INVESTIGATIVE REPORT

Study of the Exposome Ageing-related Factors in the Spanish Population

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To characterize the exposome of the Spanish population and its association with skin ageing a cross-sectional epidemiological study was conducted in men and women (18–60 years old). A total of 1,474 participants were included. Mean age (±standard deviation) was 40.84 ± 10.26 years. Most participants had Fitzpatrick skin phototype II (44.1%) and skin ageing in accordance with their current age (69.0%). In the logistic model, age, smoking habit, use of sunscreen and use of cosmetics were all significant independent predictors of skin ageing. Thus, tobacco consumption increased the score of the model towards presenting skin ageing above that expected for age, while the opposite occurred with the use of sunscreen and a complete skin care routine. The exposome therefore has an impact on skin ageing, with age, smoking habit, use of sunscreen and the use of cosmetics identified as predictors of skin ageing. Skin care routines and sunscreen use may help to prevent this process.

Key words: diet; exposome; Glogau scale; lifestyle; skin ageing; skin care.

Accepted Apr 28, 2020; Epub ahead of print May 4, 2020

Acta Derm Venereol 2020; 100: adv00153.

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The term “exposome” was first introduced in 2005 by molecular epidemiologist Christopher Wild, who described it as the totality of exposures to which an individual is subjected from conception to death (1). A refined definition was provided in 2014 by Miller & Jones (2), who proposed that the exposome should be considered as a cumulative measure of environmental influences and the subsequent associated biological responses of an individual throughout their life.

The exposome of human skin has not traditionally received much attention. Interest in reaching an accurate description of the concept, as well as in knowing its impact on the human skin, has grown in recent years, supported by the fact that the exposome may be the cause of several chronic diseases (3). Following the path of previous definitions, “the skin ageing exposome consists of external and internal factors and their interactions, affecting a human individual from conception to death as well as the response of the human body to these factors that lead to biological and clinical signs of skin aging” (4). Skin ageing exposome factors have been classified into 6 categories: (i) sun exposure, (ii) air pollution, (iii) tobacco smoke, (iv) nutrition, (v) miscellaneous factors, including stress and sleep deprivation, and (vi) cosmetics. Solar radiation is often considered as the most significant exogenous factor in skin ageing, contributing to up to 80% of its visible signs (5). Two recent epidemiological studies, performed in populations with different ethnic backgrounds (Chinese and European), have provided data supporting the relationship between sun exposure and ageing (6–8). A similar negative impact has been described for pollution. Thus, there is sufficient evidence to demonstrate that exposure to traffic-related air pollution is associated with skin ageing (6, 8, 9). Finally, diet and lifestyle are also identified as exposome factors (reviewed in Krutmann et al. (4)).

Despite the well-known individual impact of these factors on skin ageing, few studies have been conducted to evaluate the resulting net effects in relation to this process. An explanation for this may be linked to the undeniable influence of genetic and environmental factors in each subject (4), which makes it difficult to interpret results and to draw conclusions. Consequently, further research is needed that will allow current anti-ageing strategies to be improved and to develop new ones.

This study aimed to characterize the exposome of the Spanish population and its putative association with skin ageing.

MATERIALS AND METHODS

Study design

A cross-sectional, non-interventional, epidemiological study was conducted using stratified cluster sampling.

The researchers were medical specialists in dermatology and aesthetic medicine from 119 dermatological clinics who recruited an indeterminate number of subjects consecutively from Decem-

SIGNIFICANCE

This cross-sectional epidemiological study, conducted in women and men in the age range 18–60 years, aimed to characterize the exposome of the Spanish population. The results demonstrate that the exposome has an impact on skin ageing. Predictive modelling shows that skincare routines and sunscreen use may help to prevent skin ageing, while tobacco consumption may negatively impact on skin ageing.
ber 2017 to April 2018. In order to obtain a sample containing mostly healthy subjects that was representative of the population, participants were recruited from those attending consultations, as well as their companions, relatives or acquaintances. Individual data on current exposure and lifestyle factors associated with skin ageing (according to the literature) were collected by means of an electronic case report form (CRF) that also included basic demographic variables (age, sex, city of residence). Ageing score was assigned by the physician by using the Glogau scale (10). The data collected were completely anonymous and treated confidentially.

The study protocol was approved by the Research Ethics Committee of the Hospital Universitario Virgen de las Nieves de Granada following the standards of the Declaration of Helsinki. Participation in the study did not interfere with the decision of the researcher about the most appropriate care or medical treatment for participants. A signed consent was not required for each individual included, although all invited subjects received a written description of the study.

