Prevalence and determinants for xerosis cutis in the middle-aged and elderly population: A cross-sectional study

Article *in* Journal of the American Academy of Dermatology · December 2018

DOI: 10.1016/j.jaad.2018.12.038

CITATIONS
7

READS
140

7 authors, including:

Selma Mekic
Erasmus MC
5 PUBLICATIONS **110** CITATIONS
SEE PROFILE

Leonie Jacobs
Amphia Ziekenhuis
40 PUBLICATIONS **2,475** CITATIONS
SEE PROFILE

Luba Milena Pardo
Erasmus Medical Center Rotterdam
66 PUBLICATIONS **1,093** CITATIONS
SEE PROFILE

Tamar Nijsten
Erasmus MC
356 PUBLICATIONS **11,828** CITATIONS
SEE PROFILE

Ref 2 a p1

ORIGINAL ARTICLE

Prevalence and determinants for xerosis cutis in the middle-aged and elderly population: A cross-sectional study

Selma Mekić, MD,[a] Leonie C. Jacobs, MD, PhD,[a] David A. Gunn, PhD,[b] Andrew E. Mayes, PhD,[b] M. Arfan Ikram, MD, PhD,[c] Luba M. Pardo, MD, PhD,[a] and Tamar Nijsten, MD, PhD[a]
Rotterdam, The Netherlands, and Sharnbrook, Bedfordshire, United Kingdom

Background: Determinants and the extent of dry skin in healthy middle-aged and elderly populations have not been well established.

Objective: We aimed to identify the prevalence and determinants for generalized dry skin (GDS) and localized dry skin (LDS) within a large prospective population-based cohort of middle-aged and elderly individuals of the Rotterdam Study.

Methods: Dry skin was physician-graded as none, localized, or generalized. For GDS and LDS, separate multivariable logistic regression analyses were performed to search for association with participant characteristics, lifestyle factors, environmental factors, several comorbidities, and drug exposure.

Results: Among the 5547 eligible participants, 60% had dry skin, of whom a fifth had GDS. Age, female sex, skin color, body mass index, outside temperature, eczema, and chemotherapy in the past were significant determinants for both GDS and LDS. Smoking, the use of statins and diuretics, poorer self-perceived health, and several dermatologic conditions increased the likelihood of having GDS only. Daily cream use was associated with less LDS.

Limitations: Interobserver variability and residual confounding could have influenced our results. Because of our cross-sectional design, we could not infer causality.

Conclusion: We identified factors significantly associated with dry skin in a general middle-aged and elderly population, with health parameters more strongly associated with GDS. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2018.12.038.)

Key words: dry skin; elderly; middle-aged; population-based cohort; Rotterdam Study; skin aging; xerosis cutis.

Dry skin (xerosis cutis) is one of the most common skin conditions in middle-aged and elderly populations and can be considered part of the physiologic aging of skin. As the worldwide overall prevalence of dry skin is estimated at 29% to 85%,[1–5] it affects roughly every other person. Dry skin can be a very heterogeneous phenotype and can present with scaling, roughness, and even fissures. Patients usually experience itch, but the skin can also feel tight, painful, or burning. In addition, dry damaged skin can be a *porte d'entrée* for skin infections.

a

Xerosis may be a feature on its own, or it can co-occur with or be part of different skin diseases. Also, some chronic diseases, including diabetes, HIV, hypothyroidism, and renal insufficiency, and some

From the Department of Dermatology[a] and Department of Epidemiology,[c] Erasmus MC University Medical Center Rotterdam, and Unilever Research and Development, Colworth Science Park, Sharnbrook, Bedfordshire, United Kingdom.[b]

Funding sources: Dr Nijsten has received a restricted research grant from Unilever, and Dr Mekic is supported by this grant.
Disclosure: Dr Gunn and Dr Mayes are Unilever employees. Dr Mekic, Dr Jacobs, Dr Ikram, Dr Pardo, and Dr Nijsten have no conflicts of interest to disclose.

Accepted for publication December 10, 2018.
Reprint requests: Tamar Nijsten, MD, PhD, Department of Dermatology, Erasmus MC University Medical Center, PO Box 2040, 3000 CA, Rotterdam, The Netherlands. E-mail: t.nijsten@erasmusmc.nl.
Published online August 16, 2019.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2018.12.038

therapies, including the use of statins, diuretics, or chemotherapeutic agents, can be accompanied by dry skin.[2,3,6-9] Therefore, dry skin not only is a very common condition but may also be an indicator of a person's health status.

