



Epidemiological evidence that indoor air pollution from cooking with solid fuels accelerates skin aging in Chinese women



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ABSTRACT

Background: Recently, we showed that outdoor air pollution exposure from traffic and industry is associated with an increased risk of skin aging in Caucasian women. In China, indoor air pollution exposure caused by the use of solid fuels like coal is a major health problem and might also increase the risk of skin aging in Chinese women.

Objective: As cooking with solid fuels is a major source of indoor air pollution exposure in China, we aimed to test if cooking with solid fuels is associated with more pronounced skin aging in Chinese women.

Methods: We conducted two cross-sectional studies in China to assess the association between cooking with solid fuels and signs of skin aging. In Pingding (in northern China) we assessed $N = 405$ and in Taizhou (in southern China) $N = 857$ women between 30 and 90 years of age. Skin aging was evaluated by the SCINEXA™ score. Indoor air pollution exposure, sun exposure, smoking and other confounders were assessed by questionnaires. Associations were then tested by linear and logistic regression analyses adjusted for further confounders.

Results: The analysis showed that cooking with solid fuels was significantly associated with a 5–8% more severe wrinkle appearance on face and an 74% increased risk of having fine wrinkles on back of hands in both studies combined, independent of age and other influences on skin aging.

Conclusion: The present studies thus corroborate our previous finding that air pollution is associated with skin aging and extend it by showing that indoor air pollution might be another risk factor for skin aging.

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Abbreviations: AhR, arylhydrocarbon receptor; AM, arithmetic mean; AMR, arithmetic mean ratio; BMI, Body mass index; CI, confidence interval; GM, geometric mean; GMR, geometric mean ratio; MMP, matrixmetalloproteinase; OR, odds ratio; PAH, polycyclic aromatic hydrocarbon; PM, particulate matter; SCINEXA™, Score for intrinsic and extrinsic skin aging; TGF- β , transforming growth factor β .

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1. Introduction

Indoor air pollution caused by the combustion of solid fuels (coal or biomass) for cooking or heating is a major public health challenge in China [1]. In China, more than 70% of the households use solid fuels for cooking or heating [2]. The combustion of coal and biomass indoors emits a substantial amount of toxic pollutants including particulate matter (PM), polycyclic aromatic hydrocarbons (PAHs), carbon monoxide, nitrogen oxides and sulfur dioxide [3]. Various studies have been conducted to investigate the impact of indoor air pollution on health effects including respiratory illnesses, lung cancer, chronic obstructive pulmonary disease, weakening of the immune system, and reduction in lung function [4]. Exposure to indoor air pollution might also lead to more pronounced skin aging.

Clinical hallmarks of the environmentally-induced (extrinsic) skin aging process are coarse wrinkles, solar elastosis and pigment irregularities [5]. Superimposed on chronological (intrinsic) skin aging signs at chronically exposed areas of the body, these skin aging signs contribute to the appearance of looking old. Important environmental factors able to induce extrinsic skin aging include sun exposure and smoking [6,7]. Additionally, Vierkötter et al. [8] showed that exposure to outdoor air pollution from traffic and industry is associated with an increased risk for extrinsic skin aging manifestation in Caucasian women.

The current study specifically investigated the association between cooking with solid fuels and the manifestation of different

skin aging signs in two independent study populations of Chinese women. Cooking with solid fuels is a major source of indoor air pollution exposure in China. In contrast to heating with solid fuels, which is used seasonally, cooking with solid fuels causes a constant, daily exposure. Furthermore, women might be especially affected by this indoor air pollution exposure as they spend a larger proportion of their time indoors.

2. Material and methods

2.1. Study design and study populations

For our study, we made use of two independent Chinese study populations, which were recruited in the years 2012 and 2013. In both studies, we applied the same instrument for skin aging evaluation and also used validated questionnaires to assess cooking with solid fuels and further covariates of skin aging like sun exposure and smoking behaviors.