**Participant selection**

Healthy Spanish men and women aged > 18 years and < 60 years were eligible to participate. Participants were selected taking into account a balanced representation for both sexes (approximately 50%). In order to obtain a representative national sample, sampling was carried out uniformly in 4 geographical areas (20% of participants from the north, 30% from the east, 25% from the south and 25% from the centre of the country), including people from all autonomous regions in Spain.

**Measurable outcomes**

The following variables were analysed: sex, age, skin phototype according to Fitzpatrick scale (11), degree of ageing according to Glogau scale (score 1–4) (10), residential environment (rural or urban), professional occupation (indoors or outdoors and exposure time to sunlight in outdoor jobs), daily consumption of fruit and vegetables, alcohol consumption (evaluating whether consumption was daily, occasional or never), water intake, stress level (evaluated by the participant), sports activity and its type (indoors or outdoors), smoking habit (evaluating whether participants were smokers, non-smokers or ex-smokers), time sleeping, use of cosmetics, use of sunscreen and anti-ageing treatments (botulinum toxin type A (Botox), peeling or dermal fillers). All variables analysed referred to last year’s data.

The association between exposome factors and skin ageing was then determined. To that end, a variable evaluating normal ageing and excessive skin ageing was constructed, based on the scores of the Glogau scale and the chronological age of the participant. Thus, normal ageing was established when the score assigned matched the expected ageing according to chronological age, and excessive skin ageing when the score assigned was above that expected for the age of the individual (10).

**Statistical analysis**

With 2,000 individuals and assuming that 10% of these have Glogau scale values above their theoretical value, 40 variables could be simultaneously analysed, thus complying with the rule of 20 events per variable in the maximum model (12).

First, a descriptive analysis was performed. Thus, relative frequencies in the case of qualitative variables and measures of central tendency and dispersion in the case of quantitative variables were calculated. Subgroups according to demographic factors were also analysed.

Associations between the independent variables and the presence of normal/excessive skin ageing were analysed using the χ² test. A model was constructed to predict normal/excessive skin ageing based on binary logistic regression analysis (see Appendix S11) (13). A 2-sided p-value < 0.05 was considered statistically significant. Analyses were performed using STATA® version 14.1 software (Stata Corporation, College Station, TX, USA).

**RESULTS**

**Baseline characteristics of participants**

A total of 1,474 participants were included in the study. The basic characteristics of the subjects are shown in Table I. Mean age (+ standard deviation) was 40.84 ± 10.26 years and the proportion of women was 69.54% (n = 1,025). The majority of participants were between 30 and 49 years old (women n = 602, 40.84%; men n = 300, 20.35%) and lived in an urban area (n = 1,326, 90%). The most frequent locations were Barcelona (n = 184), Madrid (n = 665), Malaga (n = 256), Tarragona (n = 96), Seville (n = 62) and Zaragoza (n = 49). Regarding the skin phototype according to the Fitzpatrick scale, the most frequent was phototype II (usually burns, tans minimally; n = 650, 44.1%), followed by phototype III (sometimes mild burn, tans uniformly, n = 544, 36.9%). Finally, skin photoageing was determined by the Glogau scale, resulting in moderate ageing (group 2) in most participants (n = 727, 49.3%) and severe photoageing in only 2.9% (group 4, n = 43).

Most participants showed a degree of ageing (measured by Glogau scale) in accordance with their current

Table I. Baseline characteristics of participants, skin phototype and degree of ageing

| Characteristics | Age, n (%) |
|-----------------|------------|
| 20–29 years     | 229 (15.54) |
| 30–39 years     | 452 (30.66) |
| 40–49 years     | 450 (30.53) |
| 50–60 years     | 342 (23.23) |
| Sex, n (%)      |            |
| Men             | 1,025 (69.5%) |
| Women           | 449 (30.51)  |
| Residential environment, n (%) | |
| Rural           | 1,326 (90%)  |
| Urban           | 148 (10%)    |
| Current occupation*, n (%) | |
| Indoors         | 1,290 (87.5) |
| Outdoors        | 184 (12.5)   |
| Sun exposure time, h, mean ± standard deviation   | 3,013 ± 2,799 |
| Fitzpatrick skin phototype, n (%) | |
| I               | 106 (7.2)    |
| II              | 650 (44.5)   |
| III             | 544 (36.9)   |
| IV              | 158 (10.7)   |
| V               | 16 (1.1)     |
| Photoageing (Glogau scale), n (%) | |
| Refuse/Do not know | 1 (0.1)     |
| 1               | 355 (24.1)   |
| 2               | 727 (49.3)   |
| 3               | 348 (23.6)   |
| 4               | 43 (2.9)     |

*Related to sun exposure.
age \((n=1,017, 69.0\%)\), while 30.9\% were identified as having a skin age higher than that expected according to their chronological age.

