



## Extrinsic skin ageing in German, Chinese and Japanese women manifests differently in all three groups depending on ethnic background, age and anatomical site



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### ABSTRACT

**Background:** It has been suggested that extrinsic skin ageing manifests differently in Caucasians versus East Asians. In particular, from previous studies it was concluded that Caucasians are more prone to develop wrinkles, whereas pigment spot formation is the hallmark of extrinsic skin ageing in East Asians. However, these assumptions are based on a very limited number of studies which did not include different East Asian populations.

**Objective:** We here compare the manifestation of extrinsic skin ageing signs in German, Japanese and Chinese women by specifically elucidating the age and anatomical site dependence of any potential ethnic difference.

**Methods:** In the present study, we assessed skin ageing in N = 902 German, N = 165 Japanese and N = 1260 Chinese women ranging from 30 to 90 years by means of SCINEXA™. Linear regression analysis was used to test for ethnic differences and their age and site dependence adjusted for educational level, sun exposure, smoking and sun protection behaviours.

**Results:** Pigment spots and wrinkles on the face were present among all three ethnic groups and differences were influenced by age and anatomical sites independently of further influencing factors. Pigment spots on the forehead were most pronounced over the whole age range in Chinese and German women and least developed in Japanese. Pigment spots on cheeks were a typical extrinsic skin ageing sign in the two East Asian populations in all age groups. However, in older German women they reach the same level as observed in the two East Asian populations. In contrast, pigment spots on arms and hands were significantly more pronounced in German women ≥45 years of age. Wrinkles were not exclusively a skin ageing sign of German women, but were also very pronounced in Chinese women on forehead, between the eyebrows and in the crow's feet area.

**Conclusion:** These results corroborate the previous notion that the occurrence of pigments spots and wrinkles is different between Caucasians and East Asians. In addition, this study shows that this difference depends on age and anatomical site and that it also differs between different ethnic groups from East Asia.

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## 1. Introduction

Ageing of the skin is influenced by two separate processes. The general ageing process, which is genetically determined and occurs over time alone, is called the intrinsic skin ageing process, whereas the skin ageing process induced by environmental factors is termed the extrinsic skin ageing process. Prominent manifestations of the extrinsic skin ageing process are coarse wrinkles, solar elastosis and pigment irregularities [1]. It has been suggested that extrinsic skin ageing manifests differently in different ethnic groups [2–4]. Accordingly, Caucasians were reported to have an earlier onset of skin wrinkling and a more severe manifestation of wrinkles than East Asians [2–4]. In contrast, East Asians were found to show increased hyperpigmentation [2–4]. These differences might be attributed to intrinsic (genetic) or extrinsic (environmental) factors [5–9]. The most obvious intrinsic factor is the genetically determined skin color, which originates from an ethnic variation in melanin content and composition [5]. It has been shown that constitutive pigmentation influences the ethnic difference in the incidence of pigmentation disorders [6] and the visible signs of skin ageing, including skin wrinkling [7]. Other underlying causes might be further genetic variations beyond genes encoding skin color and/or different exposure habits to environmental factors, which influence skin ageing [2]. In this regard, we previously showed that a significant part of the ethnic difference in skin wrinkling manifestation between German and Japanese women can be explained by differences in sun exposure, smoking behaviour, and blood carotene content [8]. We also found that differences in the occurrence of pigment spots between Japanese and German women may be explained at least partially by differences in the distribution of a genetic marker in the *SLC45A2* gene, which is involved in melanin synthesis [9].

As a note of caution, however, it needs to be stated that the overall assumption that skin ageing manifests in Caucasians versus East Asians in an ethnic-specific manner, is based on a very limited number of studies ( $n=3$ ) [3,4,8]. Given the increasing interest in genetic determinants of skin phenotypes in general and gene/environment interactions in particular it thus appears that there is a need for validation studies involving larger cohorts of different ethnic backgrounds which ideally would use the same evaluation instrument for skin ageing manifestation.