One study population was located north of Shanghai at Taizhou in Jiangsu province (Fig. 1). These study participants were recruited out of an existing large prospective study, the Taizhou Longitudinal Study. The Taizhou Longitudinal Study aims to investigate environmental and genetic risk factors for common chronic diseases in China. The detailed description of the Taizhou longitudinal study was described elsewhere by Wang et al. [9]. Between August and September 2012, we investigated 857 healthy Chinese women ranging in age from 28 to 90 years out of the

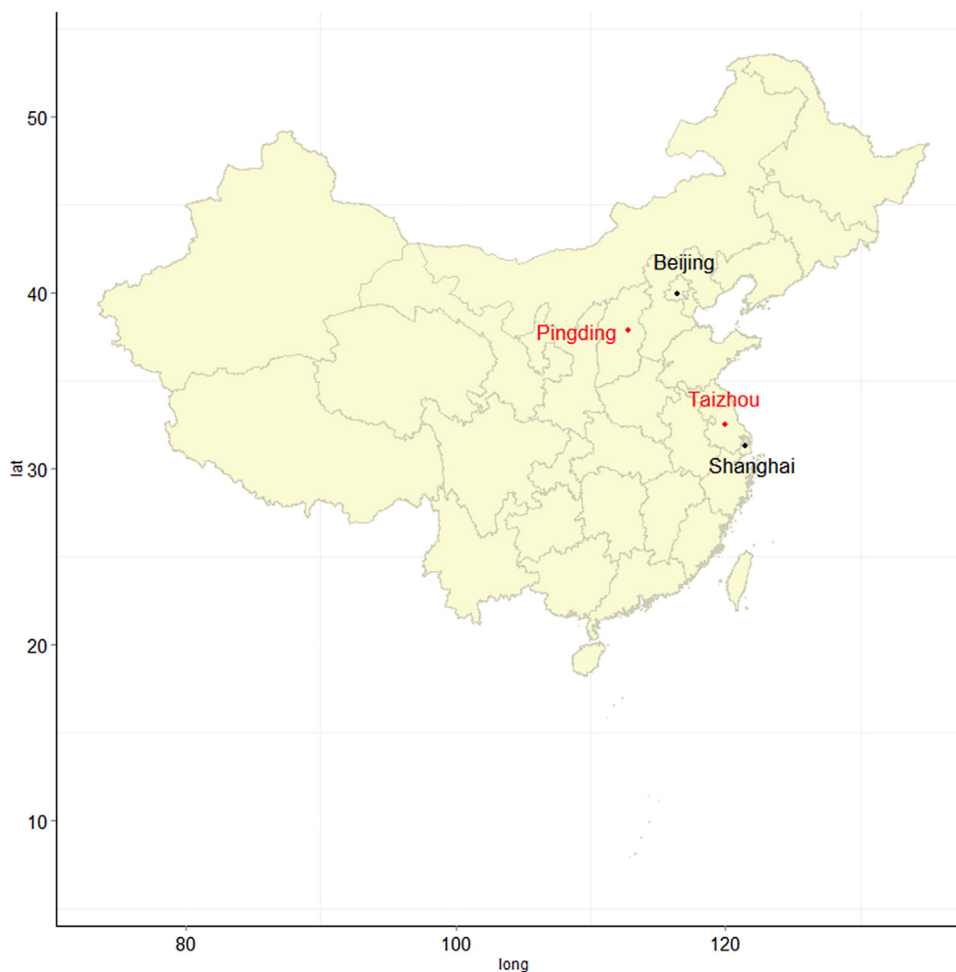


Fig. 1. Map of China with study center locations. The Pingding study population was collected at Pingding County Hospital in Shanxi Province near Beijing and the Taizhou study population was collected in Jiangsu Province near Shanghai.

Taizhou cohort. The Taizhou cohort study recruited 100,000 adults aged 30–90 years from the general population of Taizhou, through a three-stage stratified random sampling method (see detailed description in Wang et al., 2009 [9]). The present study recruited participants of the Taizhou cohort study with the following criterias: (1) women; (2) individuals with at least 15 years residential length in their current address; and (3) individuals whose residential address is less than 10 km away from the nearest air pollution monitoring station (an important criterium for a separate study focusing on outdoor air pollution). The human ethics committee of Fudan University in Shanghai approved the study. The other study population was collected in northern China near Beijing in Pingding County Hospital in Shanxi Province (Fig. 1). At this hospital the mother or mother-in-law accompanying her pregnant daughter or daughter-in-law were recruited. Only rural housewives were recruited and subjects had to meet the following inclusion criteria: (1) healthy women who are native (not immigrant) residents in the study county, (2) aged 30 to 80 years, (3) dwelling conditions (especially kitchen status regarding using solid fuels for cooking) did not change during the past 10 years, and (4) who consented to participate. A total of 405 rural housewives were recruited between 2012 and 2013. For the rural population of Shanxi Province negative effects of indoor air pollution from coal combustion have already been shown [10]. The human ethics committee of Beijing University approved the study.