Many different lifestyle and environmental factors are known to influence dry skin, including bathing behavior and weather conditions.[10] Others, such as smoking and alcohol consumption, are less well investigated. Genes also play a role, with the filaggrin gene (*FLG*) being the best-known associated gene.[11]

Most observational research on xerosis in elderly individuals has been performed in selected and relatively small populations, such as nursing home residents and those with many comorbidities.[1,2] Therefore, little evidence is provided for determinants of dry skin in general middle-aged and older populations, and few studies have investigated a broad range of possible determinants and how they relate to the extent of dry skin. In this study, we aimed to investigate the prevalence and determinants of localized dry skin (LDS) (ie, mild dry skin) or generalized dry skin (GDS) (ie, severe dry skin), as well as co-occurring diseases, in a large middle-aged and elderly population–based cohort.

CAPSULE SUMMARY

- Dry skin is a common skin discomfort among the elderly.
- Sixty percent of those in our community-based population experience dry skin. Determinants and associated diseases vary with extent of the xerosis. Greater body coverage of dry skin is more strongly linked to comorbidity and drug use.

METHODS

Study design

Participants were selected from the Rotterdam Study (RS) cohort, which is a large prospective population-based cohort situated in the Rotterdam suburb Ommoord. The study started in 1990 and is still ongoing. Details and objectives of the RS have been described elsewhere. The RS has been approved by the institutional review board (medical ethics committee) of the Erasmus Medical Center and by the review board of The Netherlands Ministry of Health, Welfare, and Sports.[12]

Identification of dry skin

Between 2010 and 2016, during routine visits at the research center, a full-body skin examination (FBSE) was performed in 5555 participants. The presence and extent of dry skin were graded in 5547 individuals by a dermatology-trained physician by observing scaly or rough skin with or without erythema that did not fit any other known skin disease. We also collected data on self-reported dry skin, but because of poor agreement with our clinical judgment of dry skin, we chose physician-based dry skin as the outcome. Dry skin was scored as absent, localized (on the extensor side of the arms and legs), or generalized (LDS and GDS, respectively). All 5547 RS participants were included in our analysis.

Characteristics

Sex and age at entry of the study were collected from the database. Self-perceived health, smoking, alcohol intake, and education level were collected from general interviews. Data on facial cream use were collected from dermatologic interviews. Skin color was graded by physicians as belonging to 1 of 3 darkness categories. Height and weight were measured at the research center and used to calculate body mass index (BMI). Mean outside temperature and air humidity over the last week before the center visit were calculated by using the weather data from Rotterdam the Hague airport.

Associated diseases

Dermatologic conditions were assessed during the FBSE. Eczema was defined as erythematous, scaly, lichenified, excoriated, and fissured patches. Seborrheic dermatitis was defined as erythema with greasy scaling on the typical locations of the scalp, face, or chest. Psoriasis was assessed as sharply demarcated erythematous, scaly thickened patches. Varicose veins were graded by using the clinical, etiology, anatomy, and pathophysiology classification (CEAP) and when present, assigned a clinical (C) score of C2 to C6. Self-reported history of itchy skin conditions, asthma, hay fever, and dust mite allergy were collected from dermatologic interviews. Diabetes mellitus was scored as present if at least 1 of the following criteria was present: fasting plasma glucose level of 7.0 mmol/L or higher, nonfasting glucose level of 11.1 mmol/L or higher, and use of antidiabetic medicine or dietary treatment for type 2 diabetes mellitus. Renal impairment was defined as having a glomerular filtration rate lower than 60. Hypothyroidism was graded as present depending on the combination of thyroid-stimulating hormone (TSH) and free thyroxine (fT4) levels as follows: high TSH level and normal or low fT4 level or normal TSH level and low fT4 level.

Abbreviations used:

BMI: body mass index
CI: confidence interval
FBSE: full-body skin examination
GDS: generalized dry skin
ft4: free thyroxine
LDS: localized dry skin
OR: odds ratio
RS: Rotterdam Study
TEWL: transepidermal water loss
TSH: thyroid-stimulating hormone

Associated medications

A trained nurse, who examined all the medication in use, assessed the current use of statins and diuretics. Ever receiving chemotherapy was self-reported in 1 of the interviews.

Statistical analysis

To investigate the various determinants in relation to dry skin, we performed a multivariable binary logistic regression, during which we adjusted for possible confounders. GDS and LDS were assessed separately. Use of an ordinal logistic regression model was considered but was not possible because the assumption of parallel lines was violated.[13] The rate of missing data was less than 15% per variable and was imputed by using multiple imputation with 20 imputations. First, we analyzed possible determinants for GDS and LDS, including age, sex, skin color, mean temperature, relative humidity, cream use, smoking, alcohol consumption, BMI, self-perceived health, and education level. Interaction between relative humidity and mean temperature was present in the GDS analysis, and therefore, the interaction term was added to the model.

