermatologists in the USA. *J. Drugs Dermatol. JDD* **16**, 97–102 (2017).
24. Evaluation of the prevalence, risk factors, clinical characteristics, and burden of acne scars among active acne patients in Brazil, France, and the USA - Journal of the American Academy of Dermatology. Available at: https://www.jaad.org/article/S0190-9622(17)31005-8/fulltext. (Accessed: 27th June 2018)
25. Fajardo, M. E. T. *et al.* PROYECTO DE INVESTIGACIÓN PREVIA A LA OBTENCION DEL TÍTULO DE LICENCIADO EN ENFERMERÍA. 80
26. Scar treatments can improve patients' quality of life | American Academy of Dermatology. Available at: https://www.aad.org/media/news-releases/scarring. (Accessed: 30th May 2018)
27. Koo, J. The psychosocial impact of acne: patients' perceptions. *J. Am. Acad. Dermatol.* **32**, S26-30 (1995).
28. Sulzberger, M. B. & Zaidens, S. H. Psychogenic Factors in Dermatologic Disorders. *Med. Clin. North Am.* **32**, 669–685 (1948).
29. Erbağci, Z. & Akçali, C. Biweekly serial glycolic acid peels vs. long-term daily use of topical low-strength glycolic acid in the treatment of atrophic acne scars. *Int. J. Dermatol.* **39**, 789–794 (2000).
30. Holland, D. B. *et al.* Inflammation in acne scarring: a comparison of the responses in lesions from patients prone and not prone to scar. *Br. J. Dermatol.* **150**, 72–81 (2004).
31. Kravvas, G. & Al-Niaimi, F. A systematic review of treatments for acne scarring. Part 1: Non-energy-based techniques. *Scars Burns Heal.* **3**, 2059513117695312 (2017).
32. Layton, A. M., Henderson, C. A. & Cunliffe, W. J. A clinical evaluation of acne scarring and its incidence. *Clin. Exp. Dermatol.* **19**, 303–308 (1994).

33. Perkins, A. C., Cheng, C. E., Hillebrand, G. G., Miyamoto, K. & Kimball, A. B. Comparison of the epidemiology of acne vulgaris among Caucasian, Asian, Continental Indian and African American women. *J. Eur. Acad. Dermatol. Venereol. JEADV* **25**, 1054–1060 (2011).
34. Davis, E. C. & Callender, V. D. A review of acne in ethnic skin: pathogenesis, clinical manifestations, and management strategies. *J. Clin. Aesthetic Dermatol.* **3**, 24–38 (2010).
35. Quarles, F. N. *et al.* Acne vulgaris in richly pigmented patients. *Dermatol. Ther.* **20**, 122–127 (2007).
36. GUÍA DE PRÁCTICA CLÍNICA PARA EL DIAGNÓSTICO Y TRATAMIENTO DEL ACNÉ. Ministerio de Salud Pública del Ecuador (2018).
37. Coello Loyola, A. M., de la Torre Carrillo, D. R., Iglesias Barzallo, P., Zeas, I. & Morocho, I. Trastornos Adaptativos en Pacientes con Acné en Consulta Externa de Dermatología del Hospital "Vicente Corral Moscoso", 2011. *Rev. Médica Hosp. José Carrasco Arteaga* **6**, 125–128 (2014).
38. Rosa Taberner Ferrer. Curso de Iconografía Dermatológica- I. (11:27:53 UTC).
39. Janssen, K. J. M. *et al.* Dealing with Missing Predictor Values When Applying Clinical Prediction Models. *Clin. Chem.* **55**, 994–1001 (2009).
40. Schafer, J. L. Multiple imputation: a primer. *Stat. Methods Med. Res.* **8**, 3–15 (1999).

Appendices.

Survey.

Survey was originally applied in Spanish, so the Spanish version is included here:

Universidad San Francisco de Quito

Colegio de Ciencias De Salud - Escuela de Medicina
Trabajo de Titulación

Encuesta para los Participantes del Estudio

Gracias por decidir participar en esta investigación. Tu ayuda es indispensable para poder alcanzar el éxito del proyecto, y así desarrollar una herramienta que permita predecir el riesgo que una persona tiene de desarrollar cicatrices por acné. Es por eso por lo que resulta indispensable la veracidad de las respuestas. A continuación, se te presenta una serie de preguntas relacionadas contigo (edad, género…), y otro grupo de preguntas relacionadas con tu proceso de acné. Las preguntas y respuestas son confidenciales, por lo que tu honestidad es apreciada al responderlas. Puedes consultar a cualquier miembro del equipo si tienes alguna duda con respecto a una pregunta durante el proceso de llenar el cuestionario. De nuevo, muchas gracias por tu ayuda.