The Declaration of Helsinki Principles was followed and all study subjects were informed in detail by written form and gave written consent.

2.2. Assessment of co-variables:

Demographic data and environmental exposure history, which might influence skin aging such as age, education (educational level categorized as primary school, junior high school, senior high school and higher education), body mass index (BMI), smoking (never, ex and current smokers as well as number of pack years), passive smoke exposure (yes/no, at home and/or at work), alcohol consumption (yes/no), sun exposure (average hours outside per day in summertime during lifetime) and sunburn history (yes/no) were collected by well-defined questionnaire-based interviews. Indoor air pollution exposure, in terms of using solid fuels (coal, firewood or straw vs. gas or electricity) for cooking at home was also obtained by questionnaires. More details regarding the applied questionnaires in the respective study can be found in Wang et al., 2009 [9] for the Taizhou study and Li et al., 2011 [10] for the Pingding study.

2.3. Assessment of skin aging symptoms:

Skin aging symptoms were evaluated by applying the skin aging score SCINEXA™ (SCore of INtrinsic and EXtrinsic skin Aging) [8,11]. Wrinkles were assessed with scores ranging from 0 (not present) to 5 (very severely present) according to photo-reference scales [12]. The number of pigment spots was evaluated as 0 = 0 pigment spots, 1 = 1 to 10 pigment spots, 2 = 11 to 50 pigment spots, 3 = more than 50 pigment spots. The manifestation of telangiectasia, solar elastosis, cutis rhomboidalis nuchae, Morbus Favre Racouchot and even pigment spots on bottom side of the arm was evaluated as present or not present. Furthermore, intrinsic skin aging symptoms, laxity of eyelids and laxity of cheeks were also assessed with scores from 0 to 5, and fine wrinkles on the back of hands were documented as present or not present. Briefly, the subjects were instructed to close their eyes and relax their face, after their face was cleaned and adapted to room temperature for 15 min. The skin aging assessment was done according to a strict protocol. Specifically, each subject was examined on site by a

dermatologist or study nurse, who had been trained prior to study start by two trainers from IUF in the correct use SCINEXA™. Specifically, A.V. and M.L. served as trainers. A.V. originally developed SCINEXA™ [11] and M.L. had received intensive training in SCINEXA™ based assessments during a one year stay at IUF. In addition to the assessment of SCINEXA™ scores, digital color photographs of participants were taken by a trained photographer. These photographs were used for quality controls, in which skin aging manifestation was evaluated a second time by an independent trained dermatologist or study nurse. If the scoring difference between the on site scoring and the scoring of photographs was larger than 1 or if there was no agreement for yes/no answers, the trainers of the SCINEXA™ decided the final score. Furthermore the trainers gave feedback to the first two scorers how to evaluate the specific skin aging trait correctly. As a result of this procedure the scores of the first two scorers deviated from each other in less than 10% of the cases.

2.4. Statistical analysis

We first analyzed the effect of cooking with solid fuels on skin aging in each study population separately by using linear and logistic regression analysis. We used two statistical models. In a first model we only adjusted for age and in a second model we further adjusted for BMI, educational level, smoking, passive smoking, alcohol consumption, sun exposure and sunburn history. Furthermore, we analyzed the effect of cooking with solid fuels on skin aging in all study subjects by combining the two study populations in order to increase power. The pooled analysis is further adjusted for study population. Moreover we tested if a pooled analysis is justified and gives an adequate estimate for the effect of indoor air pollution on skin aging manifestation. A pooled analysis is justified, if the effect of indoor air pollution on skin aging is not modified by study population. This modification was tested by interaction analysis.

The wrinkle, telangiectasia and laxity scores were normally distributed, and arithmetic means (AM) were calculated. The number of pigment spots was log-normally distributed and therefore the geometric means (GM) were given. Hence, the adjusted regression coefficients were transformed to arithmetic mean ratios (AMR) for normally distributed skin aging signs with 95% confidence intervals (CI), for log-normally distributed signs to geometric mean ratios (GMR) with 95% CI [8]. The mean ratios were relative values for continuous variables, which estimated relative change in the mean associated with a one-unit increase in the co-variables; and they were comparable in their meaning to the odds ratio (OR). Coefficients for the categorical variables solar elastosis, Morbus Favre Racouchot, cutis rhomboidalis nuchae, even pigment spots on bottom side of the arm and fine wrinkles on the back of hands were adjusted odds ratios (OR) with 95% confidence intervals (CI). The analyses were carried out using the statistical software SAS 9.2 (SAS Institute Inc., Cary, NC, USA, 2002–2003).

