


ORIGINAL ARTICLE

A cross-sectional epidemiological study conducted in Argentina to evaluate the impact of the exposome on skin aging

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Abstract

Background: Skin aging is a gradual cumulative process that may be accelerated by various exposome factors.

Aims: To investigate associations between exposome factors and facial skin aging in 11 locations in Argentina.

Patients/Methods: An observational, cross-sectional study with assessments by exposome questionnaire, Glogau photoaging classification from I to IV, AI-based algorithm analysis of 7 skin aging signs, and SCINEXA score.

Results: Of 1346 participants, most were women (82%), aged 31–50 years (62%), of skin phototype III (52%), and living in urban areas (94%). The Glogau skin age was higher than the chronological age for 28% of overall participants, 36% of men, and 45% of participants from Ciudad de Buenos Aires versus 12% from Jujuy ($p < 0.001$). Being male (OR = 1.59; 95% CI 1.18–2.13), exposed to agrochemicals (OR = 1.59; 95% CI 1.01–2.51), of lower socioeconomic levels (OR = 2.06; 95% CI 1.32–3.21) and doing outdoor physical activity (OR = 1.33; 95% CI 1.00–1.76) increased the risk for premature aging. Odds decreased with high daily intake of water (OR = 0.76; 95% CI 0.59–0.97), daily dermocosmetic use (moisturizers [OR = 0.72; 95% CI 0.55–0.94], cleansers [OR = 0.53; 95% CI 0.42–0.67], retinoids [OR = 0.61; 95% CI 0.39–0.95]), and antiaging treatments (OR = 0.74; 95% CI 0.57–0.97).

Conclusions: Some exposome factors increased the risk for premature skin aging (physical outdoor activity, exposure to agrochemicals), while others were protective factors (high water intake, antiaging treatments, use of dermocosmetics). Locations with higher pollution levels had more premature skin aging.

KEYWORDS

artificial intelligence, exposome, Glogau scale, lifestyle, skin aging

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1 | INTRODUCTION

The exposome encompasses all external and internal environmental exposures (including lifestyle factors) an individual is subjected to throughout their lifetime from conception to death.^{1,2} Skin aging is a gradual cumulative process over time that may be accelerated by various exposome factors. Skin changes are related to genetic constitution, environmental factors, nutrition, and other factors. Complementing the genome, the skin aging exposome provides a more complete environmental exposure assessment throughout the lifespan, including the external (e.g., solar radiation, pollution, climate) and internal factors (e.g., hormones and lifestyle factors [lack of sleep, stress, smoking, nutrition]), as well as the response of the human body to these factors that lead to biological and clinical signs of skin aging.³ The clinical and biological impact of the exposome factors, especially solar exposure, air pollution, hormones, nutrition, and psychological factors, that induce or modify various skin conditions have been reviewed.⁴

Aging is associated with changes in the secretory activity of both dermal papillary and reticular fibroblasts.⁵ The first signs of facial skin aging begin to appear from around 25 years of age with small, shallow fine lines at the outer corners of the eyes (crow's feet), and on the cheeks and forehead; they may be triggered by facial expression, for example, frowning. The nasolabial folds are deeper wrinkles that are associated with loss of volume. Another effect of aging on facial skin is the loss of density, over the entire surface in the form of thinner and weaker skin or associated with deeper wrinkles in certain areas, with a decrease in luminosity resulting in duller skin. From around 50 years of age in women, the decline in estrogen at the menopause may lead to important physical changes in skin and hair, as well as other symptoms and emotional changes.⁶ The skin also becomes less firm as collagen levels decrease and the skin loses structure, volume, and cohesion of the tissues.⁷

The primary objective of this study was to investigate associations between exposome factors and facial skin aging in inhabitants from 11 locations in Argentina, to determine whether the contribution of external and internal environmental factors affect people in a similar way according to chronological age or whether the facial aging process is accelerated in various locations.

2 | MATERIALS AND METHODS

2.1 | Participants

In this epidemiological, observational, cross-sectional study, participants from 11 Argentinian locations (in a total of 8 provinces) were recruited consecutively when attending a private dermatologist. Inclusion criteria were men or women aged from 25 to 60 years old, with any skin type (dry, normal, combination, oily), skin phototypes I to V, and being able to complete an anonymous exposome questionnaire.

2.2 | Assessments

2.2.1 | All assessments were performed at a single visit

The exposome questionnaire included a series of questions related to the exposome and included 14 questions on demographic variables and 27 questions on lifestyle variables covering diet, stress, physical activity, smoking, sleep, sun exposure and use of sunscreen, use of dermocosmetics and antiaging procedures.

A photograph of the face was taken and sent for central evaluation by two independent evaluating dermatologists unaware of the chronological age of the participants. The data was collected completely anonymously; the photographs were treated confidentially and, once analyzed, were deleted.

Facial aging was clinically assessed using the Glogau photoaging classification of four types from type I, "no wrinkles;" type II, "wrinkles in motion"; type III, "wrinkles at rest"; type IV, "only wrinkles."⁸ Skin aging was evaluated as normal or accelerated in relation to the chronological age of the participant. To determine the interobserver variation of the two Glogau observers performing facial aging assessments with the Glogau scale, a Kappa coefficient was calculated.