**Lifestyle and diet profile of participants**

Participants were asked about some aspects of their diet and lifestyle (Table II). Thus, most of the subjects stated that they consume fruit and vegetables daily \((n=1,162, 78.9\%)\), drink 1.5 l of water per day \((n=1,124, 76.3\%)\) and had not been on a diet in the last 5 years \((n=983, 66.7\%)\). Regarding alcohol consumption, only 15.3\% \((n=223)\) reported drinking alcohol daily, while 43.9\% \((n=646)\) said that they did so occasionally. The majority of patients reported feeling moderate stress \((n=611, 41.5\%)\). Sporting activity was reported by 59.4\% \((n=876)\) of participants, although among them, only 25.8\% \((n=226)\) practised it outdoors. Other factors, such as smoking or sleep time, were also evaluated. The participants included in the study were mainly non-smokers \((n=1,040, 70.6\%)\), followed by a lower percentage of ex-smokers \((n=251, 17\%)\). Moreover, in more than half of subjects \((n=762, 51.7\%)\), the sleep time reported was <7 h per day.

Finally, the use of sunscreen and various combinations of dermocosmetic skin care and aesthetic treatments was studied. Sunscreen was used more frequently by participants only when sunbathing \((n=647, 43.9\%)\), followed

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**Table II. Diet and lifestyle data**

| Daily consumption of fruit and vegetables, n (%) | Men       | Women     | Total     |
|-------------------------------------------------|-----------|-----------|-----------|
| No                                              | 122 (27.2) | 189 (18.5) | 311 (21.1) |
| Yes                                             | 327 (72.8) | 835 (81.5) | 1,162 (78.9) |
| Daily water intake 1.5 l/day, n (%)             |           |           |           |
| No                                              | 98 (21.8)  | 251 (24.5) | 349 (23.7) |
| Yes                                             | 351 (78.2) | 773 (75.5) | 1,124 (76.3) |
| Any weight-loss diet (last 5 years), n (%)      |           |           |           |
| No                                              | 334 (74.4) | 649 (63.4) | 983 (66.7) |
| Yes                                             | 115 (25.6) | 375 (36.6) | 490 (33.3) |
| Alcohol consumption, n (%)                      |           |           |           |
| Never                                           | 148 (33.0) | 454 (44.3) | 602 (40.9) |
| Occasionally                                    | 184 (41.0) | 462 (45.1) | 646 (43.9) |
| Daily                                           | 117 (26.1) | 108 (10.5) | 225 (15.3) |
| Stress level, n (%)                             |           |           |           |
| No stress                                       | 19 (4.2)  | 18 (1.8)  | 37 (2.5)  |
| Little                                          | 73 (16.3)  | 270 (26.4) | 343 (23.3) |
| Moderate                                        | 167 (37.2) | 444 (43.4) | 611 (41.5) |
| Quite intense                                   | 152 (33.9) | 221 (21.6) | 373 (25.3) |
| High                                            | 38 (8.5)  | 71 (6.9)  | 109 (7.4) |
| Sporting activity, n (%)                        |           |           |           |
| No                                              | 135 (30.1) | 462 (45.1) | 597 (40.5) |
| Yes                                             | 314 (69.9) | 562 (54.9) | 876 (59.4) |
| Indoors                                         | 184 (58.6) | 372 (66.2) | 556 (63.5) |
| Indoors/outdoors                                | 32 (10.2)  | 62 (11.0)  | 94 (10.7)  |
| Outdoors                                        | 98 (31.2)  | 128 (22.8) | 226 (25.8) |
| Time spent on outdoor sports, h/week, mean ± SD| 5.71 ± 6.42 | 4.24 ± 2.51 | 4.84 ± 4.58 |
| Smoking habit, n (%)                            |           |           |           |
| Non-smoker                                       | 318 (70.8) | 722 (70.5) | 1,040 (70.6) |
| Smoker                                           | 41 (9.1)  | 141 (13.8) | 182 (12.4) |
| Ex-smoker                                        | 90 (20.0)  | 161 (15.7) | 251 (17.0) |
| Sleep time, h, n (%)                            |           |           |           |
| <5                                              | 56 (12.5)  | 70 (6.8)  | 126 (8.5)  |
| ≥7                                              | 272 (60.6) | 490 (47.9) | 762 (51.7) |
| ≥12                                             | 121 (26.9) | 464 (45.3) | 585 (39.7) |
| Use of sunscreen, n (%)                          |           |           |           |
| Never                                           | 60 (13.4)  | 25 (2.4)  | 85 (5.8)  |
| Only when sunbathing                             | 262 (58.4) | 385 (35.7) | 647 (43.9) |
| Occasionally                                    | 72 (16.0)  | 201 (19.6) | 273 (18.5) |
| Daily                                           | 55 (12.2)  | 413 (40.3) | 468 (31.8) |
| Sun exposure prohibition**, n (%)                |           |           |           |
| No                                              | 443 (98.7) | 995 (97.2) | 1,438 (97.6) |
| Yes                                             | 6 (1.3)   | 29 (2.8)  | 35 (2.4)  |
| Use of cosmetics, n (%)                          |           |           |           |
| Daily cleansing                                  | 140 (31.2) | 168 (16.4) | 308 (20.9) |
| Moisturizing lotion + daily cleansing            | 121 (26.9) | 134 (13.1) | 255 (17.3) |
| Moisturizing lotion                             | 98 (21.8)  | 223 (21.8) | 321 (21.8) |
| Anti-aging cream + daily cleaning               | 12 (2.7)   | 30 (2.9)   | 42 (2.8)   |
| Anti-aging cream + moisturizing lotion          | 13 (2.9)   | 46 (4.5)   | 59 (4.0)   |
| Anti-aging cream + moisturizing lotion + daily cleaning | 11 (2.4) | 25 (2.4) | 36 (2.4) |
| Any anti-aging facial treatment* (last 2 years), n (%) | 54 (12.0) | 398 (38.9) | 452 (30.7) |
| No                                              | 377 (84.9) | 598 (58.4) | 975 (66.2) |
| Yes                                             | 72 (16.0)  | 426 (41.6) | 498 (33.8) |
## Table III. Analysis of the influence of exposome factors on the degree of ageing (according to Glogau scale)

