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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.

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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.

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 (*vi*), 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 December 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 χ^2 test. A model was constructed to predict normal/excessive skin ageing based on binary logistic regression analysis (see Appendix S1[1]) (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

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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 (23.2)
Sex, *n* (%)	
Women	1,025 (69.5)
Men	449 (30.5)
Residential environment, *n* (%)	
Urban	1,326 (90)
Rural	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 (44.1)
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

Table II. Diet and lifestyle data

	Men	Women	Total
Daily consumption of fruit and vegetables, *n* (%)			
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)
≥7	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)	1438 (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-ageing cream	12 (2.7)	30 (2.9)	42 (2.8)
Anti-ageing cream + daily cleansing	13 (2.9)	46 (4.5)	59 (4.0)
Anti-ageing cream + moisturizing lotion	11 (2.4)	25 (2.4)	36 (2.4)
Anti-ageing cream + moisturizing lotion + daily cleaning	54 (12.0)	398 (38.9)	452 (30.7)
Any anti-ageing facial treatment* (last 2 years), *n* (%)			
No	377 (84.9)	598 (58.4)	975 (66.2)
Yes	72 (16.0)	426 (41.6)	498 (33.8)

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Table III. Analysis of the influence of exposome factors on the degree of ageing (according to Glogau scale)

	Ageing in accordance with age	Ageing higher than age	*p*-value
Age, *n* (%)			**<0.001**
20–29 years	44 (19)	185 (81)	
30–39 years	329 (73)	123 (27)	
40–49 years	335 (74)	115 (26)	
50–60 years	309 (90)	33 (10)	
Sex, *n* (%)			0.213
Women	714 (69.7)	310 (30.3)	
Men	303 (67.5)	146 (32.5)	
Residential environment, *n* (%)			0.243
Urban	919 (69.36)	406 (30.64)	
Rural	98 (66.22)	50 (33.78)	
Current occupation*			
Indoors, *n* (%)	896 (69.51)	393 (30.49)	0.172
Outdoors, *n* (%)	121 (65.76)	63 (34.24)	
Sun exposure time (h), mean ± SD	3,013 ± 2,799		
Fitzpatrick skin phototype, *n* (%)			**0.020**
I	60 (57)	46 (43)	
II	464 (71)	186 (29)	
III	388 (71)	155 (29)	
IV	94 (59)	64 (41)	
V	11 (69)	5 (31)	
Daily consumption of fruit and vegetables, *n* (%)			**<0.001**
Yes	833 (72)	329 (28)	
No	184 (59)	127 (41)	
Daily water intake 1.5 l/day, *n* (%)			**0.029**
No	224 (64)	125 (36)	
Yes	793 (71)	331 (29)	
Any weight-loss diet (last 5 years), *n* (%)			**0.027**
No	660 (67)	323 (33)	
Yes	357 (73)	133 (27)	
Alcohol consumption, *n* (%)			**0.012**
Never	440 (73)	162 (27)	
Occasionally	422 (65)	224 (35)	
Daily	155 (69)	70 (31)	
Stress leve, *n* (%)			**<0.001**
No stress	23 (62)	14 (38)	
Little	241 (70)	102 (30)	
Moderate	403 (66)	208 (34)	
Quite intense	287 (77)	86 (23)	
High	63 (58)	46 (42)	
Sporting activity, *n* (%)			
No	409 (69)	188 (31)	0.378
Yes	608 (69)	268 (31)	
Indoors	143 (63)	83 (37)	
Indoors/Outdoors	65 (69)	29 (31)	0.058
Outdoors	400 (72)	156 (28)	
Time spent on outdoor sports, h, mean ± SD			0.881
Smoking habit, *n* (%)			**0.033**
Non-smoker	731 (70)	309 (30)	
Smoker	156 (62)	95 (38)	
Ex-smoker	130 (71)	52 (29)	
Sleep time, *n* (%)			0.172
<5 h	96 (76)	30 (24)	
<7 h	517 (68)	245 (32)	
≥7 h	404 (69)	181 (31)	
Use of sunscreen, *n* (%)			**<0.001**
Never	44 (51.8)	41 (48.2)	
Only when sunbathing	425 (65.7)	222 (34.3)	
Occasionally	188 (68.9)	85 (31.1)	
Daily	360 (76.9)	108 (23.1)	
Sun exposure prohibition*, *n* (%)			**0.040**
No	987 (69)	451 (31)	
Yes	30 (86)	5 (14)	
Use of cosmetics, *n* (%)			
Daily cleansing	190 (62)	118 (38)	**<0.001**
Moisturizing lotion + daily cleansing	152 (60)	103 (40)	
Moisturizing lotion	200 (62)	121 (38)	
Anti-ageing cream	31 (74)	11 (26)	
Anti-ageing cream + daily cleansing	47 (80)	12 (20)	
Anti-ageing cream + moisturizing lotion	27 (75)	9 (25)	
Anti-ageing cream + moisturizing lotion + daily cleaning	370 (82)	82 (18)	
Any anti-ageing facial treatment** (last 2 years), *n* (%)			**<0.001**
No	633 (65)	342 (35)	
Yes	384 (77)	114 (23)	

*According to medical prescription. **Botulinum toxin-A, peeling or fillers. Bold values indicate statistically significant *p*-values ($p < 0.05$).
SD: standard deviation.