The photographs were also assessed by REDACTED (REDACTED), an AI-based algorithm grading 7 facial skin aging signs (firmness, spot intensity, pore visibility, lack of radiance, under-eye wrinkles, visibility of coarse wrinkles, fine lines).⁹⁻¹¹

SCINEXA is a validated clinical tool¹² that was used to differentiate between intrinsic and extrinsic skin aging on a sample of 10–20 volunteers per location. SCINEXA calculates an overall skin aging score from the individual scores of 23 skin aging signs; comprising 5 items indicative of intrinsic or chronological aging (maximum achievable score of 15) and 18 items highly characteristic of extrinsic skin aging (maximum achievable score of 54) to simultaneously differentiate extrinsic aging from intrinsic aging factors.¹²

2.3 | Statistical analysis

Based on the Freeman formula: $[n = 10 * (k + 1)]$, where k is the number of independent variables or interactions to be considered, a sample size of 150 volunteers per region was required for a total sample size of around 1350 participants from a total of nine regions. Each of the 8 different provinces were counted as a region, except for Buenos Aires, which was counted as two regions and included a total of 293 participants from two cities (Lobos and Mar del Plata) with different climatic conditions. Assuming that 10% of the volunteers show premature skin aging according to the Glogau scale, this sample size allowed for independent variables to be analyzed simultaneously in the multivariate model and to reach the number of events per variable in the model.¹³

The relationship between each independent variable and skin aging (normal or premature aging) was analyzed by applying the χ^2 test (a bilateral p -value < 0.05 was considered

statistically significant) and odds ratio (OR) calculation (for significant variables).

For the multivariate analysis, binary logistic regression analysis was applied to model skin aging (measured by the Glogau scale) based on the set of explanatory variables or predictive factors. Logistic regression, like other multivariate statistical techniques, offers the possibility of evaluating the influence of each of the independent variables on the response variable, controlling the effect of the rest.

The Wald test was used to determine if explanatory variables were significant. The goodness of fit of the model was estimated based on the likelihood-ratio test and a *p*-value of <0.05 was considered statistically significant. The interobserver variation was assessed using kappa coefficient. Analyses were performed using IBM SPSS 25.1 version software.

2.4 | Ethical considerations

The study was carried out following the principles of the Declaration of Helsinki and in compliance with local regulations on clinical research and applicable jurisdictional laws. In accordance with current regulations and guidelines, the protocol was approved by the local regulatory authority Independent Ethics Committees: Mar del Plata CEIIC ethics committee approval (exp. 2919–2458/2021) was obtained on 17/06/2021; Lobos HCANK CCF approval (exp. 2919–2458/2021) was obtained on 17/06/2021; CABA FEFYM approval (code 4029) was obtained on 22/03/2021; Chajarí CIEIER–Paraná approval was obtained on 03/12/2021; and Bariloche FEFYM approval (resolution 3689) was obtained on 26/05/2021. Informed consent (anonymous) was obtained before participation in the study.

3 | RESULTS

3.1 | Participants

Of 1346 participants recruited between March 12, 2021 and October 7, 2021, most were women (82%), aged 31–50 years old (62%), of skin phototype III (52%), with a tertiary level of education (63%), and living in urban areas (94%) at lower than 1600m altitude (95%) (Table 1). Most (88.6%) were covered by health insurance or prepaid medical care.

3.2 | Influence of exposome factors on facial skin aging

3.2.1 | Glogau score descriptive summary

The Glogau skin age was higher than the chronological age for 28% of participants and in more men than women (36% vs. 26%; *p*=0.002).

TABLE 1 Participant characteristics.

| Characteristic | n (%) |
|--|-------------|
| Gender (female), N=1344 | 1100 (81.8) |
| Age (N=1339), n (%) | |
| 20–30 | 234 (17.5) |
| 31–50 | 834 (62.3) |
| 51–60 | 265 (19.8) |
| >60 | 6 (0.4) |
| Mean (range), years | 42 (21–62) |
| Educational level (N=1329), n (%) | |
| Incomplete primary school | 10 (0.8) |
| Complete primary school | 27 (2.0) |
| Incomplete secondary school | 50 (3.8) |
| Complete secondary school | 231 (17.4) |
| Tertiary-University incomplete studies | 179 (13.5) |
| Tertiary-University complete studies | 636 (47.9) |
| Post-University studies | 196 (14.7) |
| Medical coverage (N=1309), n (%) | |
| None | 105 (8.0) |
| Health insurance | 752 (57.4) |
| Prepaid medical care | 408 (31.2) |
| Both | 44 (3.4) |
| Local environment (N=1326), n (%) | |
| Urban | 1247 (94.0) |
| Rural | 79 (6.0) |
| Altitude of place of residence (N=1294), n (%) | |
| <1600m | 1234 (95.4) |
| >1600m | 60 (4.6) |
| Fitzpatrick skin phototype (N=1333), n (%) | |
| I | 40 (3%) |
| II | 388 (29.1%) |
| III | 691 (51.8%) |
| IV | 211 (15.8%) |
| V | 3 (0.2%) |

In the 20–30 years, 31–50 years, and 51–60 years age group, the Glogau skin age was higher than the chronological age for 25%, 31%, and 20% of participants, respectively (*p*=0.001).

Descriptive analysis of exposome factors involved in the analyses showed high percentages of participants with high daily consumption of fruit and vegetables (73%), physical activity (72%), high daily intake (1.5 L) of water (64.1%) and less than 7 h of sleep per day (65.5%).