| Age | Ageing in accordance with age | Ageing higher than age | p-value |
|-----|-------------------------------|------------------------|---------|
| 20–29 years | 44 (19) | 185 (81) | <0.001 |
| 30–39 years | 329 (75) | 123 (27) | 0.213 |
| 40–49 years | 335 (74) | 115 (26) | 0.243 |
| 50–60 years | 309 (90) | 33 (10) | 0.016 |

Sex, n (%)<br>
- Women: 714 (69.7) 310 (30.3) | 0.172 |
- Men: 303 (67.5) 146 (32.5) | 0.172 |

Residential environment, n (%)<br>
- Urban: 919 (69.36) 406 (34.24) | 0.029 |
- Rural: 98 (66.22) 50 (33.78) | 0.029 |

Current occupation*<br>
- Indoors: 896 (69.51) 393 (30.49) | 0.027 |
- Outdoors: 121 (65.76) 63 (34.24) | 0.027 |

Sun exposure time (h), mean ± SD<br>
- 3,013 ± 2,799 | 0.020 |

Fitzpatrick skin phototype, n (%)<br>
- I: 60 (57) 46 (43) | 0.020 |
- II: 464 (71) 186 (29) | 0.020 |
- III: 388 (71) 155 (29) | 0.020 |
- IV: 94 (59) 64 (41) | 0.020 |
- V: 11 (69) 5 (31) | 0.020 |

Daily consumption of fruit and vegetables, n (%)<br>
- Yes: 833 (72) 329 (28) | <0.001 |
- No: 184 (59) 127 (41) | 0.029 |

Daily water intake 1.5 l/day, n (%)<br>
- Yes: 224 (64) 125 (36) | 0.002 |
- No: 793 (71) 331 (39) | 0.002 |

Any weight-loss diet (last 5 years), n (%)<br>
- Yes: 660 (67) 323 (33) | 0.027 |
- No: 357 (73) 133 (27) | 0.027 |

Alcohol consumption, n (%)<br>
- Never: 440 (73) 162 (27) | 0.033 |
- Occasionally: 422 (65) 224 (35) | 0.033 |
- Daily: 155 (69) 70 (31) | 0.033 |

Stress leve, n (%)<br>
- No stress: 23 (62) 14 (38) | <0.001 |
- Little: 241 (70) 102 (30) | 0.378 |
- Moderate: 403 (66) 208 (34) | 0.378 |
- Quite intense: 287 (77) 86 (23) | 0.378 |
- High: 63 (58) 46 (42) | 0.378 |

Sporting activity, n (%)<br>
- No: 409 (69) 188 (31) | 0.033 |
- Yes: 608 (69) 268 (31) | 0.033 |
- Indoors: 143 (63) 83 (37) | 0.033 |
- Indoors/Outdoors: 65 (69) 29 (31) | 0.033 |
- Outdoors: 400 (72) 156 (28) | 0.033 |