3. Results

3.1. Characteristics of study populations:

In Table 1 the characteristics of the Taizhou and the Pingding study population are presented. Both study populations were restricted to complete cases for the statistical analyses with no missing data in the variables age, BMI, educational level, smoking, passive smoking, alcohol consumption, sun exposure, sunburn history and cooking with solid fuels. In the Taizhou study population there were $N = 727$ out of $N = 857$ women and in the Pingding study population there were $N = 402$ out of $N = 405$ women with complete information in these variables. All women

Table 1
Characteristics of the Taizhou (Shanghai, China) and Pingding study (Beijing, China) population.

		Taizhou study population (N = 727)	Pingding study population (N = 402)	p-Value ^a for difference in variable distribution between study populations
Age [years]	Mean (SD)	57 (11)	53 (10)	<0.0001
	Min–Max	28–90	33–82	
Body mass index (BMI) [kg/m²]	Mean (SD)	23.9 (3.1)	24.9 (3.0)	<0.0001
	Min–Max	16.4–35.6	18.0–35.1	
Education:				
Primary school or lower education	% Yes (n)	49.8 (362)	54.3 (218)	Primary school/lower education and junior high school versus senior high school and junior college/higher education: <0.0001
Junior high school	% Yes (n)	35.2 (256)	28.1 (113)	
Senior high school	% Yes (n)	12.7 (92)	9.5 (38)	
Junior college or higher education	% Yes (n)	2.3 (17)	8.2 (33)	
Smoking:				
Non-smoker	% Yes (n)	96.2 (699)	94.0 (378)	ex-smokers and current smokers versus non-smokers: <0.001
Ex-smoker	% Yes (n)	0.3 (2)	3.2 (13)	
Current smoker	% Yes (n)	3.6 (26)	2.8 (11)	
Number of packages years	Mean (SD)	0.7 (5.1)	0.7 (4.0)	0.934
	Min–Max	0.0–74.0	0.0–35.0	
Exposure to passive smoking	% Yes (n)	47.7 (347)	27.1 (109)	<0.0001
Alcohol consumption	% Yes (n)	10.0 (73)	5.5 (22)	0.009
Sun exposure:	Mean (SD)	3.1 (1.9)	4.9 (2.0)	<0.0001
Average hours outside per day in summer during lifetime	Min–Max	0.5–8.0	0.0–8.0	
Ever had sunburns	% Yes (n)	4.5 (33)	2.7 (11)	0.183
Use of solid fuels for cooking	% Yes (n)	40.4 (294)	85.3 (343)	<0.0001

^a chi² test for binary variables and *t*-test for continuous variables.

were between 30 and 90 years old. More than 50% of the women had a low educational level. Nearly all women were non-smokers but had a high passive smoke exposure. According to the average hours outside per day in summer time the women experienced a moderate sun exposure during their lifetime and only a very low percentage experienced sunburns in their lifetime. The majority of individuals within the two study populations used solid fuels for cooking. There were significant differences in the variable distribution of age, BMI, educational level, smoking, exposure to passive smoke, alcohol consumption, sun exposure and use of solid fuels for cooking between the two Chinese study populations.

3.2. Clinical skin aging manifestation:

Clinical signs of skin aging were evaluated by means of the SCINEXATM, and mean values are shown separately for the Taizhou and the Pingding study population (Online supplement table S1).

Association between cooking with solid fuels and occurrence of skin aging signs:

In Tables 2 and 3 the association between cooking with solid fuels and different skin aging signs is shown separately for the Taizhou and the Pingding study population as well as for the two study populations combined (pooled analysis). Furthermore, we tested by interaction analysis if the effect of indoor air pollution exposure is modified by study population. A significant modification by study population indicates that a pooling of study populations is not justified to test the effect of indoor air pollution on skin aging. The association results in Table 2 are only adjusted for age whereas the association results in Table 3 are additionally adjusted for BMI, educational level, smoking, passive smoking, alcohol consumption, sun exposure and sunburn history.