Odds of premature aging decreased if daily consumption of ≥1.5 L of water (OR=0.76; 95% CI 0.59–0.97), daily use of dermo-cosmetics, specifically moisturizers (OR=0.72; 95% CI 0.55–0.94), cleansers (OR=0.53; CI 95% 0.42–0.67), and retinoids (OR=0.61; 95% CI 0.39–0.95), as well as having antiaging (peeling, botox, filling or laser) treatments (OR=0.74; 95% CI 0.57–0.97) (Table 2).

TABLE 2 Influence of exposome factors with a statistically significant effect on premature aging (when the skin age according to the Glogau scale was higher than the chronological age).

| | Skin age > chronological age | p-Value | Odds ratio (95% CI) |
|---|------------------------------|---------|-------------------------|
| Educational level, n (%) | | 0.001 | OR=2.058 (1.319–3.211) |
| Lower level, incomplete secondary school | 331 (26.8%) | | |
| Higher level, completed secondary, tertiary or post-university | 37 (43.0%) | | |
| Consumption of 1.5 L of water | | 0.027 | OR=0.757 (0.591–0.970) |
| Daily | 218 (25.6%) | | |
| Occasionally, never | 149 (31.3%) | | |
| Place of carrying out physical activity | | 0.049 | OR=1.325 (1.001–1.755). |
| Outdoors | 158 (32.0%) | | |
| Indoors | 121 (26.2%) | | |
| Use of hydrating dermocosmetics | | 0.017 | OR=0.721 (0.551–0.943) |
| Yes | 262 (26.1%) | | |
| No | 110 (32.9%) | | |
| Daily use of cleansing dermocosmetics | | <0.001 | OR=0.529 (0.415–0.674) |
| Yes | 182 (22.7%) | | |
| No | 190 (35.6%) | | |
| Daily retinoid use | | 0.028 | OR=0.607 (0.388–0.950) |
| Yes | 26 (19.5%) | | |
| No | 330 (28.6%) | | |
| Antiaging treatments (peeling, botox, filling, or lasers) | | 0.029 | OR=0.742 (0.568–0.970) |
| Yes, n=413 | 98 (23.7%) | | |
| No, n=921 | 272 (29.5%) | | |
| Current exposure to agrochemicals | | 0.043 | OR=1.594 (1.011–2.512) |
| Yes | 32 (37.2%) | | |
| No | 332 (27.1%) | | |
| Daily use of sunscreen for participants living in urban areas, N=1231 | | 0.045 | OR=0.771 (0.598–0.995) |
| Yes | 135 (24.5%) | | |
| No | 202 (29.7%) | | |
| Daily use of sunscreen for nonsmokers only, N=911 | | 0.014 | OR=0.686 (0.508–0.926) |
| Yes | 93 (22.4%) | | |
| No | 147 (29.6%) | | |

Odds increased for a skin age greater than the chronological age with outdoor physical activity (OR=1.33; 95% CI 1.00–1.76), exposure to agrochemicals (OR=1.59; 95% CI 1.01–2.51), and lower socioeconomic level (OR=2.06; 95% CI 1.32–3.21) (Table 2).

There were no significant differences when comparing premature skin aging (Glogau scale skin age > chronological age) with respect to:

- Sociodemographic factors, for example, health coverage ($p=0.152$).
- Skin phototype ($p=0.582$).
- Lifestyle factors, for example, daily consumption of fruit and vegetables ($p=0.514$), daily consumption of alcoholic beverages ($p=0.675$), stress level ($p=0.098$), smoking ($p=0.077$), poor sleep

(<5 h per day or interrupted sleep; $p=0.859$), use of antiaging dermocosmetics ($p=0.933$).

- Environmental exposure, for example, rural versus urban place of residence ($p=0.167$), altitude of place of residence ($p=0.355$), working indoors or outdoors ($p=0.108$).
- Around 45% of study participants indicated they used sunscreen daily. Of those indicating they used sunscreen daily, 25.5% of had premature aging according to the Glogau scale compared to 30% for no sunscreen use, albeit a nonsignificant difference ($p=0.090$).

Although daily sunscreen use was not associated with a significantly lower probability of premature skin aging in the overall

population ($N=1328$), daily sunscreen use was significantly associated with lower premature skin aging in the subgroup of participants living in urban areas ($N=1231$; $OR=0.686$; 95% CI [0.508–0.926]), and in the subgroup of nonsmokers ($N=911$; $OR=0.771$, [95% CI 0.598–0.995]) (Table 2).

Doing physical activity was associated with a nonsignificant higher percentage of premature aging than not doing physical activity (29% vs. 24%, respectively; $p=0.052$). Of those doing physical activity ($n=961$), around half (52%) did physical activity outdoors and this increased the risk of aging 0.32 times compared to doing physical activity indoors ($p=0.049$; $OR=1.325$ [CI 95% 1.001–1.755]).

The Kappa coefficient for the variation between the two observers performing facial aging assessments on the Glogau scale was 0.869, indicating a high level of agreement, albeit with some discrepancies between scores of 2 and 3.

3.2.2 | Multivariate logistic analysis

Multivariate logistic analysis ($N=1246$) of the variables that are presented in Table 2 showed that each year of older age increased the risk of skin aging by 3.4% (OR 95% CI 1.02–1.05) and exposome factors of daily cleansing and use of antiaging treatments decreased the risk by 38% (OR 95% CI 0.47–0.81) and 29% (OR 95% CI 0.52–0.96), respectively (Table 3).