1. ¿Cuántos años tienes? (años cumplidos hasta el día de hoy) _____

2. ¿Con qué género te identificas? Marca con una X en el recuadro con tu respuesta
    a. Femenino
    b. Masculino
3. ¿Con qué etnia te identificas? Marca con una X en el recuadro con tu respuesta

a. Mestizo

b. Afroecuatoriano

c. Indígena

d. Blanco

e. Otra (especificar) _____

4. Tomando en cuenta el momento en el que tuviste el episodio más severo de acné, ¿en qué región geográfica del Ecuador vivías? Marca con una X en el recuadro con tu respuesta

a. Costa

b. Sierra

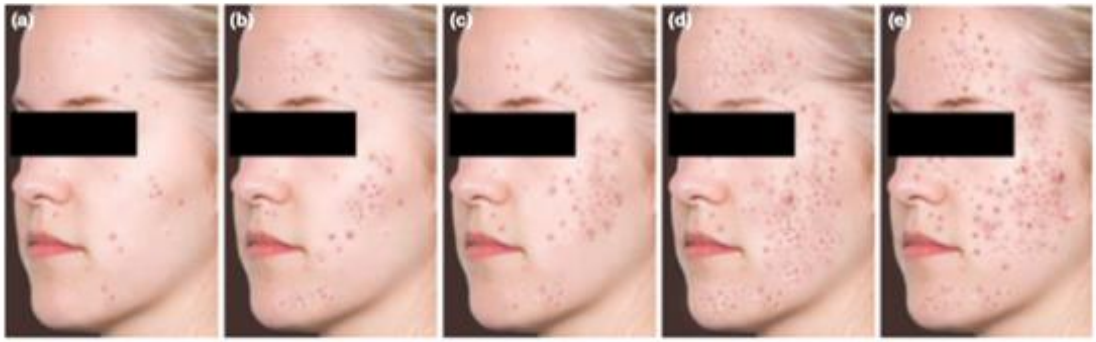
c. Amazonía

d. Galápagos

e. Otro lugar fuera del Ecuador (especificar ciudad y país) _____

5. Mira las fotografías que tienes frente a ti pegadas en la mesa bajo el cartel *"Fotografías para la pregunta 5"*[1]. Ellas muestran acné en distintos grados de severidad. Tomando en cuenta el momento en el que tuviste el episodio más severo de acné, ¿qué fotografía mejor representa tu grado de acné? Marca con una X en el recuadro con la letra que corresponda a la foto con la que te identificas.

[1] Tomada con autorización de Tan y colaboradores.



a) a

b) b

c) c

d) d

e) e

6. ¿Tus padres o hermanos/as han tenido historia de cicatrices por acné? Marca con una X en el recuadro con tu respuesta

    a. Sí

    b. No

7. ¿A qué edad empezó tu acné? (Ej. A los 13 años)

8. ¿Cuánto tiempo duró tu acné? (Ej. 5 meses. Ej. 2.- 1 año)

9. ¿Con qué frecuencia manipulabas/manipulas los granos asociados a acné? (Manipulación entendiéndose como exprimir o extraer el material de las lesiones) Marca con una X en el recuadro con tu respuesta

    a. Nunca

    b. Rara vez

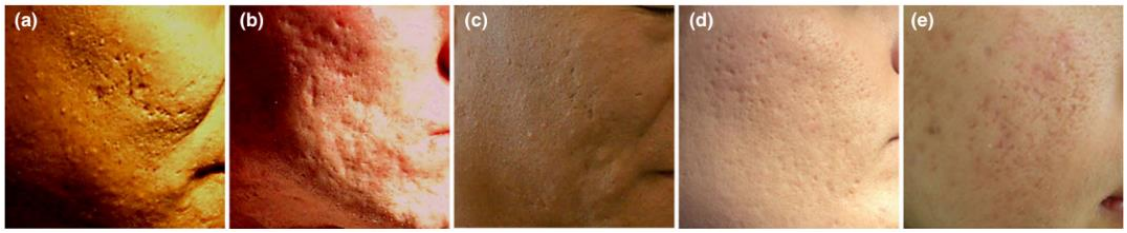
c. Algunas veces

d. Frecuentemente

e. Todo el tiempo

Mira las fotografías[2] pegadas en la mesa bajo el cartel *"Fotografías para la pregunta 10".*

Estas fotografías ilustran las diversas formas que pueden tomar las cicatrices por acné.