Second, we investigated the role of common chronic diseases and concomitant medication use and presence of GDS and LDS in a logistic regression model that was adjusted for all significant factors from the multivariable analysis. Because we selected the investigated variables on the basis of prior hypotheses as well as plausible and previously reported associations in the literature, we did not correct for multiple testing and regarded *P* values of .05 or lower as significant. All analyses were conducted by using SPSS Statistics for Windows (version 24.0, IBM Inc, Armonk, NY).

RESULTS

Demographics

This cohort included 5547 middle-aged and elderly participants (age range, 51-101 years; mean age, 70 years; 57% of our participants were female, and 60% (95% confidence interval [CI], 58%-61%) had dry skin. Of the individuals with dry skin, 1 in 5 were severely affected and had GDS, whereas the rest had dry skin only on the extensor side of the extremities (ie, LDS) (Supplemental Table I [available at http://www.jaad.org]).

Lifestyle and demographic determinants

Age was significantly associated with dry skin, more so with GDS (odds ratio [OR], 1.04; 95% CI, 1.03-1.05) than with LDS (OR, 1.009; 95% CI, 1.003-1.016). Women were more commonly affected than men: they had a 50% higher likelihood of having GDS and a 30% higher likelihood of having LDS. Individuals with a brown-black skin color experienced GDS 3 times more often than did individuals with skin in the Mediterranean skin color group (OR, 3.62; 95% CI, 1.96-6.73). However, individuals with a white skin color had LDS more often than did individuals with skin in the Mediterranean skin color group (OR, 1.18; 95% CI, 1.01-1.38). A higher BMI was associated with less GDS and LDS (Table I).

A higher mean outside temperature was strongly associated with less GDS (OR, 0.70; 95% CI, 0.56-0.88) and moderately associated with less LDS (OR, 0.95; 95% CI, 0.94-0.96). Relative outside air humidity was related to temperature and had a significant interaction with temperature in the GDS model. A higher relative humidity did not significantly interact with temperature in LDS and had a small protective association (Table I).

Interestingly, although reported for facial cream use, participants who used cream on a daily basis, had less LDS (OR, 0.77; 95% CI, 0.65-0.92), but not GDS (OR, 0.80; 95% CI, 0.60-1.02). Smokers had more GDS (OR, 1.27 1.02-1.57), whereas individuals with better self-perceived health, had less GDS (OR, 0.993; 95% CI, 0.987-0.999). Education level and alcohol use were not associated with presence of dry skin (Table I).

Comorbidities and associated medications

Of the assessed skin diseases, eczema was highly associated with having dry skin. Here, the probability of having LDS was 2.5 times higher (OR, 2.44; 95% CI, 1.85-3.25) and the likelihood of having GDS was 7 times higher in patients with eczema (OR, 7.04; 95% CI, 5.92-8.37). Other dermatologic diseases associated with GDS were seborrheic dermatitis (OR, 1.38; 95% CI, 1.06-1.79) and an itchy skin condition in the past (OR, 1.26; 95% CI, 1.14-1.39). Having psoriasis or higher C scores on the clinical, etiology, anatomy, and pathophysiology classification for venous insufficiency was not associated with dry skin (Table II).

Table I. Multivariable logistic model

Variable	OR (95% CI) of generalized vs no dry skin*	*P* value	OR (95% CI) of localized vs no dry skin†	*P* value
Age, y‡	**1.04 (1.03-1.05)**	**<.01**	**1.009 (1.003-1.016)**	**<.01**
Sex				
Female	**1.49 (1.16-1.93)**	**<.01**	**1.29 (1.10-1.52)**	**<.01**
Skin color				
Olive to light brown	Reference		Reference	
Very white to white	1.24 (0.94-1.64)	.12	**1.18 (1.01-1.38)**	**.049**
Brown to black	**3.62 (1.96-6.73)**	**<.01**	1.20 (0.76-1.90)	.43
BMI, kg/m^2§	**0.96 (0.94-0.98)**	**<.01**	**0.98 (0.97-0.99)**	**<.01**
Humidity‖	0.99 (0.96-1.02)	.39	**0.988 (0.978-0.998)**	**.01**
Temperature¶	**0.70 (0.56-0.88)**	**<.01**	**0.95 (0.94-0.96)**	**<.01**
Humidity × temperature#	**1.003 (1.001-1.006)**	**.01**		
Cream use				
No	Reference		Reference	
Yes, sometimes	1.29 (0.91-1.83)	.16	1.09 (0.87-1.36)	.46
Yes, daily	0.80 (0.60-1.02)	.11	**0.77 (0.65-0.92)**	**<.01**
Smoking**	**1.27 (1.02-1.57)**	**.03**	0.99 (0.87-1.14)	.94
Alcohol consumption††	1.00 (0.99-1.02)	.64	0.995 (0.987-1.003)	.20
Self-perceived health‡‡	**0.993 (0.987-0.999)**	**.02**	0.998 (0.994-1.002)	.40
Education level§§				
Low	Reference		Reference	
Medium	0.99 (0.74-1.34)	.96	1.05 (0.86-1.28)	.66
High	0.77 (0.55-1.08)	.13	0.84 (0.67-1.04)	.11