3.3 | AI analysis of severity of facial signs of aging

Overall, the mean total AI score was 1.33 for all participants, with the highest mean AI scores observed for dull skin (1.87 [range 0–3.1]) and under-eye wrinkles (1.65 [range 0.00–4.30]), while mean scores were lower for fine lines (1.03 [range 0–2]) and spot intensity (1.07 [range 0–2.7]).

Participants with a higher skin age than their chronological age, according to the Glogau scale ($n=372$) had a mean AI score of 1.54 compared to 1.25 for those with Glogau skin age \leq chronological age ($n=964$). The participants with a skin age greater than their chronological age had significantly ($p<0.05$) higher mean AI scores for all of the skin aging signs except for visibility of pores (Figure 1). The highest difference between participants with a skin age greater than their chronological age, compared to those who had a skin age below

or equal to their chronological age, were for visibility of coarse wrinkles and under-eye wrinkles (Figure 1).

3.4 | Differentiating between intrinsic and extrinsic skin aging

Of 171 participants who completed the SCINEXA questionnaire, 80.7% of participants had a higher weight of extrinsic factors, 11.7% had a higher weight of intrinsic factors, and both were equal in 7.6% of participants. The mean SCINEXA score was 1.88 (range 0.45–11).

The most important extrinsic factors were freckles and sunburn on the shoulders, and those with the least weight were Favre-Racouchot syndrome, squamous cell carcinoma, and melanoma. The intrinsic factors with the greatest and least weight were irregular pigmentation and benign tumors, respectively.

3.5 | Differences between men and women

According to the Glogau score, a statistically significant higher percentage of men had a skin age higher than their chronological age than women (36% vs. 26%; $p=0.002$) and, according to the multivariate analysis, odds increased for a skin age greater than the chronological age if male ($OR=1.59$; 95% CI 1.18–2.13).

Women had statistically significantly higher daily consumption of fruit and vegetables (76% vs. 61% men), high or moderate stress (80% vs. 72% men), daily use of dermocosmetics (hydrating [84% vs. 35%]; antiaging [44.5% vs. 4.5%]; cleansing products [69% vs. 20.5%]; complete skincare routine [36% vs. 2.5%]), and retinoids (12% vs. 4% men), and more antiaging treatments (36% vs. 7% men) than men (all $p<0.05$). Conversely, men had statistically significant higher daily consumption of alcohol (9% vs. 5% women, $p=0.008$). While men did more outdoor physical activity (60% vs. 50% women, $p=0.016$) and had a higher frequency of occupational sun exposure (28.5% men vs. 12% women, $p<0.001$), higher daily use of sunscreen was observed for more women (52% women vs. 13% men, $p<0.001$), as was higher sun exposure avoidance (18% women vs. 8% men, $p<0.001$).

In general, the AI scores were higher for men. Men had higher AI scores for pronounced wrinkles (1.68 for men vs. 1.42 for women), lack of luminosity (1.99 men vs. 1.85 women), and lack of skin firmness (1.26 men vs. 1.11 women) (all $p<0.05$).

TABLE 3 Results of logistic regression analysis to estimate factors associated with skin aging (predictive model), $N=1246$ (100 cases were excluded due to lack of complete data).

| Variable | Wald | <i>p</i> | OR | 95% CI |
|--------------------------------|--------|----------|-------|-------------|
| Age | 24.571 | <0.001 | 1.034 | 1.020–1.047 |
| Physical activity | 4.657 | 0.031 | 1.383 | 1.030–1.856 |
| Exposure to agrochemicals | 4.379 | 0.036 | 1.660 | 1.033–2.668 |
| Use of daily cleansing product | 12.439 | <0.001 | 0.618 | 0.473–0.807 |
| Antiaging treatments | 5.049 | 0.025 | 0.706 | 0.521–0.957 |

Note: $p<0.001$ /Overall = 72.3%.

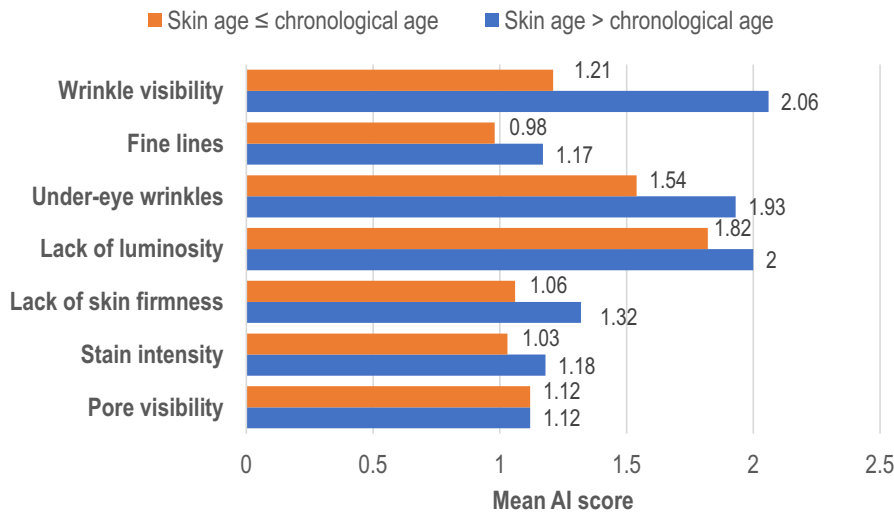


FIGURE 1 Mean AI scores for participants with a skin age higher than their chronological age ($N=372$) versus skin age less than or equal to their chronological age ($N=964$).