Therefore, we here conducted the largest study, a total of 2326 women of three different populations (German, Chinese and Japanese) in order to systematically investigate the ethnic-specific manifestation of extrinsic skin ageing, with a special emphasis on its age and anatomical site dependence.

## 2. Material and methods

### 2.1. Study design and study populations

For the present analysis, we made use of three ethnically different populations which we had previously investigated in four independent studies, which are: (i) The Study of the influence of Air pollution on Lung function, Inflammation and Ageing (SALIA), which includes German women living in the Ruhr Area, (ii) the study of extrinsic skin ageing of Japanese and German women (JAGE), which assessed Japanese women living in Nagoya (Japan) and German women living in Duisburg (Germany) and (iii) the Taizhou study as well as (iv) the Pingding study, which investigated Han-Chinese women from either Taizhou or Pingding (China). Specifically, skin ageing assessment was performed in the follow-up 2008/2009 of the SALIA study and included  $N=806$  elderly German women. Detailed descriptions of the SALIA study can be found in Schikowski et al. [10] and

Voussoughi et al. [11]. The JAGE study was performed in 2011/2012 and included  $N=96$  German women and  $N=165$  Japanese women in the age from 30 to 70 years. Han-Chinese women aged 30–90 years were assessed in context of a study located in Taizhou near Shanghai in Jiangsu province (Taizhou study,  $N=857$ ) and in a second study located in Pingding near Beijing (Pingding study;  $N=403$ ). The latter two studies were conducted in 2012/2013. A detailed description of the Taizhou and the Pingding studies can be found in Wang et al. [12] and Li et al. [13]. In all studies, we applied the same instrument for skin ageing evaluation. All studies were approved by the respective human ethics committees and the Declaration of Helsinki Principles was followed. All study subjects were informed in detail by written form and gave written consent.

### 2.2. Assessment of skin ageing symptoms

Assessment of skin ageing was conducted in a standardised manner according to a protocol which was identical for all four studies. In brief, skin ageing symptoms were visually evaluated by applying the skin ageing score SCINEXA™ (SCore of INtrinsic and EXtrinsic skin Ageing) [14–16]. SCINEXA™ comprises a set of extrinsic and intrinsic skin ageing symptoms. However, we here only evaluate the extrinsic skin ageing signs pigment spots and coarse wrinkles as these are the signs, which seem to manifest in an ethnic-specific manner. Pigment and wrinkle scores were assessed with scores ranging from 0 (not present) to 5 (very severely present) according to photo-reference scales [3]. The pigment score refers to the size of the spots, whereas the wrinkle score refers to the severity of wrinkles in respect of their number, depths and length. Additionally, the number of pigment spots was evaluated as 0 = 0 pigment spots, 1 = 1–10 pigment spots, 2 = 11–50 pigment spots, 3 = more than 50 pigment spots. Before the assessment the face was cleaned and adapted to room temperature for 15 min and during the assessment the subjects were instructed to close their eyes and relax their face. In the SALIA study the SCINEXA™ evaluation was performed by A.V. In the other studies, each subject was examined on site by a dermatologist or study nurse, who had been trained prior to study start by A.V. in the correct use of SCINEXA™. In addition to the on-site assessment of SCINEXA™ scores, digital color photographs of participants were taken by a trained photographer in the Taizhou and Pingding studies. These photographs were used for quality controls, in which skin ageing manifestation was evaluated a second time by an independent trained dermatologist or study nurse. In the cases of (i) a scoring difference between the on-site scoring and the scoring of photographs larger than 1 or (ii) a disagreement for yes/no answers, the trainer (A.V.) of the SCINEXA™ decided the final score. Furthermore A.V. gave feedback to the on-site scorers how to evaluate the specific skin ageing trait correctly. As a result of this procedure the scores of the on-site scorers deviated from each other in less than 10% of the cases.