Boldface indicates statistical significance.
BMI, Body mass index; *CI*, confidence interval; *OR*, odds ratio.
*The OR expresses the odds for having generalized dry skin versus no dry skin per tested variable. This analysis is adjusted for the following factors: sex, age, temperature, relative humidity, temperature times relative humidity, cream use, smoking, alcohol consumption, BMI, quality of life, and education level.
†The OR expresses the odds for having localized dry skin versus no dry skin per tested variable. This analysis is adjusted for the following factors: sex, age, temperature, relative humidity, cream use, smoking, alcohol consumption, BMI, quality of life, and education level.
‡Per 1-year increase.
§BMI in kg/m^2 per point.
‖Rolling relative humidity over the last week, %.
¶Rolling average temperature over the last week in degrees Celsius.
#Interaction term *rolling relative humidity* times the term *rolling average temperature*. Not significant in localized model and hence excluded.
**Ever-smoking versus never-smoking.
††Alcohol consumption, g/d.
‡‡Self-perceived health score based on overall health; scores between 0 and 100 (where 0 is the lowest quality and 100 is the highest quality) per point.
§§Low means primary education, medium means lower vocational/lower secondary/intermediate vocational education, and high means general secondary or higher vocational education or university education.

Other tested medical conditions included diabetes, which was a determinant for LDS only (OR, 1.22; 95% CI, 1.04-1.45) (Table II). Renal impairment, hypothyroidism, and atopic constitution (asthma, hay fever, or dust mite allergy) were not associated with dry skin.

The use of certain medications were also linked to dry skin. Using statins (OR, 1.28; 95% CI, 1.05-1.57) and using diuretics (OR, 1.37; 95% CI, 1.06-1.75) were both significantly associated with GDS but not with LDS. Ever having received chemotherapy was associated with LDS (OR, 1.56; 95% CI, 1.05-2.32) and with GDS (OR, 1.69; 95% CI, 0.97-2.95), with similar odds ratios but with the odds of LDS being statistically significant.

DISCUSSION

In this study, the prevalence of dry skin in people with an average age of 70 years was 60%, which corresponds well with the range of 29% to 85% previously reported in the literature.[1-4] The known risk factors of increasing age, female sex, eczema, and lower outside temperature were replicated in this study. Less well known determinants included skin color (white and brown to black) and lower BMI. GDS was less common, but it was a more severe condition than LDS. Additional determinants for GDS included smoking, some dermatologic conditions, and use of certain medication. Moreover, self-perceived health was significantly poorer in individuals with GDS. Interestingly,

Table II. Associated diseases and medication regression model

Disease or medication	OR (95% CI) of generalized vs no dry skin*	*P* value	OR (95% CI) of localized vs no dry skin†	*P* value
Dermatologic diseases				
Eczema	**7.04 (5.92-8.37)**	**<.01**	**2.44 (1.85-3.25)**	**<.01**
Seborrheic dermatitis	**1.38 (1.06-1.79)**	**.02**	1.05 (0.88-1.26)	.57
Psoriasis	1.01 (0.60-1.68)	.99	0.89 (0.64-1.24)	.50
Itchy skin condition‡	**1.26 (1.14-1.39)**	**.02**	1.08 (0.95-1.22)	.25
Varicose veins	0.90 (0.73-1.11)	.34	0.97 (0.85-1.10)	.62
Other diseases				
Diabetes	1.04 (0.80-1.36)	.76	**1.22 (1.04-1.45)**	**.02**
Renal impairment	1.20 (0.92-1.57)	.18	1.08 (0.90-1.30)	.42
Hypothyroidism	1.15 (0.85-1.56)	.36	0.96 (0.78-1.18)	.71
Atopy	0.95 (0.74-1.21)	.68	1.01 (0.87-1.17)	.91
Medication				
Statins	**1.28 (1.05-1.57)**	**.02**	1.08 (0.95-1.24)	.25
Diuretics	**1.37 (1.06-1.75)**	**.01**	1.11 (0.94-1.32)	.22
Chemotherapy	**1.69 (0.97-2.95)**	**.07**	**1.56 (1.05-2.32)**	**.03**