10. En base a estas fotografías, ¿consideras tú que tienes cicatrices por acné? Marca con una X en el recuadro con tu respuesta

    a. Sí

    b. No

11. ¿Tienes cicatrices en la cara por eventos diferentes al acné (caídas, cirugías, varicela, quemaduras…)? Marca con una X en el recuadro con tu respuesta

    a. Sí

    b. No

12. ¿Has usado o usas actualmente algún tratamiento no prescrito por un médico para el tratamiento de tu acné (jabones, pastillas o cremas que no te fueron recetadas por un médico)? Marca con una X en el recuadro con tu respuesta

[2] Fotografías tomadas con permiso de Tan y colaboradores.

a. Sí

b. No

13. En algún momento de la evolución de tu acné, ¿consultaste a un médico dermatólogo? Marca con una X en el recuadro con tu respuesta

a. Sí

b. No

Si contesta No, ir a la pregunta 17.

14. En caso de haber respondido Sí a la pregunta anterior, ¿recibiste o recibes algún tratamiento prescrito por parte del médico que visitaste? (jabones, pastillas, cremas) Marca con una X en el recuadro con tu respuesta

a. Sí

b. No

Si contesta No, ir a la pregunta 17

15. En caso de haber respondido Sí a la pregunta anterior, ¿completaste el tratamiento de la manera en que te indicó el médico? Marca con una X en el recuadro con tu respuesta

a. Si

b. No

c. Sigo en el tratamiento

16. Después de haber utilizado el tratamiento prescrito por el médico (completo o incompleto), tú crees que las lesiones de acné: (Marca con una X en el recuadro con tu respuesta)

a. Desaparecieron

b. Mejoraron, pero no desaparecieron completamente

c. No hubo ningún cambio (no mejoraron)

17. Mientras tenías los episodios de acné, ¿tú fumabas cigarrillo? Marca con una X en el recuadro con tu respuesta

a. Sí

b. No

18. En relación con el peor episodio de acné, tú crees que en ese momento estabas con: (Marca con una X en el recuadro con tu respuesta)

a. Peso normal

b. Obesidad

19. ¿Tienes una piel seborreica (grasosa), ya sea porque un médico te lo ha dicho o por tu impresión propia? Marca con una X en el recuadro con tu respuesta

a. Sí

b. No

20. Durante el episodio más severo de acné que tuviste, ¿consideras que tu alimentación era rica en grasa? Marca con una X en el recuadro con tu respuesta

a. Sí

b. No

21. Durante el episodio más severo de acné que tuviste, ¿consideras que estuviste sometido a un estrés psicológico y emocional más fuerte del usual? Marca con una X en el recuadro con tu respuesta

    a. Sí

    b. No

El acné puede estar presente en varias regiones del cuerpo. A continuación, se presenta una tabla con las localizaciones más frecuentes del acné. Por favor encierra la palabra “Sí” en caso de que hayas tenido o tengas acné en esa región, o la palabra “No” en caso de que no tengas acné en ninguna de estas regiones.

22. Cara	Sí	No
23. Cuello	Sí	No
24. Espalda	Sí	No
25. Pecho	Sí	No

Informed Consent.

Comité de Ética de Investigación en Seres Humanos

Universidad San Francisco de Quito

El Comité de Revisión Institucional de la USFQ

The Institutional Review Board of the USFQ

Formulario Consentimiento Informado

Título de la investigación: Evaluación y adaptación de una herramienta para estimar el riesgo de tener cicatrices inducidas por acné en una población ecuatoriana

Organización del investigador: Universidad San Francisco de Quito

Nombre del investigador principal: Jonathan R. Guillemot

Datos de localización del investigador principal: jrguillemot@usfq.edu.ec

+593980528404

Coinvestigadores: Mikaela Dominique Camacho Olalla, Jorge Antonio Estrella Porter, María Isabel Viteri Suárez

DESCRIPCIÓN DEL ESTUDIO
Introducción
El acné es una enfermedad muy prevalente a nivel mundial; se estima que hasta casi 10% de la población actual del mundo tiene acné. Las cicatrices que el acné puede generar se consideran uno de sus principales problemas, por el alto malestar psicológico y emocional asociados. Un tratamiento

oportuno del acné puede evitar, en muchos de los casos, la formación de cicatrices. Es por eso que resulta indispensable desarrollar una herramienta que permita predecir el riesgo de que una persona con acné desarrolle cicatrices, para motivarla a recibir el tratamiento adecuado de forma oportuna. No existe todavía una herramienta aplicable a una población ecuatoriana.