### 2.3. Statistical analysis

We pooled the German women from two studies (SALIA, JAGE) to one German population and the Chinese women from two studies (Taizhou, Pingding) to one Chinese population. Japanese women were only investigated in the JAGE study. Skin ageing manifestation was then described for each ethnic group (German, Japanese, Chinese) and further for three different age groups: (30–45) years, (45–60) years and (60–90) years of age separately. As the distribution of wrinkle and pigment scores were normally distributed, arithmetic means (AM) were calculated. The distribution of a pigment spot number was log-normally distributed and therefore the geometric means (GM) were given.

**Table 1**  
Description of study population characteristics.

	SALIA	JAGE (German population)	JAGE (Japanese population)	Taizhou	Pingding
N	510	88	157	749	403
Age range, AM (Min–Max)	73.5 (66.7–79.7)	51.7 (31.1–73.6)	45.9 (30.0–70.0)	57.5 (31.8–89.7)	53.7 (33.9–82.5)
Educational level					
<10 years of school education	179 (35.1%)	31 (35.2%)	7 (4.5%)	385 (51.4%)	219 (54.3%)
=10 years of school education	234 (45.9%)	13 (14.8%)	0 (0.0%)	261 (34.8%)	113 (28.0%)
>10 years of school education	97 (19.0%)	44 (50.0%)	150 (95.5%)	103 (13.8%)	71 (17.6%)
Smoking behaviour					
Never-smokers, n (% Yes)	411 (80.6%)	38 (43.2%)	117 (74.5%)	721 (96.3%)	378 (93.8%)
Ex-smokers, n (% Yes)	84 (16.5%)	35 (39.8%)	25 (15.9%)	2 (0.3%)	14 (3.5%)
Current smokers, n (% Yes)	15 (2.9%)	15 (17.0%)	15 (9.6%)	26 (3.5%)	11 (2.7%)
Sun exposure <sup>a</sup> , AM (SD)	2.6 (1.2)	5.0 (2.2)	2.2 (1.1)	3.2 (2.0)	4.7 (2.0)
Sun protection <sup>b</sup> , n (% Yes)	318 (62.4%)	74 (84.1%)	129 (82.2%)	43 (5.7%)	23 (5.7%)

AM: arithmetic mean, SD: standard deviation.

<sup>a</sup> Sun exposure: average hours outside per day in summer during lifetime.<sup>b</sup> Sun protection: usage of cream with sun protection factor.

Differences in skin ageing manifestation between the different populations and different age groups were calculated by linear regression analysis. The linear regression analysis was further adjusted for age as each age group included a range of 15 or more years as well as for study (SALIA, JAGE (Japan), JAGE (Germany), Taizhou and Pingding) in order to account for differences in study conceptions. Additionally the statistical model was adjusted for social status indicated by school education and major environmental factors influencing skin ageing like: (i) educational level (<10 years, =10 years and >10 years of school education), (ii) smoking behaviour: never-smokers, ex-smokers, current smokers, (iii) sun exposure: average hours outside per day in summer during lifetime and (iv) sun protection behaviour: usage of cream with sun protection factor. The adjusted regression coefficients were transformed to arithmetic mean ratios (AMRs) for normally distributed skin ageing signs with 95% confidence intervals (CI) and to geometric mean ratios (GMRs) with 95% CI for log-normally distributed signs according to Vierkötter et al. [14]. The mean ratios are relative values for continuous variables, which estimated relative change in the mean associated with a one-unit increase in the co-variables; they are comparable in their meaning to the odds ratio (OR). The analyses were carried out using the statistical software R 3.1.2 (R Core Team 2014).