Table IV. Analysis of the exposome factors in the regression model

Exposome factors	*n*	*p*-value
Age	1,473	< 0.001
Fitzpatrick scale	1,473	0.782
Daily consumption of fruit and vegetables	1,473	< 0.001
Daily water intake 1.5 l	1,473	0.025
Alcohol consumption	1,473	0.048
Stress level	1,473	0.723
Smoking habit	1,473	0.026
Use of sunscreen	1,473	< 0.001
Use of cosmetics	1,473	< 0.001
Sun exposure prohibition	1,473	0.031
Any weight-loss diet (last 5 years)	1,473	0.025
Anti-ageing treatments (in the last 2 years)	1,473	< 0.001

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

Table V. Coefficients of the binary logistic regression equation

Variable	Coefficient	*p*-value
Age	−0.954	< 0.001
Smoking habit	0.310	< 0.001
Use of sunscreen	−0.177	0.016
Use of cosmetics	−0.076	0.015
Constant	1.562	< 0.001

$$Y = -0.954 \times \text{age (years)} + 0.310 \times \text{smoke habit} - 0.177 \times \text{use of sunscreens} - 0.076 \times \text{use of cosmetics} + 1.562;$$

- **Smoke habit:** non-smoker = 0; ex-smoker = 1; smoker = 2.
- **Use of sunscreens:** never = 0; only when sunbathing = 1; occasionally = 2; daily = 3.
- **Use of cosmetics:** daily cleaning = 0; moisturizing lotion = 1; moisturizing lotion + daily cleaning = 2; anti-aging cream = 3; anti-aging + daily cleaning = 4; anti-aging + moisturizing lotion = 5; anti-aging cream + moisturizing lotion + daily cleaning = 6.

Fig. 1. Predictive model for skin ageing.

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 (χ^2 322.993, 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 photoageing. 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 have 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

Table VI. Quality assessment of the logistic model

		Predicted		
		Ageing in accordance with age	Ageing higher than age	Correct percentage (%)
Observed	Ageing in accordance with age	932	82	91.6
	Ageing higher than age	231	225	49.3
	Total percentage			78.5

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).

According to the Glogau scale, most participants showed a degree of ageing corresponding to their actual age, which is in

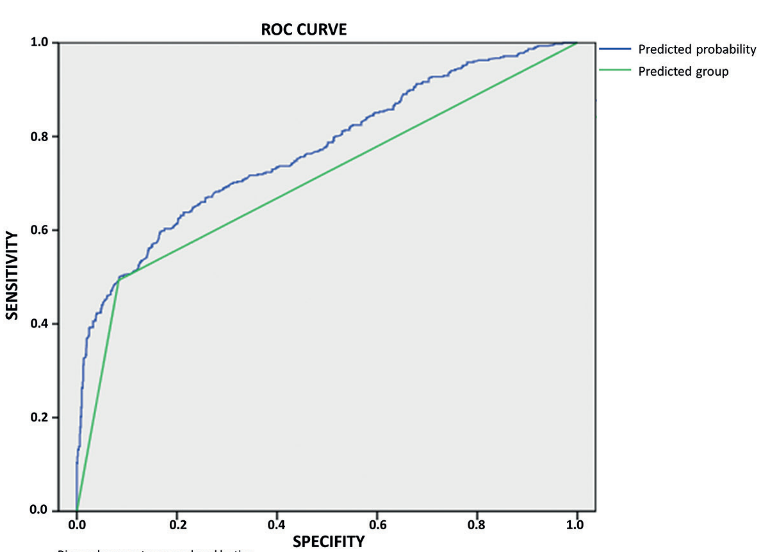

Fig. 2. Receiver operating characteristic (ROC) curve to validate the logistic regression model.

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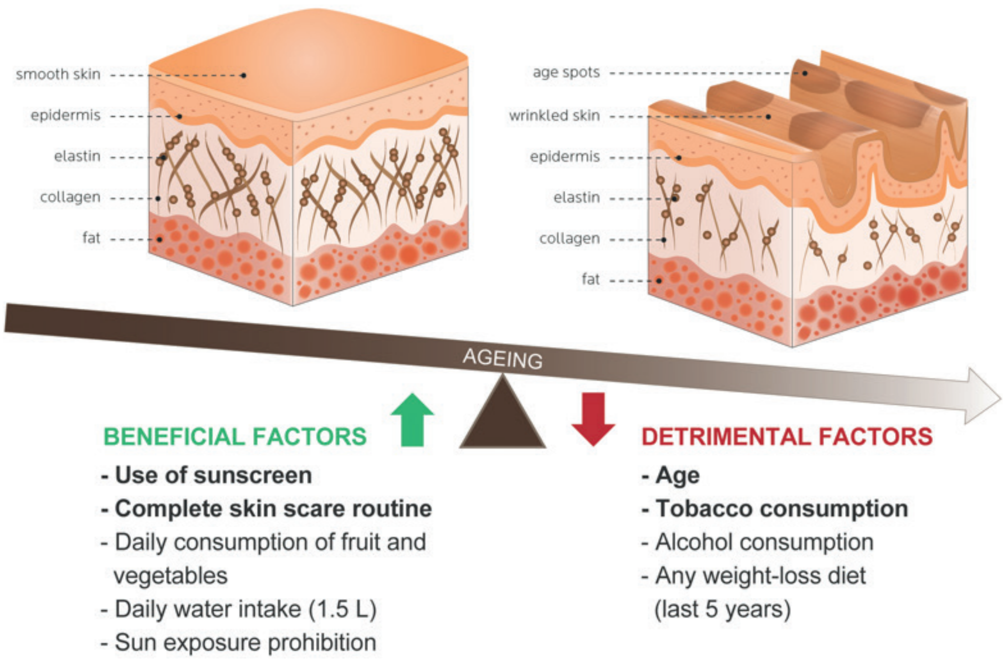

Fig. 3. Factors that help to predict skin ageing in the final model along with contributing/preventive factors. *Complete skin care routine consisting of daily cleansing, an anti-ageing cream and moisturizing lotion.

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 photoprotection, 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.

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