Propósito del estudio

El presente estudio busca validar un cuestionario desarrollado en una población de Francia, Estados Unidos y Brasil, para la predicción del riesgo de desarrollar cicatrices por acné (alto o bajo). Esta herramienta se probará en una población ecuatoriana. Participarán alrededor de 500 personas entre 18-25 años de la USFQ. De validarse, el cuestionario será útil para que varios médicos puedan aplicarlo a personas que tienen acné, y puedan determinar qué tan alto o bajo es el riesgo de que desarrollen cicatrices. De esta forma, las personas con acné podrán decidir qué tan urgente y necesario es que se apliquen un tratamiento para su acné, con el fin de evitar las cicatrices asociadas.

Descripción de los procedimientos

Para su participación dentro del estudio, necesitamos que cada persona nos colabore con 8 minutos de su tiempo. Los primeros 4 minutos se utilizarán para llenar una encuesta, en la que se harán preguntas sobre el participante (edad, sexo…) y sobre su acné (intensidad, duración…) Terminada la encuesta, cada participante pasará a un fotomatón, donde se le tomarán 3 fotos de sus rostros, con unas gafas que permitirán mantener anónima su identidad. La toma de fotografías tardará alrededor de 4 minutos. Los participantes concluyen su aporte al proyecto con estos dos pasos (llenar encuesta y acceder a la toma de 3 fotografías). Las fotografías serán luego analizadas por un equipo de 3 dermatólogos para determinar la presencia o ausencia de cicatrices por acné. Las fotografías pueden ser accedidas únicamente por el equipo de investigación, y serán destruidas al cabo de un año. El anonimato de los participantes se mantendrá durante todo el proceso.

Riesgos y Beneficios

Riesgos:

El estudio como tal no presenta ningún riesgo para el participante, pues consiste sólo en la toma de datos y de fotografías. La única situación riesgosa de algún modo es que las fotos se filtren. Sin embargo, eso no ocurrirá pues existen varias medidas para garantizar la confidencialidad del proceso.

Beneficios:

El beneficio principal del estudio recae sobre la población ecuatoriana con acné, pues tendrán a disposición suya y de médicos un cuestionario que actuará como herramienta para predecir el riesgo de desarrollar cicatrices. De esta forma, tendrán más información para decidir sobre la necesidad de acudir a un especialista para recibir un tratamiento oportuno y urgente.

Confidencialidad de los datos

Para nosotros es muy importante mantener su privacidad, por lo cual aplicaremos las medidas necesarias para que nadie conozca su identidad ni tenga acceso a sus datos personales:

- No se solicitará a los participantes que proporcionen sus datos personales en ningún momento del estudio, excepto el epidemiológico requerido en la resolución de la encuesta (edad, sexo ...).
- Durante la toma de fotografías, cada participante usará gafas negras delgadas, diseñadas por el equipo de investigación, que les permitirán taparse los ojos. Esto asegurará el anonimato parcial de los dermatólogos y el equipo de investigación. Mientras que cubrir

los ojos es una medida de anonimato insuficiente, la dispersión limitada de la fotografía (dermatólogos y equipo de investigación), la cobertura ocular se estima suficiente.

- Las fotografías se almacenarán en la nube, y solo los investigadores principales y los dermatólogos del equipo (bajo la supervisión de los miembros del equipo) tendrán acceso a ellos; estarán protegidos por contraseña.
- Las fotografías serán destruidas desde 1 año después de ser tomadas.
- Las fotografías tomadas como parte del estudio no se utilizarán para ninguna comunicación académica o no académica
- Solo el equipo de investigación tendrá acceso al conjunto de datos.
- Su nombre no será mencionado en los reportes o publicaciones.
- El Comité de Bioética de la USFQ podrá tener acceso a sus datos en caso de que surgieran problemas en cuando a la seguridad y confidencialidad de la información o de la ética en el estudio.