Cooking with solid fuels was significantly associated with more severe coarse wrinkles, more pronounced laxity and the occurrence of fine wrinkles in the pooled analysis adjusted for age as well as in the pooled analysis further adjusted for BMI, educational level, sun exposure, smoking and alcohol intake. The significant protective effect of indoor air pollution exposure on pigment spot

occurrence on cheeks shown in Table 2 vanishes after further adjustment shown in Table 3. After further adjustment in Table 3 the pooling seems to be justified to test the effect of indoor air pollution on skin aging for nearly all skin aging signs, except for the wrinkle type nasolabialfold. Here the significant p-value for interaction indicates that the effect of cooking with solid fuels is more pronounced in the Pingding study than in the Taizhou study.

4. Discussion

The current study provides epidemiological evidence that indoor air pollution exposure from cooking with solid fuels is associated with a higher rate of wrinkle manifestation in Chinese women. This conclusion is based on observations in two independent study populations from two geographically different areas of China, which both showed significant positive associations with coarse wrinkle manifestation on the face and fine wrinkle manifestation on back of the hands after adjustment for further confounders.

Regarding the effect of air pollutants on the manifestation of skin aging, a previous epidemiological study of Caucasian women investigated the association between outdoor, mainly traffic-related air pollution exposure, and its influence on skin aging occurrence [8]. In that study, the exposure to soot in particular was associated with more pronounced pigment spot and wrinkle manifestation. It was assumed that PAHs are the major components, which induce skin aging, as they are lipophilic and can easily penetrate through the skin and furthermore, they are ligands of the arylhydrocarbon receptor (AhR). By the induction of the AhR pathway melanogenesis [13] and wrinkle development [14,15] can be induced.

Possible mechanistic explanations for the association between air pollutants and skin aging induction are further provided by *in-vitro* studies, which have examined the effects of tobacco-smoke extract exposure in cultured human skin fibroblasts. Tobacco smoke is also a complex mixture of pollutants similar to air pollution and it also induces skin aging, mainly wrinkle

Table 2

Association between cooking with solid fuels and skin aging manifestation in the Taizhou (Shanghai, China) and Pingding (Beijing, China) study population as well as for both studies combined (pooled analysis) adjusted for age (significant associations with $p < 0.05$ are in bold, the p -value for interaction indicates if there is a significant modification by study population).

		Taizhou study population (N=727)	Pingding study population (N=402)	pooled analysis (N=1129)	p for interaction between study population and indoor air pollution exposure
Number of pigment spots:					
On forehead	GMR (95% CI)	0.99 (0.89–1.12)	0.79 (0.61–1.02)	0.93 (0.83–1.05)	0.025
On cheeks	GMR (95% CI)	0.95 (0.87–1.01)	0.67 (0.49–0.92)	0.89 (0.79–0.98)	0.005
On arms	GMR (95% CI)	0.93 (0.81–1.05)	1.29 (0.96–1.74)	0.99 (0.89–1.12)	0.024
On back of hands	GMR (95% CI)	1.00 (0.89–1.12)	1.30 (0.95–1.77)	1.07 (0.95–1.20)	0.034
Score of coarse wrinkles:					
On forehead	AMR (95% CI)	1.14 (1.08–1.19)	1.17 (1.08–1.27)	1.14 (1.10–1.19)	0.511
Frownlines	AMR (95% CI)	1.06 (1.00–1.11)	1.18 (1.07–1.28)	1.08 (1.03–1.13)	0.041
Crow's feets	AMR (95% CI)	1.09 (1.05–1.14)	1.14 (1.04–1.24)	1.07 (1.03–1.12)	0.005
Under the eyes	AMR (95% CI)	1.03 (0.99–1.08)	1.19 (1.10–1.28)	1.11 (1.07–1.15)	<0.0001
On upper lip	AMR (95% CI)	1.12 (1.05–1.19)	1.22 (1.10–1.34)	1.14 (1.03–1.11)	0.175
Nasolabial	AMR (95% CI)	1.07 (1.03–1.10)	1.23 (1.15–1.32)	1.10 (1.07–1.14)	0.0001
Score of further skin aging symptoms:					
Teleangiectasia	AMR (95% CI)	1.05 (0.65–1.45)	1.45 (1.24–1.65)	1.21 (1.06–1.37)	<0.0001
Laxity of eyelids	AMR (95% CI)	1.08 (1.04–1.13)	1.20 (1.12–1.29)	1.11 (1.07–1.16)	0.009
Laxity of cheeks	AMR (95% CI)	1.07 (1.01–1.13)	1.16 (1.07–1.25)	1.09 (1.05–1.14)	0.002
Presence of further skin aging symptoms:					
Solar elastosis on cheeks	OR (95% CI)	1.17 (0.79–1.73)	2.38 (0.83–6.78)	1.28 (0.90–1.82)	0.249
Cutis rhomboidalis nuchae	OR (95% CI)	1.20 (0.84–1.69)	1.53 (0.72–3.25)	1.28 (0.93–1.75)	0.397
Morbus favre racouchot	OR (95% CI)	n.a.	n.a.	n.a.	n.a.
Even pigmentation on bottom side of the arms	OR (95% CI)	1.17 (0.84–1.62)	0.39 (0.13–1.21)	1.02 (0.75–1.38)	0.024
Fine wrinkles on back of hands	OR (95% CI)	2.04 (1.29–3.24)	3.44 (1.81–6.52)	2.03 (1.44–2.87)	0.838