### 3. Results

#### 3.1. Characteristics of study populations

In Table 1 the characteristics of the different study populations are described. Only women with complete information on relevant skin ageing items and on assessed influencing factors such as age, educational level, smoking and sun exposure behaviour are presented. SALIA included elderly German women with a mean age of 73.5 years and an age range of 67–80 years. Most of the women in SALIA had 10 years of school education and were never smokers. They spent around 2.6 h outside per day in summer time and more than 60% have used cream containing sun protection factor. The SALIA study population was pooled with the German population of the JAGE study with a lower mean age of 51.7 years and a broader age range of 31–74 years. The German population of the JAGE study included mainly never smoking women with more than 10 years of school education. They have spent in average 5 h outside per day in a summer time, but mainly with using sun protection cream. The Japanese population of the JAGE study has a mean age of 45.9 with an age range of 30–70 years. Nearly all

Japanese women have more than 10 years of school education, more than 70% were never smokers and more than 80% used cream with sun protection factor. Japanese women only spent 2.2 h per day on the average outside in summer, which was the lowest sun exposure time per day of all included populations. The two Chinese studies have a mean age of 57.5 and 53.7 years, respectively, and an age range from 31 to 90 years. The Chinese studies also included mainly never smoking women with a school education less than 10 years, who spent 3.2–4.7 h outside per day in summer. Only a very small fraction of the Chinese women used cream with sun protection factor. The two Chinese studies were also pooled together.

We finally assessed the ethnic difference in N=598 German women, in N=157 Japanese women and in N=1152 Chinese women (Table 2) with complete information on relevant skin ageing items and assessed influencing factors as presented in Table 1. In Table 2 the distribution of study participants in the different age groups of the respective ethnic populations is described in detail.

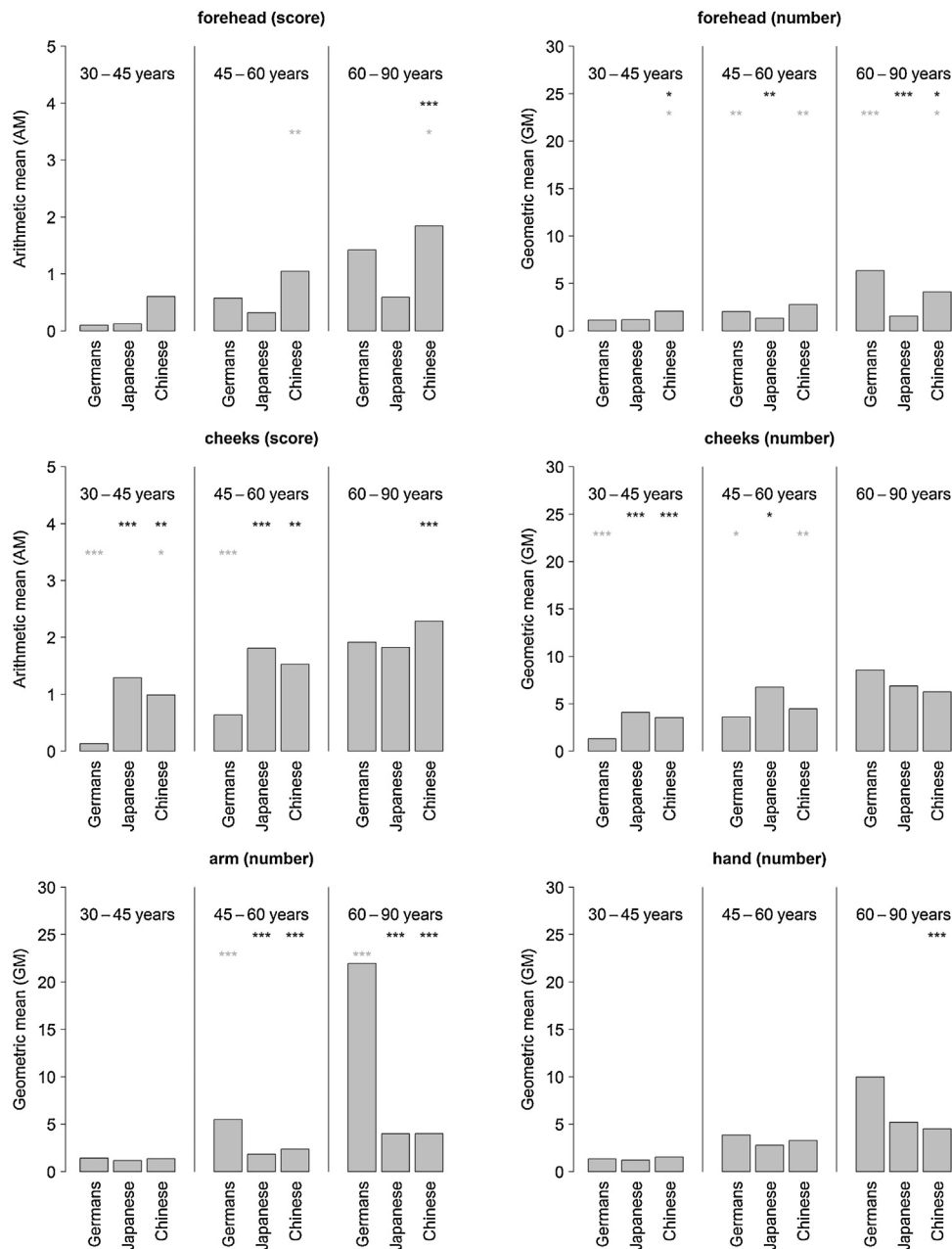
#### 3.2. Ethnic difference in extrinsic skin ageing manifestation