Boldface indicates statistical significance.
CI, Confidence interval; *OR*, odds ratio.
*The OR represents the odds for having generalized dry skin versus no dry skin when having a certain disease or when using a certain medication. This analysis is adjusted for the following factors: age, sex, skin color, temperature, relative humidity, humidity times temperature, BMI, smoking, and quality of life.
†The OR represents the odds for having localized dry skin versus no dry skin when having a certain disease or when using a certain medication. This analysis is adjusted for the following factors: age, sex, skin color, temperature, relative humidity, BMI, and cream use.
‡Ever having had an itchy skin condition (based on question from dermatologic questionnaire).

individuals who used facial moisturizing cream on a daily basis over the past year had significantly less LDS, even though they were instructed not to wear cream 24 hours before the FBSE. If use of a facial moisturizer is assumed to be a proxy of use of a body moisturizer, this implies that emollients may have a beneficial effect on dry skin for longer than 24 hours.

Fluctuations in intercellular lipid levels, water metabolism, and changes in the keratinization process play a role in the development of dry skin.[10,14] With aging, the skin's barrier function weakens as the lipid film on the skin surface decreases and keratinocyte proliferation declines, leading to transepidermal water loss (TEWL) and dry skin.[15,16] Sebum production in male skin is higher and more stable throughout life, which could explain why men experience dry skin less than women do.[17] Cream use may to a certain extent mimic this lipid film and therefore prevent TEWL. Interestingly, light- and dark-skinned individuals have significantly more dry skin than do those in the group in between. Research into ethnic skin differences has shown that black skin has a higher TEWL and a 2.5 times greater desquamation rate compared with white skin.[18] Consistent evidence in Mediterranean skin color is lacking, although our results suggest that these individuals experience dry skin less than individuals with white and dark skin color do.

An increased BMI resulted in a lower risk of dry skin, which has been previously reported.[2] It is clear that malnourished individuals have drier skin on account of lack of sufficient nutrients to maintain a healthy skin barrier, with the mechanisms explaining the other side of the spectrum remaining to be fully understood. An increase in the availability of lipids for the stratum corneum with increased body mass could play a role.

Low outside temperature was highly associated with dry skin. Surprisingly, outside air humidity had a weaker association, which might be due to the difference between humidity outside and that indoors. Therefore, we hypothesize that air humidity is important, but actual exposure to humidity indoors and out is required to further understand its importance for dry skin.

Smoking was associated with GDS. It is well known that smoking stimulates skin aging, but less well known is that it leads to dry skin. Recently, it was found that in animal models administration of nicotine disrupted the dermoepidermal junction, reduced the formation of rete ridges, and disorganized collagen bundles, all of which may affect the barrier function and increase the risk of dry skin.[19]

Eczema is well known to occur with an impaired skin barrier, but seborrheic dermatitis is now also being recognized as an impaired barrier skin

disease.[20,21] This could clarify the increased likelihood of dry skin in both skin conditions. We also found that ever having had an itchy skin condition is associated with GDS. Itch is an important symptom of dry skin; this association is well known,[2,3,22] and itch is most likely a symptom of dry skin.

Patients with diabetes showed more LDS. The association with dry skin is well known but not well understood, although it may be related to damage of dermal proteins and formation of advanced glycation end products in individuals with diabetes.[7,23] That the association was seen only on the extremities might be due to alterations to the microvascularization in the arms and legs of individuals with diabetes. Previous studies showed that hypothyroidism and renal insufficiency are associated with xerosis,[6,9] but the prevalence of these conditions in our group of healthy subjects was very low, which could clarify why we did not find such an association. We did confirm known associations with culprit drugs, including statins, diuretics,[24,25] and chemotherapy agents (which have known toxic effects on the human body, including the skin).[26]

It was notable that GDS was more strongly associated with several comorbidities than LDS was. The systemic effects of most diseases could explain this finding, and conversely, it would imply that GDS is a symptom of diseases or even a biomarker of deteriorating health. This suggests that dry skin on the extremities is mainly a cosmetic condition in healthy individuals but becomes more widespread over the body with decreasing health. Hence, longitudinal studies are required to determine the degree to which dry skin might be pre-empting the prevalence of skin and systemic disease.