GMR: geometric mean ratio, AMR: arithmetic mean ratio; OR: Odds ratio, 95% CI: 95% confidence interval; n.a.: not applicable.

development [6]. In this regard, it has been shown that tobacco smoke extract affects collagen metabolism in cultured skin fibroblasts [16]. After tobacco smoke exposure the production of the collagen precursors procollagen types I and III was decreased significantly in the supernatants of cultured fibroblasts, whereas

the matrix-metalloproteinases (MMPs)-1 and MMP-3 were induced. However, the expression of tissue inhibitors of MMPs remained unchanged. In total, after tobacco smoke extract exposure the balance is shifted to collagen degradation from collagen production. Further, tobacco smoke extract also induces

Table 3

Association between cooking with solid fuels and skin aging manifestation in the Taizhou (Shanghai, China) and Pingding (Beijing, China) study population as well as for both studies combined (pooled analysis) adjusted for age, body mass index (BMI), educational level, smoking, passive smoking, alcohol consumption, sun exposure and sunburn history (significant associations with $p < 0.05$ are in bold, the p -value for interaction indicates if there is a significant modification by study population).

		Taizhou study population (N=727)	Pingding study population (N=402)	Pooled analysis (N=1129)	p for interaction between study population and indoor air pollution exposure
Number of pigment spots:					
on forehead	GMR (95% CI)	0.96 (0.85–1.08)	0.75 (0.55–1.02)	0.93 (0.83–1.05)	0.005
on cheeks	GMR (95% CI)	0.95 (0.85–1.05)	0.80 (0.55–1.16)	0.93 (0.83–1.05)	0.019
on arms	GMR (95% CI)	0.95 (0.84–1.07)	1.35 (0.94–1.93)	1.02 (0.89–1.01)	0.068
on back of hands	GMR (95% CI)	0.97 (0.87–1.08)	1.38 (0.95–2.02)	1.04 (0.93–1.17)	0.285
Score of coarse wrinkles:					
on forehead	AMR (95% CI)	1.11 (1.06–1.17)	0.97 (0.86–1.08)	1.09 (1.05–1.14)	0.284
frownlines	AMR (95% CI)	1.05 (1.00–1.11)	1.08 (0.95–1.21)	1.05 (1.01–1.11)	0.237
crow's feets	AMR (95% CI)	1.07 (1.03–1.12)	1.01 (0.89–1.12)	1.06 (1.02–1.11)	0.198
under the eyes	AMR (95% CI)	1.03 (0.98–1.08)	1.05 (0.94–1.16)	1.04 (1.00–1.09)	0.010
on upper lip	AMR (95% CI)	1.08 (1.01–1.15)	1.09 (0.95–1.24)	1.07 (1.01–1.13)	0.841
Nasolabial	AMR (95% CI)	1.06 (1.03–1.09)	1.14 (1.04–1.25)	1.08 (1.04–1.11)	0.012
Score of further skin aging symptoms:					
Teleangiectasia	AMR (95% CI)	0.98 (0.57–1.39)	1.23 (0.98–1.48)	1.01 (0.91–1.23)	0.0001
Laxity of eyelids	AMR (95% CI)	1.06 (1.01–1.10)	1.08 (0.97–1.18)	1.06 (1.02–1.11)	0.338
Laxity of cheeks	AMR (95% CI)	1.06 (0.99–1.12)	1.04 (0.94–1.15)	1.06 (1.01–1.11)	0.352
Presence of further skin aging symptoms:					
solar elastosis on cheeks	OR (95% CI)	1.09 (0.72–1.63)	1.19 (0.36–3.87)	1.17 (0.80–1.70)	0.555
cutis rhomboidalis nuchae	OR (95% CI)	1.04 (0.72–1.51)	0.48 (0.18–1.25)	0.98 (0.69–1.37)	0.278
morbus favre racouchot	OR (95% CI)	n.a.	n.a.	n.a.	n.a.
even pigmentation on bottom side of the skin	OR (95% CI)	1.11 (0.79–1.56)	0.30 (0.08–1.08)	0.96 (0.70–1.33)	0.026
fine wrinkles on back of hands	OR (95% CI)	1.70 (1.04–2.79)	2.89 (1.29–6.51)	1.74 (1.20–2.55)	0.806