Time spent on outdoor sports, h, mean ± SD<br>
- 0.88 ± 0.79 | 0.033 |

Smoking habit, n (%)<br>
- Non-smoker: 731 (70) 309 (30) | 0.033 |
- Smoker: 156 (62) 95 (38) | 0.033 |
- Ex-smoker: 130 (71) 52 (29) | 0.033 |

Sleep time, n (%)<br>
- <5 h: 96 (76) 30 (24) | 0.172 |
- 6-7 h: 517 (68) 245 (32) | 0.172 |
- ≥7 h: 404 (69) 181 (31) | 0.172 |

Use of sunscreen, n (%)<br>
- Never: 44 (51.8) 41 (48.2) | <0.001 |
- Only when sunbathing: 425 (65.5) 222 (34.3) | 0.001 |
- Occasionally: 188 (68.9) 85 (31.1) | 0.001 |
- Daily: 360 (76.9) 108 (23.1) | 0.001 |

Sun exposure prohibition*, n (%)<br>
- No: 987 (69) 451 (31) | 0.040 |
- Yes: 30 (86) 5 (14) | 0.040 |

Use of cosmetics, n (%)<br>
- Daily cleansing: 190 (62) 118 (38) | <0.001 |
- Moisturizing lotion + daily cleansing: 152 (60) 103 (40) | 0.001 |
- Moisturizing lotion: 200 (62) 121 (38) | 0.001 |
- Anti-ageing cream: 31 (74) 11 (26) | 0.001 |
- Anti-ageing cream + daily cleansing: 47 (80) 12 (20) | 0.001 |
- Anti-ageing cream + moisturizing lotion: 27 (75) 9 (25) | 0.001 |
- Anti-ageing cream + moisturizing lotion + daily cleaning: 370 (82) 82 (18) | 0.001 |

Any anti-ageing facial treatment**, (last 2 years), n (%)<br>
- No: 633 (65) 342 (35) | <0.001 |
- Yes: 384 (77) 114 (23) | <0.001 |

*According to medical prescription. **Botulinum toxin-A, peeling or fillers. Bold values indicate statistically significant p-values (p < 0.05). SD: standard deviation.
by daily use (n = 468, 31.8%). Furthermore, only 2.4% of participants (n = 35) reported that sun exposure was prohibited by medical prescription. Regarding cosmetics, most participants reported that they perform a complete skin care routine, consisting of daily cleansing, an anti-ageing cream and moisturizing lotion (n = 452, 30.7%), while a specific anti-ageing treatment (Botox, peeling or dermal fillers) in the last 2 years was reported in only 33.8% of subjects (n = 498).

**Analysis of the association between the exposome factors and the degree of ageing**

The analysis of the influence of the exposome factors on the degree of skin ageing (normal/excessive for chronological age) is shown in Table III (univariate analysis). All analysed variables, except for sex, residential environment, current occupation, sporting activity and sleep time, showed a statistically significant association with the degree of ageing.

### Logistic predictive model

All variables showing an association with the degree of ageing were subsequently included in the logistic regression model. Table IV shows the p-value obtained for each variable in the model. From the variables introduced, the coefficient that each variable adopts in the final model is shown in Table V. As observed, not all variables showing an association in the univariate analyses were statistically significant in the logistic regression model. Thus, age, smoking habit, use of sunscreen and use of cosmetics were all significant independent predictors of the degree of ageing.

The predictive model for skin ageing is shown in Fig. 1. Thus, the resulting Y is a score between 0 and 100. A value < 50 indicates that ageing exceeds the participant’s age, while a score > 50 indicates that ageing matches the participant’s age. Thus, the coefficients of the regression model equation allowed us to conclude that tobacco consumption increases the score towards presenting skin ageing above that expected for age. On the other hand, the more frequently sunscreen is used and the more complete the skin care routine, the lower the score will be, towards presenting skin ageing that matches the real age.

Omnibus tests of model coefficients were statistically significant (χ² 322.993, p < 0.001). Furthermore, the quality of classification was assessed. As shown in Table VI, the overall classification rate was 78.5%, with sensitivity and specificity values of 49.3% and 91.6%, respectively. Finally, the area under the curve (AUC) was 0.77 (Fig. 2).

The results reveal that the exposome has a real impact on skin ageing, with age, smoking habit, use of sunscreen and the use of cosmetics identified as predictors of phot ageing. Importantly, skin care routines and sunscreen use may help to prevent this process (Fig. 3).