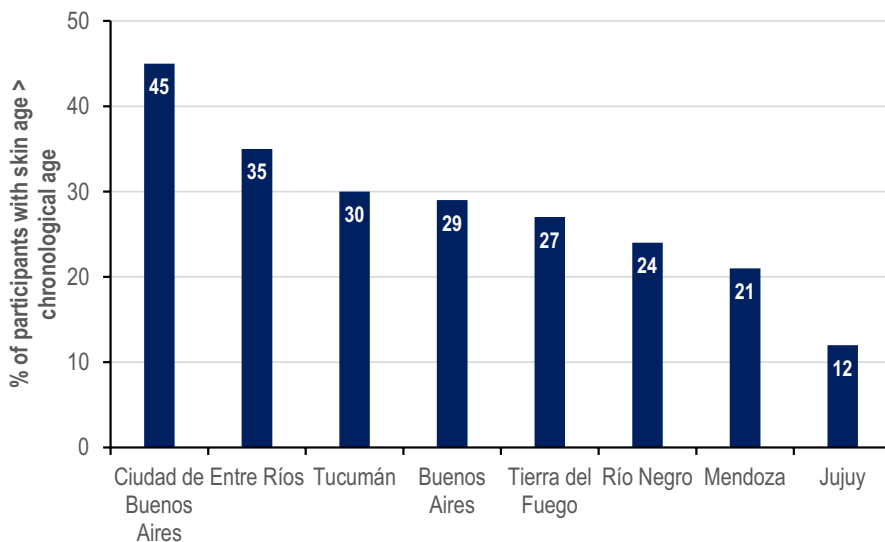


FIGURE 2 Percentage of participants from the various provinces with a skin age higher than their chronological age.

3.6 | Differences between localities

Participants were from 11 different localities in 8 geographically diverse provinces: San Salvador de Jujuy (Jujuy province); San Miguel de Tucumán (Tucumán province); Chajarí (Entre Ríos province); Ciudad de Buenos Aires (CABA province); Mendoza (Mendoza province); San Carlos de Bariloche (Río Negro province); Río Grande and Ushuaia (Tierra del Fuego province); and Lobos and Mar del Plata (both in Buenos Aires province).

According to the Glogau score, the region with the highest percentage of participants with a skin age higher than the chronological age was CABA and the lowest was Jujuy (45% vs. 12%, $p < 0.001$; Figure 2).

A descriptive summary table of exposure to various exposome factors for all 8 provinces is provided in Table S1. Comparing Jujuy (lowest premature aging rate) to CABA (highest premature aging rate): Jujuy had more female participants (90% vs. 79% in CABA), more participants aged >50 years (17% vs. 15% CABA), more participants consumed >1.5L water per day (85% vs. 67% in CABA), more used hydrating products (85% vs. 75% in CABA), cleansing products

(96% vs. 65% in CABA) and sunscreen (55% vs. 49% in CABA), and fewer performed outdoor physical activity (51% vs. 68% in CABA). However, while there was similar retinoid use (8% and 9% in Jujuy and CABA, respectively) and similar exposure to agrochemicals (both 3%), there was lower use of antiaging treatments (24% vs. 51% for Jujuy vs. CABA, respectively).

Of the 8 provinces, the altitude ranges from 11m for Tierra del Fuego province (site: Ushuaia) to 3468m for Jujuy (site: La Quiaca), the average annual UV exposure ranges from 3.74 for Tierra del Fuego (Ushuaia) to 14.29 for Jujuy (La Quiaca), and average annual atmospheric pollution levels are lowest in Tierra del Fuego and highest in CABA (Figure 3A,B and Table S2). The highest sun exposure avoidance (41% of participants), along with high use of sunscreen (55% of participants), was observed for participants from Jujuy, which is the location at the highest altitude with the highest average annual UV index (Figure 3C). The highest percentages of the population with occupational sun exposure were in Jujuy and Río Negro at 25% and 23%, respectively, while the lowest percentages were in Tierra del Fuego and Buenos Aires at 9% and 10%, respectively (Figure 3C).

A summary of the results from the application of the logistic regression model, to each province separately, shows that aging was influenced by different risk and protection factors in the various provinces (Table 4). In the case of Jujuy and Entre Ríos none of the variables included in the model were found to statistically significantly influence facial skin aging.

According to the AI analysis for participants from the 8 provinces, participants from Jujuy (lowest Glogau premature aging rate) had fewer fine lines (mean score 0.89) while CABA (highest Glogau premature aging rate) had the highest score for fine lines (1.18). Jujuy participants also had the best skin firmness score (0.95), whereas Entre Ríos had the worst score for lack of skin firmness (1.27) (Table 5). Conversely, participants from Jujuy had the most visible pores (1.37) but visibility of pores was not a statistically significant factor in the overall study population in the participants with a higher age than their chronological age. CABA had the highest mean spot intensity score (1.24), while the participants from Tierra del Fuego had the lowest score for spot intensity (0.81) and they also had the lowest score for under-eye wrinkles.