Derechos y opciones del participante

- Usted puede decidir no participar en el estudio si considera que no está de acuerdo con cualquier parte de este. Aunque haya firmado el consentimiento informado, usted puede retirarse del estudio en cualquier momento del mismo.
- Como participante, tiene derecho a que los investigadores respondan cada una de sus preguntas durante todo el proceso.
- Tiene derecho a recibir respuestas claras y honestas.
- Usted no recibirá ningún pago ni tendrá que pagar absolutamente nada por participar en este estudio, aunque su tiempo y esfuerzo será agradecido con un bono de 10 dólares

estadounidenses para el consumo de alimentos y bebidas dentro de la cafetería de la universidad.
Información de contacto
Si usted tiene alguna pregunta sobre el estudio por favor llame al siguiente teléfono 0980528404 que pertenece a Jonathan Guillemot, o envíe un correo electrónico a jrguillemot@usfq.edu.ec Si usted tiene preguntas sobre este formulario puede contactar al Dr. William F. Waters, presidente del Comité de Bioética de la USFQ, al siguiente correo electrónico: comitebioetica@usfq.edu.ec
Consentimiento informado
Comprendo mi participación en este estudio. Me han explicado los riesgos y beneficios de participar en un lenguaje claro y sencillo. Todas mis preguntas fueron contestadas. Me permitieron contar con tiempo suficiente para tomar la decisión de participar y me entregaron una copia de este formulario de consentimiento informado. Acepto voluntariamente participar en esta investigación.

Firma del participante	Fecha
Firma del testigo *(si aplica)*	Fecha
Nombre del investigador que obtiene el consentimiento informado	Fecha
Firma del investigador	Fecha

Invitation message to students for project participation .

English Version.

Good morning. We are 5th and 6th year medical students from USFQ, and we are working on a research project we would like to invite you to. What we want to do in this study is to adjust a questionnaire to Ecuador. The questionnaire aims to predict the risk of developing scars due to acne. For this reason, we need to recruit 300-400 participants, and we would very much like you to be part of our project. We need students between 18-25 years who have suffered or currently suffer from acne. What it requires from you is to fill out a survey of 15 questions and let us take three photos. The photos will be anonymized and used only for the purpose of this research project. These photos will be reviewed by dermatologists to assess your skin, so we can relate to your survey responses. We will be installed [location] from [date range], from [time range]. Your help is indispensable. Participants will receive an incentive of 10 dollars of consumption within the cafeteria of the university for their help in the process. We hope to count with your participation.

Spanish Version

Buenos días. Somos estudiantes de medicina de quinto y sexto año de la USFQ, y estamos trabajando en un proyecto de investigación al que nos gustaría invitarles. Lo que queremos hacer en este estudio es ajustar un cuestionario a Ecuador. El cuestionario tiene como objetivo predecir el riesgo de desarrollar cicatrices debido al acné. Por esta razón, necesitamos reclutar entre 300 y 400 participantes, y nos gustaría que ustedes sean parte de nuestro proyecto. Necesitamos estudiantes entre 18 y 25 años que hayan sufrido o que actualmente tengan acné. Lo que requieren ustedes es completar una encuesta de 15 preguntas y tomarse tres fotos. Las fotos serán anonimizadas y utilizadas solo para el

propósito de este proyecto de investigación. Estas fotos serán revisadas por dermatólogos para evaluar su piel, para que podamos relacionarnos con las respuestas de su encuesta. Se instalará [ubicación] desde [rango de fechas], desde [intervalo de tiempo]. Tu ayuda es indispensable. Los participantes recibirán un incentivo de 10 dólares de consumo dentro de la cafetería de la universidad por su ayuda en el proceso. Esperamos contar con tu participación.

Invitation poster to students for project participation.

Figure 1. Tentative model of the poster to be used.

The following message will be shared with the poster:

"The Health Research Group of the USFQ School of Medicine is working on an unprecedented project in the country, and we need your help. What we want to do in this study is to validate in an Ecuadorian population a tool (questionnaire), developed by a French study, to predict the risk of developing acne scars, that is, to see if this instrument can adequately predict the risk of developing scarring in patients who have suffered or suffer from acne. For this, we need to recruit 500 participants, and we would very much like you to be part of the process. We need students between 18-25 years of age who have suffered or currently suffer from

acne, who are willing to fill out a survey of 15 questions and take three photos (which will adequately preserve the anonymity of each one) in a specially constructed photo booth. These photos will be evaluated by a team of 3 dermatologists to define the presence or absence of scars due to acne, so we can determine if the questionnaire given to you may or may not predict those patients who have higher or lower risk of developing acne scarring. We will be installed next to the Coliseum these days (define days), from 10h00-12h00 and from 14h00-16h00. Your help is indispensable. Participants will receive an incentive of 10 dollars of consumption within the cafeteria of the university for their help in the process. We hope count with your participation."