### DISCUSSION

Epidemiological approaches to the impact of different factors that form part of the exposome have traditionally focused on individual exposures or a class of exposures (14). However, by definition, the exposome encompasses the totality of exposures to which an individual is subjected throughout their life (2) and, consequently, studies addressing the interaction of these factors and their net effect are necessary. Although a paper by Tamayo-Uria et al. (15) recently described the early-life exposome in 6 European countries, including Spain, characterization of the exposome in relation to skin ageing is a topic that has not yet been addressed. This study has described the exposome of the Spanish population, and have demonstrated for the first time that a large part of the analysed factors has a significant impact on the degree of skin ageing.

Firstly, our demographic data show that, contrary to popular belief, there is a prevailing “dark” Mediterranean skin; the majority of participants were phototype II, followed by phototype III, according to the Fitzpatrick scale. This prevalence does not seem to be exclusive to the Spanish population, since similar results have been described in other Mediterranean countries, such as...
as Turkey or Greece (14, 16), and might be related to the residential environment (mostly urban) and/or the current professional occupation (mostly indoor work). Furthermore, most participants presented moderate ageing (group 2), which is in agreement with the fact that the median age determined in this study was 40.84 years, a value within the expected range in this population group (10). Thus, both age and phototype classification showed a statistically significant association with the degree of ageing assessed by the specialists.

Secondly, this study evaluated several factors related to dietary habits and lifestyle, which are relevant when defining the exposome (17). The daily intake of fruit and vegetables and 1.5 L of water, occasional alcohol consumption and the absence of weight-loss diets in the last 5 years defined our study population. The other characteristics reported more frequently included a moderate stress level, regular sporting activity, no smoking habit and sleep time between 5 and 7 h per day. Finally, regarding skin care, most participants declared that they used sunscreen only when sunbathing and had no medical prohibition related to sun exposure, but stated that they perform a complete skin care routine, consisting of daily cleansing, an anti-ageing cream and moisturizing lotion. Interestingly, the association study demonstrated that almost all of those factors were significantly related to the degree of ageing, confirming previous scientific evidence. It is well known that sun exposure causes skin damage and ageing (6, 8, 18). Importantly, it must be taken into account that sunlight is composed of electromagnetic rays of different wavelengths, ranging from the highly energetic ultraviolet (UV) radiation to visible light and to the low energy infrared radiation. All of these are present in different amounts and penetrate to different skin levels (19). Specifically, all UVA wavelengths are known to contribute to skin photoageing, with UVA1 being a major contributor. Skin ageing is consequently the result of daily exposure to non-extreme, low doses of radiation that does not produce visible changes immediately, but that alters biological processes leading to noticeable long-term changes (4). Nutrition has been suggested to be strongly linked to skin ageing, where a high intake of vegetables, olive oil and legumes appeared to be protective against cutaneous damage, while a high intake of meat, dairy and butter appeared to be adverse (20). In the same way, a diet rich in anti-oxidants (highly present in fruits and vegetables) and a reduction in alcohol consumption may delay ageing effects (21). Tobacco is included among the factors that negatively impact skin ageing, by altering biological processes in this organ (4). In smokers, skin ageing is evidenced by typical facial changes, such as wrinkles around the mouth, upper lip and eyes (22), as well as hyperpigmentation of the oral mucosa or “smoker’s melanosis” (23). Other factors, such as water intake or stress, although not directly proven to be linked to skin ageing, are known to play important roles in maintaining the integrity and properties of the skin (4, 24). Finally, the use of cosmetics deserves special attention since, contrary to other exposome factors, these products are used voluntarily. Indeed, the effectiveness of different anti-ageing and moisturizing lotions has been reported previously (25–27). To achieve their desirable effects, skin care products must contain active ingredients focused on reducing the damage and preventing and/or delaying ageing. Apart from chemical or physical sunscreens, anti-oxidants, such as N-acetyl cysteine or vitamin C, retinol, peptides such as Pal-KTTS and tripeptide copper complex (GHK-Cu), and alpha hydroxy acids have been demonstrated to stimulate collagen production, showing clinical improvement in photoaged skin (28–32).

![Fig. 2. Receiver operating characteristic (ROC) curve to validate the logistic regression model.](https://www.medicaljournals.se/acta)
agreement with the participant’s profile drawn in the study. As described above, this profile includes relevant aspects regarding skin phototype, and nutritional and lifestyle habits.

Given the importance of exposome factors in skin ageing, a logistic model was constructed. As shown, age, smoking habit, use of sunscreen and the use of cosmetics are exposome factors that allow predictions to be made relative to skin photoageing. Our results highlight the importance of healthy habits and of using cosmetics and sunscreens. Indeed, the Spanish population represented here cared about their skin and the ageing process and declared that they actively take measures to prevent it. However, they did not pay special attention to photo-protection, which stresses the importance of making people aware of the risks of sunlight, not only in terms of photoageing, but also in terms of the well-established increased risk of skin cancer (33). Considering that subclinical signs of skin damage induced by UV exposure are already present at 15 years of age in the setting of normal exposure (34), and that visible skin modifications are found even in unexposed skin areas by the early 30s (35, 36), there is strong evidence to support regular use of sunscreen, as well as the implementation of other sun protection habits to delay the skin photoageing process (37, 38).