We here describe the observed ethnic difference in skin ageing manifestation depending on age and different anatomical sites. We further considered educational level, sun exposure, smoking and sun protection behaviours as important influences of skin ageing manifestation, which might impact the observed ethnic difference by age and anatomical site. This means that in the following the presented ethnic difference by age and anatomical site is independent from educational level, sun exposure, smoking or sun protection behaviours.

In Figs. 1 and 2 the mean skin ageing manifestation for each of the three ethnic populations (German, Japanese, Chinese) and for three age groups ((30–45) years, (45–60) years and (60–90) years)

**Table 2**  
Number of study participants in each age group of the different ethnic populations.

age group:	German population N in respective age group	Japanese population	Chinese population
(30–45)	28	80	239
(45–60)	37	61	451
(60–90)	533	16	462
Total	598	157	1152



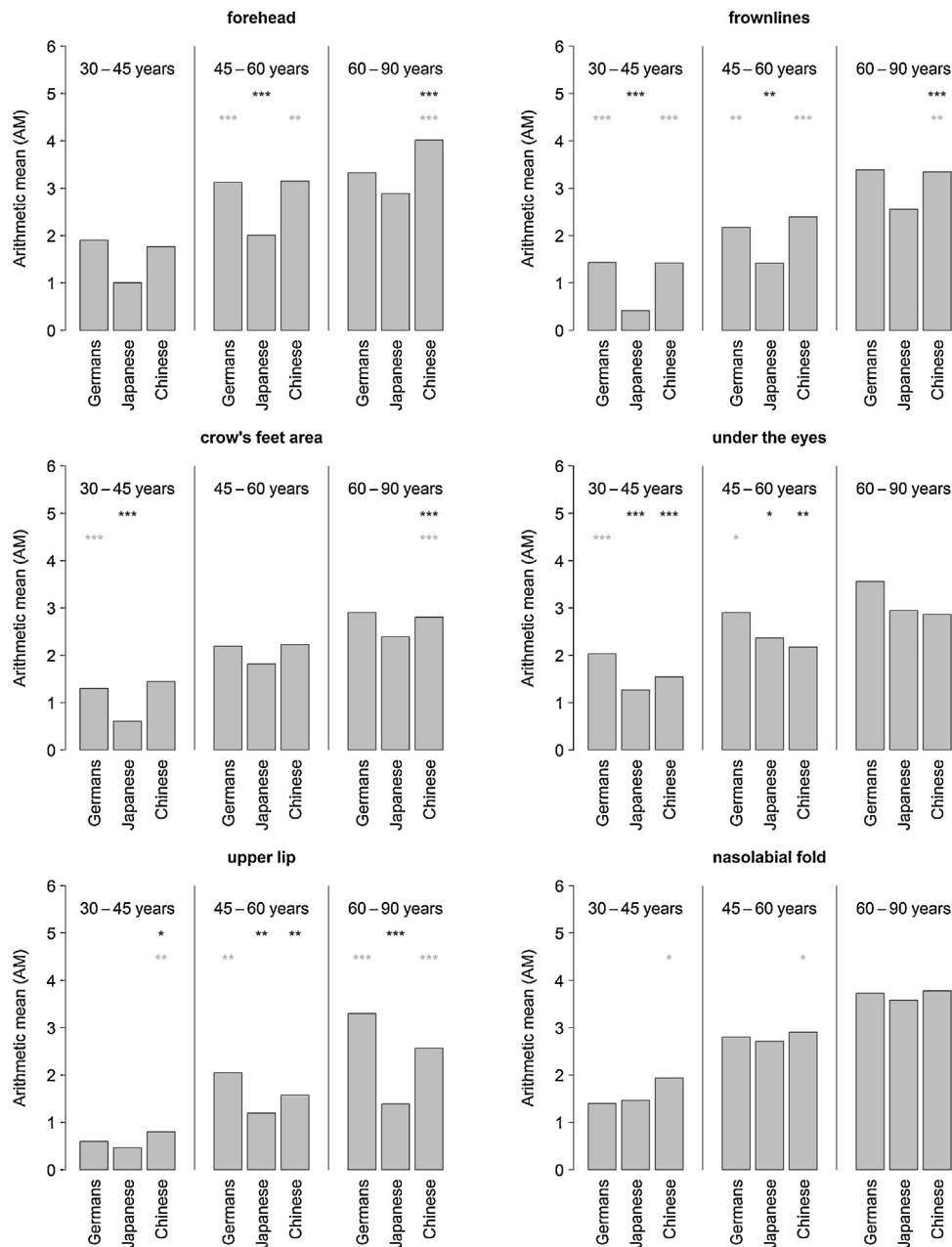
**Fig. 1.** Mean score or number of pigment spots on different anatomical sites separately for the three ethnic populations (German, Japanese, Chinese) and the three age groups: (30–45) years, (45–60) years and (60–90) years of age. Significant ethnic differences in skin ageing sign manifestation between two different populations gained from adjusted linear