The main strength of our study is that we investigated a large population-based sample of middle-aged and elderly individuals living in the community. Also, the diagnoses were done by physicians and stratified on the basis of severity of dry skin to assess differences in a wide range of determinants for severe dry skin and LDS. We assume that physician scoring of skin as dry is more reliable than self-reporting of dry skin, as it is an independent evaluation that should be more comparable across individuals than self-report diagnoses are. Case definition might be a limitation of the study because we did not use validated questionnaire diagnostic criteria for dry skin and it was not feasible to measure TEWL. Nevertheless, consensus on the best scoring method for dry skin is lacking and the outcome assessment might suffer from inter-rater and intrarater variability, which also makes it difficult to compare the observations with those of other studies. Residual confounding, such as the lack of data on bathing behavior, could also have influenced our results. Finally, because of the cross-sectional design of our study, no causal relationship can be proved.

In conclusion, dry skin is a highly prevalent skin condition, affecting 60% of our middle-aged and elderly population. We have identified new and replicated known determinants for dry skin, which are similar between healthy community-based populations and nursing home populations, and that dry skin is more strongly associated with health parameters such as drug use and skin disease when more widely spread across the body.

REFERENCES

1. Hahnel E, Lichterfeld A, Blume-Peytavi U, Kottner J. The epidemiology of skin conditions in the aged: a systematic review. *J Tissue Viability*. 2017;26(1):20-28.
2. Lichterfeld A, Lahmann N, Blume-Peytavi U, Kottner J. Dry skin in nursing care receivers: a multi-centre cross-sectional prevalence study in hospitals and nursing homes. *Int J Nurs Stud*. 2016;56(Supplement C):37-44.
3. Paul C, Maumus-Robert S, Mazereeuw-Hautier J, Guyen CN, Saudez X, Schmitt AM. Prevalence and risk factors for xerosis in the elderly: a cross-sectional epidemiological study in primary care. *Dermatology*. 2011;223(3):260-265.
4. Smith DR, Atkinson R, Tang S, Yamagata Z. A survey of skin disease among patients in an Australian nursing home. *J Epidemiol*. 2002;12(4):336-340.
5. Augustin M, Kirsten N, Körber A, et al. Prevalence, predictors and comorbidity of dry skin in the general population. *J Eur Acad Dermatol Venereol*. 2019. https://doi.org/10.1111/jdv.15157 [Epub ahead of print]. Accessed June 28, 2018.
6. Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. *Lancet*. 2017;390(10101):1550-1562.
7. de Macedo GMC, Nunes S, Barreto T. Skin disorders in diabetes mellitus: an epidemiology and physiopathology review. *Diabetol Metabc Syndr*. 2016;8(1):63.
8. Lee D, Benson CA, Lewis CE, Grunfeld C, Scherzer R. Prevalence and factors associated with dry skin in HIV infection: the FRAM study. *AIDS*. 2007;21(15):2051-2057.
9. Solak B, Acikgoz SB, Sipahi S, Erdem T. Epidemiology and determinants of pruritus in pre-dialysis chronic kidney disease patients. *Int Urol Nephrol*. 2016;48(4):585-591.
10. Pons-Guiraud A. Dry skin in dermatology: a complex physiopathology. *J Eur Acad Dermatol Venereol*. 2007;21:1-4.
11. Sandilands A, Sutherland C, Irvine AD, McLean WH. Filaggrin in the frontline: role in skin barrier function and disease. *J Cell Sci*. 2009;122(Pt 9):1285-1294.
12. Ikram MA, Brusselle GGO, Murad SD, et al. The Rotterdam Study: 2018 update on objectives, design and main results. *Eur J Epidemiol*. 2017;32(9):807-850.
13. Harrell FE. *Ordinal Logistic Regression. Regression Modeling Strategies*. New York, NY: Springer; 2001.
14. Verdier-Sévrain S, Bonté F. Skin hydration: a review on its molecular mechanisms. *J Cosmet Dermatol*. 2007;6(2):75-82.
15. Chalyk NE, Bandaletova TY, Kyle NH, Petyaev IM. Age-related differences in morphological characteristics of residual skin surface components collected from the surface of facial skin of healthy male volunteers. *Skin Res Technol*. 2017;23(2):212-220.