Finally, we have demonstrated that our model is valid and helps to explain the event, i.e. the independent variables (exposome factors) explain the dependent variable (degree of ageing). This is also confirmed by a classification rate >50% and an AUC >0.75.

This study also has some limitations. Despite a balanced recruitment approach, stratified cluster sampling might lead to overrepresentation or underrepresentation of some of the groups, reducing the strength of the conclusions obtained. Indeed, a higher representation of women was observed. Furthermore, since sampling was not random, a bias towards a population particularly worried about their skin (those who attended dermatological consultations) might have been introduced. On the other hand, some important exposome factors must also be taken into account, such as pollution levels; in addition, the real exposure to UV radiation could not be measured due to the complicated methodology required. Finally, this was a self-reported study, which implies intrinsic limitations that cannot be dismissed. Despite its weaknesses, the results presented here are robust and the objectives proposed were met.

In summary, this study describes the exposome of the Spanish population for the first time, and demonstrates its relationship with the degree of skin ageing. The results support the need for a healthy lifestyle, in which smoking should be avoided, and the importance of active skin care through the use of sunscreens and cosmetics that help to prevent skin ageing.

ACKNOWLEDGEMENTS

The authors thank Dr Almudena Fuster-Manzano and Dr Blanca Piedrafita for providing scientific support.

This work was funded by Vichy.

Conflicts of interest: LP and MA are employees of Vichy. AB-E and SAS declare no conflicts of interest.