4 | DISCUSSION

In this study, we have characterized the exposome in relation to skin aging in 1346 participants in Argentina. The risk factors for skin aging identified by bivariate analysis were being male, aged 51–60 years, performing physical activity outdoors, and exposure to agrochemicals. Protection factors were high water uptake (>1.5 L daily), use of hydrating and cleansing dermocosmetics, daily use of retinoids, and use of antiaging treatments (peeling, botulinum toxin, filling, or lasers).

The majority of the study population (70%) had skin FPT III or above. Of those who used sunscreen daily (45% of study participants), 25.5% had premature aging according to the Glogau scale compared to 30% for no sunscreen use, albeit this difference was not statistically significant ($p=0.09$) in the overall population. Furthermore, some participants would avoid sun exposure by seeking shade and wearing sun-protective clothing, as was the case for almost half of participants (41%) from Jujuy, which has the highest annual UV index. Interestingly, daily sunscreen use was associated with a statistically significantly lower probability of premature skin aging in the subgroup of participants living in urban areas, suggesting that sunlight and pollution might synergistically increase skin aging. Previous *in vitro* studies in keratinocytes exposed to ultraviolet A rays showed a combined effect of pollution and UV on the skin causing impaired redox homeostasis, the so-called photo-pollution concept.¹⁴ Comparing Jujuy, which had the lowest premature aging rate to CABA, which had the highest premature aging rate (12% vs. 45%, $p<0.001$), Jujuy is at much higher altitude and has the highest UV index, but it also has lower levels of pollution while CABA is the most polluted location. These findings highlight the need for dermocosmetics containing antioxidants to combat the effects of pollution and not just sun protection factors.^{15,16} Recent reviews on research

findings and updated approaches to environmental or atmospheric aging highlight the importance of photoprotection, antioxidants, chelating agents, and DNA repair enzymes.^{17,18}

Skin age was greater than chronological age in more participants who did physical activity compared to those who did not (29.2% vs. 23.9%, respectively; $p=0.052$), possibly reflecting the fact that the place of activity had significant effect. Indeed, half (51.7%) did physical activity outdoors and so their skin may have been exposed to pollution and photodamage.

The multivariate analysis found that the factors that increase the risk of skin aging were age, physical activity, and exposure to agrochemicals, while the protection factors were daily cleansing and the use of antiaging treatments.

As the exposome encompasses the totality of exposures to which an individual is exposed to throughout their lifetime studies addressing the interaction of these factors and their net effects are necessary.^{2,19} As physically measuring the contribution of each exposome factor, as has been done for individual exposome factors such as pollution,^{20,21} is not practical, we used an exposome questionnaire to obtain data for multiple exposome factors. Also, comparing the exposome questionnaire results from different localities with known environmental data for each locality (UV, pollution, altitude), we were able to provide further insights into which factors contributed most to premature aging.

Understanding how exposome factors impact skin aging can help in the design of tailored preventive strategies for specific populations. Previous studies on exposome factors contributing to skin aging have been performed in various countries including Spain,²² Chile,²³ Turkey,²⁴ Mongolia,²⁵ and in Russia.²⁶ A review on skin aging exposome factors including sun radiation, air pollution, tobacco smoke, nutrition, and cosmetic products, concluded that ultraviolet radiation, smoking, and pollution were the three main factors that induce skin aging.³ A recent systematic review and meta-analysis conducted to define skin aging risk factors identified seven risk factors for various skin aging phenotypes: specifically, age, gender, ethnicity, air pollution, nutrition, smoking, and sun exposure.²⁷ In a further study of middle-aged women, aged >40 years, with a high polygenetic risk score for wrinkles (PRS), lifestyle factors of menopause and UV exposure increased PRS, while avoiding UV exposure by applying sunscreen, maintaining sufficient water intake, and managing estrogen deficiency may reduce the risk of wrinkles.²⁸

5 | LIMITATIONS

The limitations of this study are related to the inherent limitations of using self-assessed questionnaire responses rather than measurements. Also, the majority of participants were well-educated women aged 31–50 years old, and all participants were recruited when attending a private dermatology office and so are not representative of the general public of Argentina.