regression analyses (see supplemental Tables 4–6) are indicated by stars (\*:  $p < 0.05$ ; \*\*:  $p < 0.001$ ; \*\*\*:  $p < 0.0001$ ). Black stars indicate a significant difference in skin ageing sign manifestation of Japanese or Chinese women in comparison to German women (German women used as reference group) and grey stars indicate a significant difference of German or Chinese women in comparison to Japanese women (Japanese women used as reference group).

is shown. Further, in these figures significant differences in skin ageing sign manifestation between ethnic populations gained from adjusted linear regression analysis (supplemental Tables 4–6) are indicated by stars (\*:  $p < 0.05$ ; \*\*:  $p < 0.001$ ; \*\*\*:  $p < 0.0001$ ).

In Fig. 1 the mean score (referring to spot size) and the mean number of pigment spots on different anatomical sites (forehead, cheeks, arm and hand) is presented (mean values are listed in Supplemental Tables 1–3). For pigment spots on forehead, the score as well as the number were most pronounced in Chinese women. However, this difference became less with age. In the group of individuals  $\geq 60$  years of age Chinese women still showed 1.4 times larger pigment spots than German ( $p < 0.001$ ) and 1.5 times larger pigment spots than Japanese ( $p = 0.045$ ), but German

women had the most pigment spots of all three groups (Supplemental Table 6).

