

Hidradenitis suppurativa tarda: defining an understudied elderly population

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Abstract

Background Hidradenitis suppurativa (HS) is a chronic, devastating, multifactorial skin disease. Patients generally develop HS after puberty and the prevalence of the disease is assumed to decrease with higher age. Data outside the usual age range are limited, especially for elderly patients.

Objectives To investigate the prevalence, clinical characteristics and associated comorbidities among the elderly HS population.

Methods Data were collected through a population-wide survey-based study within the Lifelines Cohort Study in the Netherlands. The clinical characteristics of elderly patients with HS (≥ 60 years) were compared with an adult population (< 60 years) with HS. The comorbidities in elderly patients with HS were compared with those of a non-HS sex- and age-matched elderly population in a 1 : 4 ratio. HS in the elderly was defined as active HS in patients aged 60 years and older. Within the HS elderly group, two subgroups were defined, late-onset HS (HS developed after 60 years of age) and persistent HS (HS developed from a younger age but continuing after 60 years of age).

Results Within the Lifelines cohort 209 elderly patients with HS were identified as well as an adult (< 60 years) group with HS ($n=793$) and a non-HS sex- and age-matched control elderly group ($n=810$). The prevalence of HS among the elderly bootstrap analysis population was 0.8% [95% confidence interval (CI) 0.4–1.2]. A significantly higher age of HS symptom onset was found compared with the adult HS group: respectively, 40 vs. 23 years (odds ratio 1.056, 95% CI 1.05–1.07). Among the elderly HS cohort (in the Discussion, the HS tarda cohort) a female : male ratio of 1.7 : 1.0 and a higher family history for HS were found. Moreover, elderly patients with HS had a significantly higher risk of having HS-associated comorbidities compared with the sex- and age-matched controls.

Conclusions The prevalence of HS in the elderly is not rare. Among the elderly a shift from female predominance towards a lower female : male ratio in HS is observed. In addition, HS in the elderly showed significant variation in age of onset and involved body areas. Moreover, elderly patients with HS were more susceptible to multimorbidity. Finally, we propose defining HS in the elderly as 'HS tarda' and subdividing it as late-onset and persistent HS tarda.

What is already known about this topic?

- Patients generally develop hidradenitis suppurativa (HS) after puberty and the prevalence of the disease is assumed to decrease with higher age.
- Data outside this known age range are limited.

What does this study add?

- New insights concerning the epidemiological characteristics and disease characteristics of HS among the elderly in a large prospective cohort.
- Extending knowledge in who is at risk for developing HS at older age.
- Proposal of defining HS in the elderly as 'HS tarda' with subdivisions for late-onset and persistent HS tarda.
- Possible contribution to new steps in diagnostic approaches and clinical management of HS.

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic, inflammatory and heterogeneous skin disease characterized by recurrent and painful abscesses, nodules, draining sinuses and scarring.¹ HS is considered a common

skin disorder, with a prevalence of 1–4% worldwide.² Prens *et al.* reported a prevalence of up to 2.1% in the northern Netherlands.³ Risk factors for developing the disease are female sex (female: male ratio 2.8 : 1.0), a positive family

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history, smoking and being overweight.^{3,4} Treatment of HS includes lifestyle modifications, medication such as antibiotics and biologics, and surgical procedures.⁵ Hormonal background is thought to play an important role as HS is more prevalent in females, the onset of the disease is around puberty and HS has been reported to decrease after menopause.^{3,6,7}

In the last few decades, increasing levels of data have shown the presence of the disease outside the known age range, specifically in childhood populations. Deckers *et al.* reported that 7.7% of the patients with HS had an onset of disease before 13 years of age.⁸ Additionally, the prevalence of associated comorbidities differs between the paediatric and adult populations, as shown by Hallock *et al.*⁹ Despite this growing knowledge of HS in childhood, data concerning HS in older adults remain scarce. However, older patients with HS are seen commonly at the outpatient clinic of tertiary referral centres. Blum *et al.* recently described the clinical presentation and management of HS in 26 patients with HS aged 65 years or older and compared the older patients with HS with an adult population younger than 65 years.¹⁰ They discovered a significantly higher age at disease onset in older patients with HS and showed that older patients with HS were more likely to be current or ex-smokers.¹⁰

Because we face an ageing population worldwide, from 461 million people older than 65 years in 2004 to approximately 2 billion expected by 2050, physicians may start encountering this understudied elderly HS population even more.¹¹ Healthcare practitioners should pay more attention to disease presentation in the elderly to provide the best diagnostic and tailored treatment for these patients. Therefore, we aimed to assess the prevalence, clinical characteristics and comorbidities of HS in the elderly of the general population in the northern Netherlands.

Patients and methods

Study design

A cross-sectional study within the framework of the Lifelines Cohort Study was performed. Lifelines is a multidisciplinary, prospective, population-based cohort study examining the health and health-related behaviours of 167 729 persons living in the north of the Netherlands. It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioural, physical and psychological factors contributing to the health and disease of the general population, with a particular focus on multimorbidity and complex genetics. The Lifelines Cohort Study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the University Medical Centre Groningen, the Netherlands (reference number: METc 2007/152; reference number for the current add-on study: METc 2019/571).