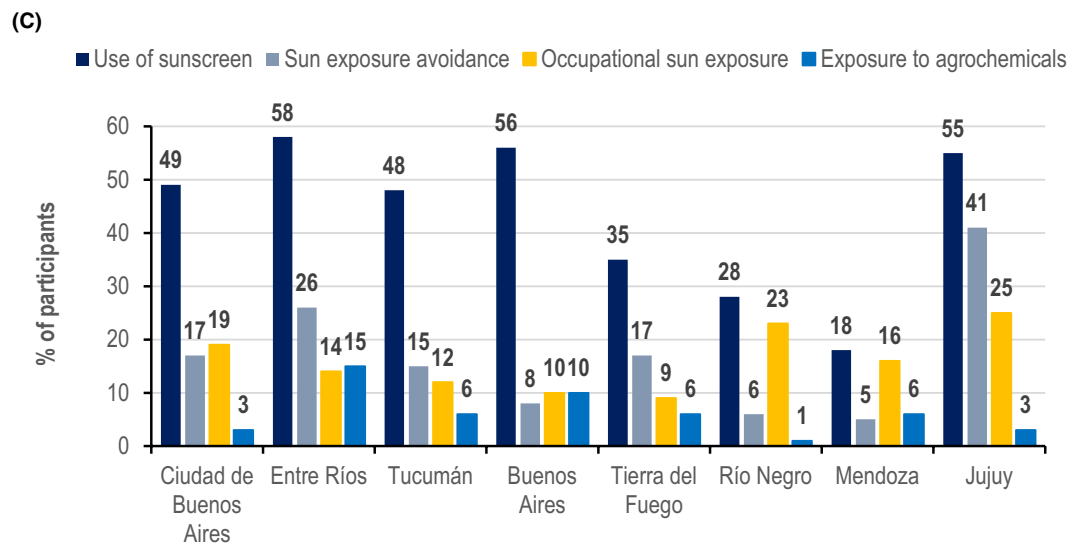
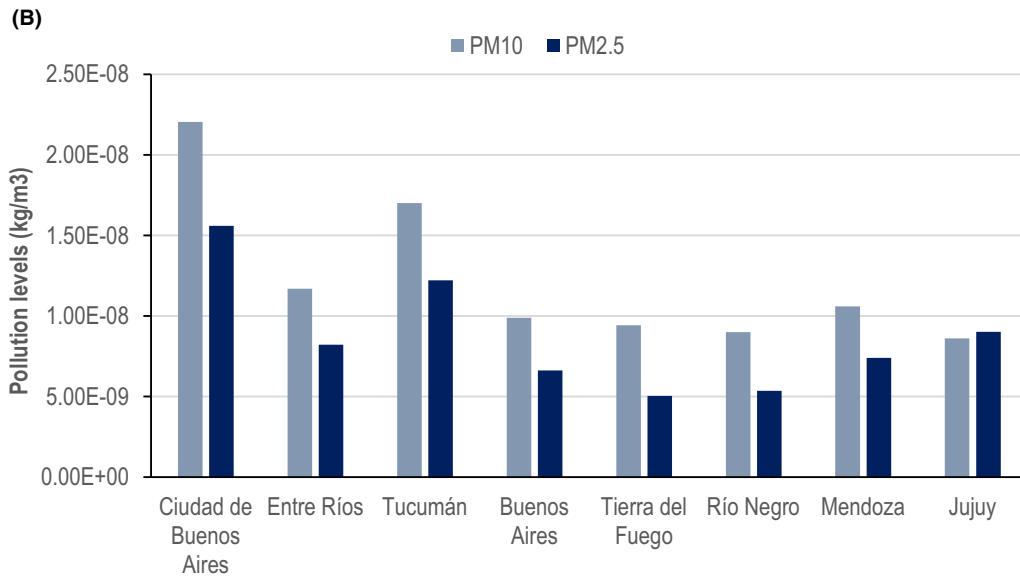
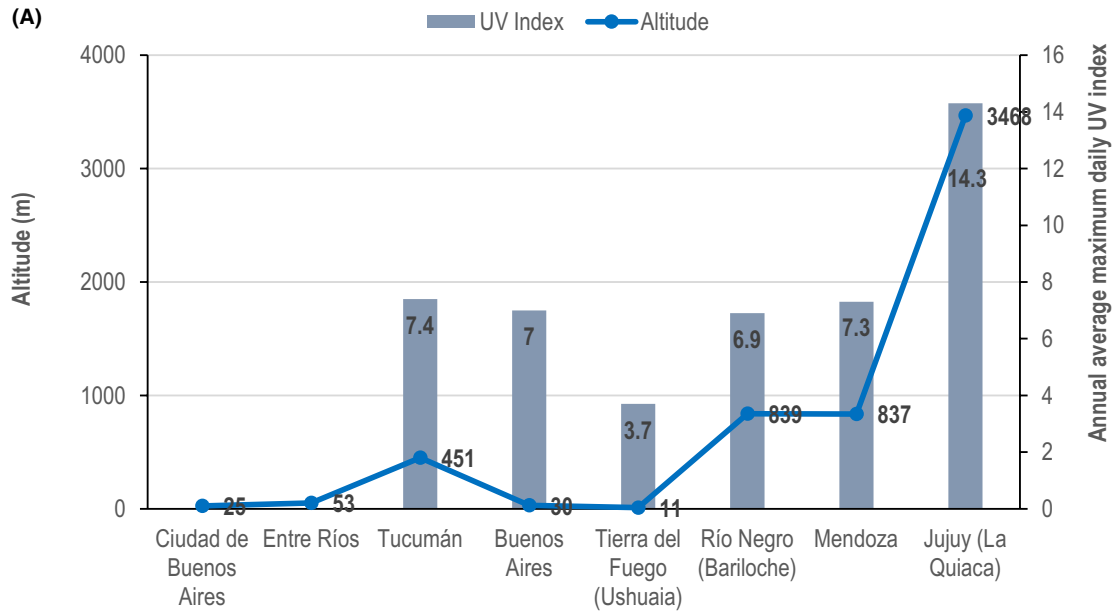


FIGURE 3 For each of the 8 provinces: (A) Altitude and annual average of maximum daily UV index, (B) annual average pollution levels (PM10 and PM2.5) and (C) percentage of participants who indicated they used sunscreen, avoided the sun, had occupational exposure to sun or agrochemicals. Annual average of maximum daily UV index data for Ciudad de Buenos Aires and Entre Rios were not available from the National Meteorology Service of Argentina.