For pigment spots on cheeks, mean score and number were highest in the two East Asian populations, but increased in the German population with age, finally being equivalent to levels observed in the two East Asian populations (Fig. 1). Accordingly, at the age of 30–45 year, Japanese women showed 2.1 times larger and 2.9 times more pigment spots than German women ( $p < 0.001$ ) and Chinese women showed 1.7 times larger and 2.5 times more pigment spots than German women ( $p < 0.01$ ) (supplemental Table 4). In the oldest age group, however, East Asian women still showed larger pigment spots than German women, but there was no significant difference in the number of pigment spots on cheeks



**Fig. 2.** Mean wrinkle score on different anatomical sites separately for the three ethnic populations (German, Japanese, Chinese) and the three age groups: (30–45) years, (45–60) years and (60–90) years of age. Significant ethnic differences in skin ageing sign manifestation between two different populations gained from adjusted linear regression analyses (see supplemental Tables 4–6) are indicated by stars (\*:  $p < 0.05$ ; \*\*:  $p < 0.001$ ; \*\*\*:  $p < 0.0001$ ). Black stars indicate a significant difference in skin ageing sign manifestation of Japanese or Chinese women in comparison to German women (German women used as reference group) and grey stars indicate a significant difference of German or Chinese women in comparison to Japanese women (Japanese women used as reference group).

between the East Asian populations and the German population (Fig. 1 and Supplemental Table 6). In contrast, pigment spots on arms and hands were most pronounced in German women in the age from 45 to 90 years in comparison to the two East Asian groups. There was no significant difference in the number of pigment spots on arm and hands between Japanese and Chinese women (Fig. 1 and Supplemental Table 4–6).

In Fig. 2 the mean wrinkle score (referring to wrinkle depth and length) on different anatomical sites (forehead, frownlines, crow's feet, under eyes, upper lip, nasolabial) is shown (mean values are listed in Supplemental Tables 1–3). Wrinkle scores were more pronounced in Chinese and German women for the anatomical sites forehead, frownlines and in the crow's feet area in

comparison to Japanese women. In this regard Chinese women, for example, showed 10% to 30% more severe wrinkles on forehead than Japanese women over the whole age range (Supplemental Tables 4–6). Further, 30–45 year old Chinese women showed 70% more severe frownlines compared to Japanese women (Supplemental Table 4). This difference decreased with age, but in the oldest age group Chinese women still showed 20% more severe frownlines than Japanese women (Supplemental Table 6). For wrinkles in the crow's feet area Chinese women showed 10–30% more severe wrinkles over the whole age range (Supplemental Tables 4–6). Wrinkle scores on the anatomical sites under the eyes and on upper lips were generally more pronounced in German women in comparison to the East Asian populations (Fig. 2).



Regarding wrinkles under the eyes the ethnic difference was more pronounced in the youngest age group. Japanese and Chinese women showed 40% to 50% less severe wrinkles under the eyes compared to German women (Supplemental Table 4). This ethnic difference decreased with age. Regarding wrinkles on upper lips, the ethnic difference was especially pronounced in the middle-aged age group. Here East Asian women showed 30% less severe wrinkles on upper lip than German women (Supplemental Table 5). Nasolabial folds were similarly pronounced in all three ethnic populations (Fig. 2).

#### 4. Discussion

In the current study we confirm the previous findings that extrinsic skin ageing manifests in an ethnic-specific manner when comparing Caucasians and East Asians [2,3,7]. We also unambiguously show, however, that the assumption that Caucasians develop more pronounced wrinkles earlier, whereas Asians develop more pronounced pigment spots earlier, [1–3] is not entirely true, but most likely represents an oversimplification. This may be the case because (i) these differences depend on age and anatomical site and (ii) differences between different ethnic groups in East Asian countries need to be considered. Further, we here show for the first time, that the observed ethnic difference in skin ageing manifestation is independent from educational level, personal sun exposure, smoking and sun protection behaviour.