16. Kottner J, Lichterfeld A, Blume-Peytavi U. Maintaining skin integrity in the aged: a systematic review. *Br J Dermatol*. 2013; 169(3):528-542.
17. Luebberding S, Krueger N, Kerscher M. Skin physiology in men and women: in vivo evaluation of 300 people including TEWL, SC hydration, sebum content and skin surface pH. *Int J Cosmet Sci*. 2013;35(5):477-483.
18. Wesley NO, Maibach HI. Racial (ethnic) differences in skin properties: the objective data. *Am J Clin Dermatol*. 2003;4(12): 843-860.
19. Eltony SA, Ali SS. Histological study on the effect of nicotine on adult male guinea pig thin skin. *Anat Cell Biol*. 2017;50(3):187-199.
20. Cork MJ, Danby SG, Vasilopoulos Y, et al. Epidermal barrier dysfunction in atopic dermatitis. *J Invest Dermatol*. 2009; 129(8):1892-1908.
21. DeAngelis YM, Gemmer CM, Kaczvinsky JR, Kenneally DC, Schwartz JR, Dawson TL. Three etiologic facets of dandruff and seborrheic dermatitis: malassezia fungi, sebaceous lipids, and individual sensitivity. *J Investig Dermatol Symp Proc*. 2005; 10(3):295-297.
22. Reich A, Ständer S, Szepietowski JC. Pruritus in the elderly. *Clin Dermatol*. 2011;29(1):15-23.
23. Gkogkolou P, Bohm M. Advanced glycation end products: key players in skin aging? *Dermatoendocrinol*. 2012;4(3): 259-270.
24. Golomb BA, Evans MA. Statin adverse effects: a review of the literature and evidence for a mitochondrial mechanism. *Am J Cardiovasc Drugs*. 2008;8(6):373-418.
25. Elias PM, Ghadially R. The aged epidermal permeability barrier: basis for functional abnormalities. *Clin Geriatr Med*. 2002;18(1): 103-120.
26. Heidary N, Naik H, Burgin S. Chemotherapeutic agents and the skin: an update. *J Am Acad Dermatol*. 2008;58(4): 545-570.

Supplemental Table I. Population characteristics

Variable	Generalized dry skin* (n = 642)	Localized dry skin (n = 2667)	No dry skin (n = 2238)
Median age, (IQR)	72.4 (64.0-81.7)	69.3 (62.3-77.7)	67.6 (60.7-76.8)
Sex, n (%)			
Male	259 (40.3)	1128 (42.3)	1020 (45.6)
Female	383 (59.7)	1539 (57.7)	1218 (54.4)
Skin color, n (%)			
Very white to white	544 (84.7)	2253 (84.5)	1829 (81.7)
White to olive-light brown	77 (12.0)	369 (13.8)	368 (16.4)
Brown-black	21 (3.3)	45 (1.7)	41 (1.8)
Median temperature (IQR)	8.2 (4.2-12.2)	8.9 (4.8-13.0)	11.0 (7.2-14.7)
Median humidity (IQR)	83.9 (81.0-86.8)	82.9 (79.3-86.5)	82.6 (78.7-86.5)
Cream use, n (%)			
No	164 (25.5)	777 (29.1)	721 (32.2)
Yes, few times a week	67 (10.4)	244 (9.1)	192 (8.6)
Yes, daily	292 (45.5)	1284 (48.1)	1238 (55.3)
Missing	119 (18.5)	362 (13.6)	87 (3.9)
Smoking,† n (%)			
No	445 (69.3)	1939 (72.7)	1595 (71.3)
Yes	195 (30.4)	721 (27.0)	640 (28.6)
Missing	2 (0.3)	7 (0.3)	3 (0.1)
Alcohol consumption‡			
Median (IQR)	8.6 (1.6-8.6)	8.6 (1.6-8.6)	8.6 (1.6-8.6)
Missing, n (%)	103 (16.0)	391 (14.7)	343(15.3)
BMI, kg/m^2,§ n (%)			
<20	19 (3.0)	40 (1.5)	39 (1.7)
20-25	177 (27.6)	713 (26.7)	607 (27.1)
>25	446 (69.4)	1906 (71.5)	1589 (71.0)
Missing	0 (0.0)	8 (0.3)	3 (0.1)
QoL‖			
Mean (SD)	77.11 (13.9)	78.13 (14.1)	78.52 (14.7)
Missing, n (%)	2 (0.3)	9 (0.3)	9 (0.4)
Education level,¶ n (%)			
Low	75 (11.7)	267 (10.0)	212 (9.5)
Medium	410 (63.9)	1667 (62.5)	1300 (58.1)
High	149 (23.2)	696 (26.1)	698 (31.2)
Missing	8 (1.2)	37 (1.4)	28 (1.2)
Self-reported dry skin,# n (%)			
No	278 (43.3)	1517 (56.9)	1464 (65.4)
Yes	326 (50.8)	1073 (40.2)	746 (33.3)
Missing	38 (5.9)	77 (2.9)	28 (1.3)
Dermatologic diseases			
Eczema, n (%)			
No	535 (83.3)	2475 (92.8)	2167 (96.8)
Yes	107 (16.7)	191 (7.2)	71 (3.2)
Missing	0 (0.0)	1 (0.0)	0 (0.0)
Seborrheic dermatitis, n (%)			
No	536 (83.5)	2326 (87.2)	1972 (88.1)
Yes	103 (16.0)	338 (12.7)	265 (11.8)
Missing	3 (0.5)	3 (0.1)	1 (0.1)
Psoriasis, n (%)			
No	621 (96.7)	2586 (97.0)	2166 (96.8)
Yes	21 (3.3)	79 (3.0)	72 (3.2)
Missing	0 (0.0)	2 (0.0)	0 (0.0)
Varicose veins**			
Yes	464 (72.3)	1949 (73.1)	1629 (72.8)
No	177 (27.6)	716 (26.8)	605 (27.0)
Missing	1 (0.2)	2 (0.1)	4 (0.2)