GMR: geometric mean ratio, AMR: arithmetic mean ratio; OR: Odds ratio, 95% CI: 95% confidence interval; n.a.: not applicable.

the non-functional latent form of transforming growth factor- β (TGF- β) in supernatants of cultured skin fibroblasts [17]. This results in decreased synthesis of extracellular matrix proteins. Moreover, PAHs included in tobacco smoke can trigger AhR signaling pathway. In this regard, it has been shown that tobacco smoke extract can induce MMP-1 expression over the AhR signaling pathway in cultured human fibroblast and keratinocytes [14,15]. In conclusion, the tobacco smoke extract-induced imbalance towards collagen degradation as well as the induced degradation of the extracellular matrix is most probably responsible for the smoking-induced wrinkle manifestation. In addition, recent *in-vitro* studies indicate that stimulation of primary human keratinocytes with two different standard preparations of diesel exhaust particles increase MMP-1 expression via activation of the AhR signaling pathway [18]. It is thus likely that exposure to indoor combustion of solid fuels might induce the same molecular pathways in skin cells and thereby cause wrinkle formation.

In the German study population the association between traffic-related air pollution and skin aging manifestation was strongest for pigment spot formation [8], which we did not observe in the present study. This difference might be due to (i) qualitative differences between indoor versus outdoor pollution and/or (ii) the higher baseline risk for pigment spot development in Asian populations [12,18], which might obscure the relatively small effect of air pollution on pigment spot occurrence and/or (iii) genetic differences between Caucasians and Chinese.

One major limitation of our study is that we used only questionnaire based data to assess indoor air pollution exposure from cooking and did not have instrumental monitoring measurements. Also, it is probable that there are differences in the composition of indoor air pollution exposure geographically, resulting from different mixtures of solid fuels. Strikingly, some of the significant association effects with coarse wrinkles vanish after further adjustment in the Pingding study population. This seems to be mainly due to the confounding effect of educational level in the Pingding study population, which cannot be observed in the Taizhou study. Also the estimation of major confounders relied on questionnaire-based data. The most critical confounder might be sun exposure. However, we assume similar general sun exposure for both areas as both areas have very similar elevation and climatic conditions. The average summer temperatures are 21–26 °C in Pingding and 24–31 °C in Taizhou and both areas are not highly elevated. Furthermore, another source of indoor air pollution might be heating with solid fuels. However, heating with solid fuels is used seasonally and thus contributes only a small part to indoor exposure, whereas cooking with solid fuels leads to chronic daily exposure. Finally the recruitment of mother or mother-in-law accompanying her pregnant daughter or daughter-in-law in the Pingding study might have introduced some bias in the way that we might not have reached a random selection out of our target population. However, it is very unlikely that this recruitment procedure has influenced the effect of indoor air pollution on skin aging manifestation as participation did not depend on their exposure and also not on their skin aging manifestation.

The strength of our study is that we could show similar associations between indoor air pollution from cooking with solid fuels and skin aging manifestation in two independent study populations in China. This makes the observed associations more reliable.

To our knowledge this is the first study showing an association between indoor air pollution exposure by cooking and skin aging manifestation. The current study confirms the previously seen associations between outdoor air pollution and skin aging

manifestation in Caucasian women in that air pollution in the form of particulates and PAHs are associated with an increased risk of pigment spots and facial wrinkles. There are differences in the specific details of skin aging manifestations between this study population and the Caucasian study, however, echoing the ethnic differences reported previously between Caucasian and Japanese populations [19]. It will therefore be important to test for gene-environment interactions in further studies.