Specifically, we here report that skin wrinkling on different facial regions is significantly more pronounced in German women than in Japanese women until the age of 60 years. In older women this difference becomes smaller, as also reported by Tschachler et al. [2]. In marked contrast, facial skin wrinkling is not significantly more pronounced in German women when compared with Chinese women over the whole age range. In fact, Chinese women even develop more pronounced wrinkles on forehead, between the eyebrows and in the crow's feet area than German women above the age of 60. This is in line with a previous report indicating that Chinese women aged 40–50 years old might be particularly prone to wrinkle formation [3]. We therefore conclude that the assumption that Caucasian women are more prone to developing wrinkles as compared with East Asian women might be incorrect as this difference clearly depends on which East Asian populations are being considered.

We also here observe that pigment spots on forehead may not be regarded as a unique skin ageing sign in East Asians, because they are less pronounced in Japanese women than in German women and they increase with age in German women reaching similar levels than in Chinese women. In contrast, pigment spots on cheeks were more pronounced in both Japanese and Chinese women as compared with German women (at least until the age of 60), thus confirming a previous observation by Tschachler et al. [2]. The relevance of anatomical site for pigment spot development is further emphasized by the observation that the opposite seems to be true for pigment spots on the upper side of the arm and back of the hands, for which German women show higher values than women from the two East Asian populations. We therefore conclude that the assumption that East Asians are more prone to develop pigment spots than Caucasians might not be entirely correct; this might be only true for pigment spots on cheeks up to 60 years of age, but not for pigment spots on foreheads, and the opposite seems to be true for pigment spots on an upper side of the arms and back of hands. These results thus again underline the importance of anatomical site, age as well as differences between different East Asian populations.

One limitation of our study is that there was not an equal distribution over the investigated age range in our study populations. This leads for some age groups to relatively small

sample sizes, especially for the Japanese study population, where in total  $N = 165$  study subjects were included. As a consequence, we might have missed some ethnic differences in skin ageing manifestation due to low power. Further, we did a lot of statistical analysis to analyse the ethnic difference of 12 skin ageing sign outcomes, 3 age groups and 3 ethnic populations, which might have led to some significant results by chance. Further, it is noteworthy, that pigment spots on different anatomical sites as well as wrinkles on different anatomical sites are moderately to highly correlated with each other (correlation coefficients ( $r^2$ ): 0.3–0.7) and thus ethnic differences in highly correlated skin ageing signs might be similar. Our statistical analysis is adjusted for major environmental and behavioral influencing factors on skin ageing, but other environmental and behavioral factors like air pollution exposure and the use of cosmetics might explain further fractions of the observed ethnic difference. There might be also some women, who have had corrective or reparative dermatological treatments which might have led to skin ageing misclassification.

The strengths of our study is that we included three different ethnic populations with relatively big sample sizes and that we investigated skin ageing similarly in all three study populations by applying the same instrument i.e. the SCINEXA™. Further we also adjusted for educational level and personal sun exposure, smoking and sun protection behaviour, in order to show the ethnic difference in skin ageing manifestation, which occur independent from these factors.

In conclusion, the present study corroborates the previous notion that the occurrence of pigments spots and wrinkles is different between Caucasians and East Asians. In addition, this study shows that this difference depends on age and anatomical site and that it also differs between different ethnic groups from East Asia. The ethnic difference in skin ageing manifestation by age and anatomical site was independent from educational level and personal exposure habits towards the sun and cigarette smoke as well as independent from personal sun protection behaviour, meaning that most probably genetic predispositions and/or the interplay between the ethnic specific genetic make-up and the exposure to relevant environmental factors like sun exposure and smoking are relevant for the observed ethnic difference in skin ageing manifestation and have to be elucidated in more detail in the future. In this regard, in a previous publication, we already could show that genetic variation in the *SLC45A2* gene, which has been shown to influence skin, hair and eye color, might be associated with the ethnic specific occurrence of pigment spots in Caucasians and Asians.

#### Conflict of interest

Jean Krutmann, Akimichi Morita, Zhiwen Li, Li Jin and Sijia Wang received financial support by research grants from 'The Estee Lauder Companies' for the conduction of the presented epidemiological studies. Mary Matsui is an employee of 'The Estee Lauder Companies'.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jdermsci.2016.05.011>.

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