Continued

Supplemental Table I. Cont'd

Variable	Generalized dry skin* (n = 642)	Localized dry skin (n = 2667)	No dry skin (n = 2238)
Itchy skin condition,†† n (%)			
No	390 (60.7)	1740 (65.2)	1516 (67.7)
Yes	216 (33.6)	845 (31.7)	692 (30.9)
Missing	36 (5.6)	82 (3.1)	30 (1.3)
Other diseases			
Diabetes,‡‡ n (%)			
Yes	94 (14.6)	429 (16.1)	304 (13.6)
No	538 (83.8)	2201 (82.5)	1890 (84.5)
Missing	10 (1.6)	37 (1.4)	44 (1.9)
Renal impairment,§§ n (%)			
Yes	108 (16.8)	346 (13.0)	254 (11.3)
No	485 (75.5)	2163 (81.1)	1852 (82.8)
Missing	49 (7.6)	158 (5.9)	132 (5.9)
Hypothyroidism,‖‖ n (%)			
Yes	68 (10.6)	233 (8.7)	196 (8.7)
No	517 (80.5)	2227 (83.5)	1879 (84.0)
Missing	57 (8.9)	207 (7.8)	163 (7.3)
Atopy,¶¶ n (%)			
Yes	110 (17.1)	502 (18.8)	433 (18.8)
No	515 (80.2)	2107 (79.0)	1757 (78.5)
Missing	17 (2.6)	58 (2.2)	48 (2.7)
Medication			
Statins, n (%)			
Yes	206 (32.1)	725 (27.2)	580 (25.9)
No	432 (67.3)	1920 (72.0)	1642 (73.4)
Missing	4 (0.6)	22 (0.8)	16 (0.7)
Diuretics, n (%)			
Yes	118 (18.4)	399 (15.0)	301 (13.5)
No	520 (81.0)	2246 (84.2)	1921 (85.8)
Missing	4 (0.6)	22 (0.8)	16 (0.7)
Chemotherapy,## n (%)			
Yes	21 (3.3)	76 (2.9)	39 (1.7)
No	614 (95.6)	2556 (95.8)	2173 (97.1)
Missing	7 (1.1)	35 (1.3)	26 (1.2)

BMI, Body mass index; *IQR*, interquartile range; *QoL*, quality of life, *SD*, standard deviation.

*Dry skin graded by physician as localized, generalized, or no dry skin.

†No indicates never smoking, yes indicates ever smoking.

‡Alcohol consumption in g/d.

§BMI per point.

‖Self-perceived health score based on overall health; scores between 0 and 100 (where 0 is the lowest quality and 100 is the highest quality).

¶Low means primary education, medium means lower vocational/lower secondary/intermediate vocational education, and high means general secondary or higher vocational education or university education.

#Based on the question from the questionnaire Have you experienced dry skin over the last year?

**Varicose veins indicated by a score of 2 to 6 according to theclinical, etiology, anatomy, pathophysiology classification of chronic venous disorders, where 0 indicates no signs of venous disease, 1 indicates spider or reticular veins, 2 indicates varicose veins, 3 indicates edema without skin lesions, 4 indicates skin changes without ulceration, 5 indicates skin changes with healed ulceration, and 6 indicates skin changes with active ulceration.

††Question from the questionnaire Have you ever had an itchy skin condition?

‡‡Diabetes mellitus present if at least 1 of the following criteria was present: fasting plasma glucose level of 7.0 mmol/L or higher, nonfasting glucose level of 11.1 mmol/L or higher, and use of antidiabetic medicine or dietary treatment for type 2 diabetes mellitus.

§§Renal impairment, where yes means a glomerular filtration rate less than 60 and no means a glomerular filtration rate of 60 or higher.

‖‖Hypothyroidism if thyroid-stimulating hormone level is high and free thyroxine level is normal or low or thyroid-stimulating hormone level is normal and free thyroxine level is low.

¶¶Atopic constitution: self-reported asthma, hay fever, and dust mite allergy.

##Ever having received chemotherapy.