TABLE 4 Percentage of participants from the various provinces with premature aging (according to the Glogau scale), exposome factors associated with premature aging, and summary of the multivariate analysis by province.

| Province | Skin age > chronological age, n (%) | Factors associated with greater aging | Multivariate analysis | |
|------------------|-------------------------------------|--|--|---|
| | | | Risk factors | Protection factors |
| CABA | 68 (45.3%) | | Age (OR 1.078; 95% CI 1.026–1.133) | Female (OR 0.41; 95% CI 0.171–0.993) |
| Entre Ríos | 51 (34.7%) | No hydrating product use No cleansing product use No consumption of 1.5 L of water Age < 50 | | |
| Tucumán | 45 (30.0%) | | Physical activity (OR 2.510; 95% CI 1.052–5.986) | Use of daily cleansing (OR 0.408; 95% CI 0.188–0.886) |
| Buenos Aires | 83 (28.6%) | Male Age < 50 No daily cleansing use Smoking | Exposure to agrochemicals (OR 2.751; 95% CI 1.164–6.499) | Antiaging treatments (OR 0.303; 95% CI 0.170–0.541) |
| Tierra del Fuego | 40 (26.5%) | No cleansing product use | Age (OR 1.052; 95% CI 1.008–1.098) Physical activity (OR 3.342; 95% CI 1.305–8.559) | Female (OR 0.363; 95% CI 0.165–0.797) |
| Río Negro | 36 (24.0%) | | Age (OR 1.064; 95% CI 1.022–1.107) | |
| Mendoza | 31 (20.8%) | No hydrating product use | Age (OR 1.072; 95% CI 1.029–1.118) | Use of daily cleansing (OR 0.227; 95% CI 0.072–0.716) |
| Jujuy | 18 (12.1%) | Daily alcohol consumption Smoking | – | – |

TABLE 5 Mean AI scores for 7 skin aging signs for participants from 8 provinces in Argentina.

| | Buenos Aires (N = 293) | CABA (N = 150) | Entre Ríos (N = 151) | Jujuy (N = 150) | Mendoza (N = 150) | Río Negro (N = 151) | T. del Fuego (N = 151) | Tucumán (N = 150) |
|----------------------------------|------------------------|----------------|----------------------|-----------------|-------------------|---------------------|------------------------|-------------------|
| Skin age > chronological age | 28.6% | 45.3% | 34.7% | 12.1% | 20.8% | 24.0% | 26.5% | 30.0% |
| Lack of Skin firmness | 1.24 | 1.17 | 1.27 | 0.95 | 1.14 | 1.11 | 1.04 | 1.06 |
| Spot intensity | 1.17 | 1.24 | 1.21 | 1.05 | 0.98 | 1.10 | 0.81 | 0.90 |
| Pore visibility | 1.16 | 1.08 | 1.21 | 1.37 | 1.05 | 0.92 | 1.11 | 1.03 |
| Lack of luminosity | 1.98 | 1.92 | 1.91 | 1.93 | 1.83 | 1.87 | 1.75 | 1.69 |
| Under-eye wrinkles | 1.90 | 1.77 | 1.66 | 1.47 | 1.67 | 1.84 | 1.32 | 1.37 |
| Visibility of prominent wrinkles | 1.82 | 1.62 | 1.40 | 1.15 | 1.43 | 1.85 | 1.13 | 0.96 |
| Fine lines | 1.12 | 1.18 | 1.06 | 0.89 | 0.96 | 1.12 | 0.91 | 0.92 |

6 | CONCLUSIONS

In conclusion, exposome factors found to increase the risk for premature skin aging included physical outdoor activity and exposure to agrochemicals, while protection factors were high water uptake, the use of antiaging treatments, and daily use of dermocosmetics (moisturizers, cleansers, and retinoids). The province (Jujuy) with the highest UV index but lowest levels of pollution had the lowest Glogau premature aging rate, highlighting the importance of dermocosmetics containing antioxidants to counteract the effects of pollution in addition to photoprotection and sun avoidance.

AUTHOR CONTRIBUTIONS

Marina Giselle Claros involved in conceptualization, data curation, investigation, methodology, supervision, validation, visualization, review, and editing. Mariana Lequio, Santiago Cheli, Agustin Bollea Garlatti, Noelia Cecilia, Lucrecia Juarez, Mario Bittar, María José Leiva, María Laura Hernandez, Juan Manuel Márquez, and Guillermo Badaracco involved in investigation, review, and editing. Stephanie Leclerc-Mercier involved in writing the original draft, review, and editing. Maite Iglesias Leal involved in conceptualization, funding acquisition, methodology, project administration, resources, software, supervision, validation, visualization, review, and editing.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was carried out following the principles of the Declaration of Helsinki and in compliance with local regulations on clinical research and applicable jurisdictional laws. In accordance with current regulations and guidelines, the protocol was approved by the local regulatory authority Independent Ethics Committees: Mar del Plata CEIIC ethics committee approval (exp. 2919-2458/2021) was obtained on 17/06/2021; Lobos HCANK CCF approval (exp. 2919-2458/2021) was obtained on 17/06/2021; CABA FEFYM approval (code 4029) was obtained on 22/03/2021; Chajarí CIEIER—Paraná approval was obtained on 03/12/2021; and Bariloche FEFYM approval (resolution 3689) was obtained on 26/05/2021. Informed consent (anonymous) was obtained before participation in the study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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