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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.2015.04.001>.

References

- [1] Bruce N, Perez-Padilla R, Albalak R. Indoor air pollution in developing countries: a major environmental and public health challenge. *Bull World Health Organ* 2000;78(9):1078–92.
- [2] Jin Y, Zhou Z, He G, Wei H, Liu J, Liu F, et al. Geographical, spatial, and temporal distributions of multiple indoor air pollutants in four Chinese provinces. *Environ Sci Technol* 2005;39(24):9431–9.
- [3] Ge S, Xu X, Chow JC, Watson J, Sheng Q, Liu W, et al. Emissions of air pollutants from household stoves: honeycomb coal versus coal cake. *Environ Sci Technol* 2004;38(17):4612–8.
- [4] Zhang JJ, Smith KR. Household air pollution from coal and biomass fuels in China: measurements, health impacts, and interventions. *Environ Health Perspect* 2007;115(6):848–55.
- [5] Yaar M. Clinical and histological features of intrinsic versus extrinsic skin aging. In: Gilchrist BA, Krutmann J, editors. *Skin aging*. Berlin: Springer Verlag; 2006. p. 9–22.
- [6] Daniell HW. Smoker's wrinkles. A study in the epidemiology of crow's feet. *Ann Intern Med* 1971;75:873–80.
- [7] Gilchrist BA. Photoaging. *J Invest Dermatol* 2013;133(E1):E2–6.
- [8] Vierkötter A, Schikowski T, Ranft U, Sugiri D, Matsui M, Krämer U, et al. Airborne particle exposure and extrinsic skin aging. *J Invest Dermatol* 2010;130(12):2719–26.
- [9] Wang X, Lu M, Qian J, Yang Y, Li S, Lu D, et al. Rationales, design and recruitment of the Taizhou Longitudinal Study. *BMC Public Health* 2009;9:223.
- [10] Li Z, Zhang L, Ye R, Pei L, Liu J, Zheng X, Ren A. Indoor air pollution from coal combustion and the risk of neural tube defects in a rural population in Shanxi Province. *China Am J Epidemiol* 2011;174(4):451–8.
- [11] Vierkötter A, Ranft U, Krämer U, Sugiri D, Reimann V, Krutmann J. The SCINEXA: a novel, validated score to simultaneously assess and differentiate between intrinsic and extrinsic skin ageing. *J Dermatol Sci* 2009;53(3):207–11.
- [12] Tschachler E, Morizot F. Ethnic differences in skin aging. In: Gilchrist BA, Krutmann J, editors. *Skin Aging*. Berlin: Springer Verlag; 2006. p. 23–32.
- [13] Luecke S, Backlund M, Jux B, Esser C, Krutmann J, Rannug A. The aryl hydrocarbon receptor (AHR), a novel regulator of human melanogenesis. *Pigment Cell Melanoma Res*. 2010 Dec;23(6):828–33.
- [14] Morita A, Torii K, Maeda A, Yamaguchi Y. Molecular basis of tobacco smoke-induced premature skin aging. *J Invest Dermatol Symp* 2009;14(1):53–5.

- [15] Ono Y, Torii K, Fritsche E, Shintani Y, Nishida E, Nakamura M, et al. Role of the aryl hydrocarbon receptor in tobacco smoke extract-induced matrix metalloproteinase-1 expression. *Exp Dermatol* 2013;22(5):349–53.
- [16] Yin L, Morita A, Tsuji T. Alterations of extracellular matrix induced by tobacco smoke extract. *Arch Dermatol Res* 2000;292(4):188–94.
- [17] Yin L, Morita A, Tsuji T. Tobacco smoke extract induces age-related changes due to modulation of TGF-beta. *Exp Dermatol* 2003;12(Suppl 2):51–6.
- [18] Krutmann J, Liu W, Li L, Pan X, Crawford M, Sore G, Seite S. Pollution skin. From epidemiological and mechanistic studies to clinical implications. *J Dermatol Sci* 2014 Dec;76(3):163–8.
- [19] Nouveau-Richard S, Yang Z, Mac-Mary S, Li L, Bastien P, Tardy I, Bouillon C, Humbert P, de Lacharrière O. Skin ageing: a comparison between Chinese and European populations. A pilot study. *J Dermatol Sci* 2005;40(3):187–93.