REFERENCES

1. Wild CP. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol

Fig. 3. Factors that help to predict skin ageing in the final model along with contributing/preventive factors. *Complete skin care routine consisting of daily cleansing, an anti-ageing cream and moisturizing lotion.
Biomarkers Prev 2005; 14: 1847–1850.
2. Miller GW, Jones DP. The nature of nurture: refining the definition of the exposome. Toxicol Sci 2014; 137: 1–2.
3. Rappaport SM. Genetic factors are not the major causes of chronic diseases. PLoS One 2016; 11: e0154387.
4. Krutmajer J, Bouloc A, Sore G, Bernard BA, Passeron T. The skin aging exposome. J Dermatol Sci 2017; 85: 152–161.
5. Grant WB. The effect of solar UVB doses and vitamin D production, skin cancer action spectra, and smoking in explaining links between skin cancers and solid tumours. Eur J Cancer 2008; 44: 12–15.
6. Li M, Vierkotter A, Schikowski T, Huls A, Ding A, Matsui MS, et al. Epidemiological evidence that indoor air pollution from cooking with solid fuels accelerates skin aging in Chinese women. J Dermatol Sci 2015; 79: 148–154.
7. Marionnet C, Pierrard C, Lejeune F, Sok J, Thomas M, Bernard F. Different oxidative stress response in keratinocytes and fibroblasts of reconstructed skin exposed to non extreme daily-ultraviolet radiation. PLoS One 2010; 5: e12059.
8. Vierkotter A, Schikowski T, Ranft U, Sugiri D, Matsui M, Kramer U, et al. Airborne particle exposure and extrinsic skin aging. J Invest Dermatol 2010; 130: 2719–2726.
9. Huls A, Vierkotter A, Gao W, Kramer U, Yang Y, Ding A, et al. Traffic-related air pollution contributes to development of facial lentigines: further epidemiological evidence from Caucasians and Asians. J Invest Dermatol 2016; 136: 1053–1056.
10. Glogau RG. Aesthetic and anatomic analysis of the aging skin. Semin Cutan Med Surg 1995; 14: 134–138.
11. Roberts WE. Skin type classification systems old and new. Dermatol Clin 2009; 27: 529–533, viii.
12. Austin PC, Steyerberg EW. Events per variable (EPV) and the relative performance of different strategies for estimating the out-of-sample validity of logistic regression models. Stat Methods Med Res 2017; 26: 796–808.
13. Sperandei S. Understanding logistic regression analysis. Biochimia Medica 2014; 24: 12–18.
14. Stratigos A, Nikolau V, Kedicoglou S, Antoniou C, Stefanaki I, Haidemenos G, et al. Melanoma/skin cancer screening in a Mediterranean country: results of the Euromelanoma Screening Day Campaign in Greece. J Eur Acad Dermatol Venereol 2007; 21: 56–62.
15. Tamayo-Uria I, Maitre L, Thomsen C, Nieuwenhuijzen MJ, Chatzi L, Siroux V, et al. The early-life exposome: description and patterns in six European countries. Environ Int 2019; 123: 189–200.
16. Ekiz O, Yuce G, Ulasli SS, Ekiz F, Yuce S, Basar O. Factors influencing skin ageing in a Mediterranean population from Turkey. Clin Exp Dermatol 2012; 37: 494–496.
17. Vrijheid M. The exposome: a new paradigm to study the impact of environment on health. Thorax 2014; 69: 876–878.
18. Kligman AM. Early destructive effect of sunlight on human skin. JAMA 1969; 210: 2377–2380.
19. Dupont E, Gomez J, Bilodeau D. Beyond UV radiation: a skin under challenge. Int J Cosmet Sci 2013; 35: 224–232.
20. Purba MB, Kouris-Blazos A, Wattanapenpaiboon N, Lukito W, Rothenberg EM, Steen BC, et al. Skin wrinkling: can food make a difference? J Am Coll Nutr 2001; 20: 71–80.
21. Rowe DJ, Guoyron B. Environmental and genetic factors in facial aging in twins. Textbook of aging skin. Berlin: Springer.
22. Aizen E, Gilhar A. Smoking effect on skin wrinkling in the aged population. Int J Dermatol 2008; 40: 431–433.
23. Hedin C. Smokers’ melanosis: Occurrence and localization in the attached gingiva. Arch Dermatol 1977; 113: 1533–1538.
24. Palma L, Marques LT, Bujan J, Rodrigues LM. Dietary water affects human skin hydration and biomechanics. Clin Cosmet Investig Dermatol 2015; 8: 413–421.
25. Pinska MA. Efficacy and safety of an anti-aging technology for the treatment of facial wrinkles and skin moisturization. J Clin Aesthet Dermatol 2017; 10: 27–35.
26. Verschoore M, Nielsom N. The rationale of anti-aging cosmetic ingredients. J Drugs Dermatol 2017; 16: 594–597.
27. Watson REB, Ogden S, Cotterell LF, Bowden JJ, Bastrilles JY, Long SP, et al. A cosmetic ‘anti-aging’ product improves photoaged skin: a double-blind, randomized controlled trial. Br J Dermatol 2009; 161: 419–426.
28. Farris PK. Topical vitamin C: a useful agent for treating photaging and other dermatologic conditions. Dermatol Surg 2005; 31: 814–817; discussion 818.
29. Kafi R, Kwak HS, Schumacher WE, Cho S, Hanft VN, Hamilton TA, et al. Improvement of naturally aged skin with vitamin A (retinol). Arch Dermatol 2007; 143: 606–612.
30. Kang S, Chung JH, Lee JH, Fisher GJ, Wan YS, Duell EA, et al. Topical N-acetyl cysteine and genistein prevent ultraviolet-light-induced signaling that leads to photoaging in human skin in vivo. J Invest Dermatol 2003; 120: 835–841.
31. Sachs DL, Voorhees JJ. Age-reversing drugs and devices in dermatology. Clin Pharmacol Ther 2011; 89: 34–43.
32. Van Scott EJ, Yu RJ. Control of keratinization with alpha-hydroxy acids and related compounds. I. Topical treatment of ichthyotic disorders. Arch Dermatol 1974; 110: 586–590.
33. Silva ESD, Tavares R, Paulitsch FDS, Zhang L. Use of sunscreen and risk of melanoma and non-melanoma skin cancer: a systematic review and meta-analysis. Eur J Dermatol 2018; 28: 186–201.
34. Green BG, Bluth J. Measuring the chemosensory irritability of human skin. J Toxicol 1995; 44: 23–48.
35. Bergfeld WF. The aging skin. Int J Fertil Womens Med 1997; 42: 57–66.
36. Martini F. Fundamentals of anatomy and physiology. San Francisco: Springer; 2004.
37. Buendia Eisman A, Arias Santiago S, Moreno-Gimenez JC, Cabrera-Leon A, Prieto L, Castillo J, et al. An Internet-based programme to promote adequate UV exposure behaviour in adolescents in Spain. J Eur Acad Dermatol Venereol 2013; 27: 442–453.
38. Buendia-Eisman A, Palau-Lazaro MC, Arias-Santiago S, Cabrera-Leon A, Ferrande-Ortega S. Prevalence of melanoctytic nevi in 8- to 10-year-old children in southern Spain and analysis of associated factors. J Eur Acad Dermatol Venereol 2012; 26: 1558–1564.