The participants provided written informed consent. An add-on study was conducted, for which a digital questionnaire (SKIQ, initiated by the University Medical Center Groningen Department of Dermatology with the aim to gain more insight into HS and other skin diseases in the general population) was sent out to the Lifelines participants between February and May 2020. This digital questionnaire

consisted of 23 questions related to HS and was sent by email to 135 950 Lifelines participants. An overview of the questions used for identifying HS status are found in the supplementary material of Prens *et al.*³ Participants were allocated to the HS group in two ways. Firstly, when they answered 'yes' to the question: 'Did you ever (during your life) get the diagnosis hidradenitis suppurativa (HS)?' If participants answered 'no', two validated questions were asked for self-diagnosing HS, determined by Esmann *et al.* and Vinding *et al.*^{12,13} For self-diagnosing HS, the first question ('Do you have painful, recurring abscesses or boils in your armpits, groin, buttocks, or on other locations, as seen in the images below?') has a sensitivity of 97% and specificity of 82%, with a positive predictive value of 85%. The second question ('Did you have at least two outbreaks of abscesses or boils within a period of 6 months?') has a sensitivity of 90%, a specificity of 97% and a positive predictive value of 96%.^{12,13} Additionally, with the questions for self-diagnosing HS, images of HS lesions corresponding with the Hurley stages were shown to the participants, enabling potential patients to self-assess the presence and the stage of HS.

Patient characteristics

The demographic characteristics of the add-on questionnaire were used for the database, including sex, age, smoking, body mass index (BMI) and smoking status. Smoking status was categorized into nonsmokers, ex-smokers and current smokers. All identified HS cases were asked questions concerning their clinical characteristics, including disease duration, current HS activity, disease course, disease severity, involved HS areas, family history of HS, and any HS-associated comorbidities. The history of comorbidities was acquired from the questionnaires taken during the baseline visits and included the following comorbidities: history of acne, psoriasis, chronic obstructive pulmonary disease (COPD), asthma, heart failure or heart infarct or valve dysfunction, hypertension, kidney disease or dysfunction, diabetes, Crohn disease, irritable bowel disease, arthrosis, rheumatoid arthritis, fibromyalgia and history of polycystic ovary syndrome (PCOS).

Defining subgroups of hidradenitis suppurativa in the elderly

HS in the elderly was defined as active HS in patients aged 60 years and older. This cutoff was chosen because HS has been reported to decrease after the menopause.^{3,6,7} The menopausal transition begins at a median of 51 years, with a distribution ranging from 40 until 58 years.⁷ In addition, HS in the elderly was subdivided into differences in the age of onset. Late-onset HS is defined as HS that develops after 60 years of age, whereas persistent HS in the elderly has an onset earlier in life and continues after 60 years of age (Figure 1).

Data analysis

Descriptive statistics were used to characterize the elderly population with HS. Categorical data were presented with a frequency distribution. Continuous data were reported

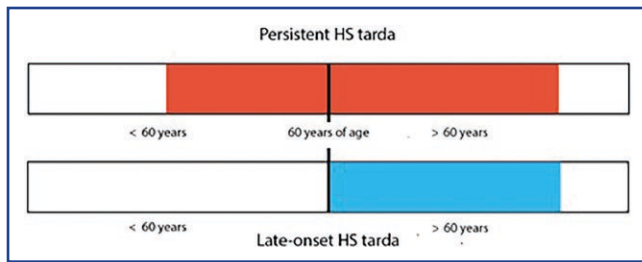


Figure 1 Schematic visualization of the differences in age at symptom onset between the persistent HS tarda group and the late-onset HS tarda group. HS, hidradenitis suppurativa.

with a median (interquartile range) or mean (SD). To sustain the anonymity of the Lifelines participants, frequencies below $n=10$ were noted as $n < 10$ ($< x\%$, using 10 as the numerator). Additionally, to maintain patient anonymity, the missing cases are noted as NR_A and are not reported in the descriptive notes when $n < 10$. The prevalence of the identified elderly patients with HS was calculated using a 95% confidence interval (CI) through binominal exact calculations. As HS is more prevalent among women and to minimize potential uneven distribution among male and female respondents, 2500 randomly selected males and 2500 randomly selected females in the total cohort, as well as 1000 randomly selected males and 1000 randomly selected females in the elderly cohort, were extracted. The bootstrap method was used to recalculate the prevalence of HS among the elderly in the total cohort, with an equal proportion of men and women.

To reduce selection bias in the comorbidity risk analysis, group matching was utilized to match the age and sex of the identified elderly HS cases with the elderly control cases at a 1 : 4 ratio. Univariable and multivariable logistic regression analyses were performed to assess the differences in clinical characteristics between the elderly patients with HS and adult patients with HS and between the late-onset HS group and the persistent HS group while adjusting for sex, BMI and smoking status. For the univariable regression analysis, the forced enter selection procedure was used. For multivariable regression analysis, the backward elimination procedure was used. The odds ratio (OR) was used to report the strength of associations with a 95% CI. All statistical tests were two-sided, and a P -value of ≤ 0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA).

Results

Analysing the dataset

The HS questionnaire was sent to 135 950 Lifelines participants. The response rate was 42.8%, as 58 198 participants filled in the questionnaire. A total of 1356 participants did not answer the HS-related questions and were therefore excluded from the study. In addition, 753 participants aged < 18 years were excluded, resulting in 56 089 participants eligible for analysis. In the cohort a division was made between participants under age 60 years and participants

60 years and older, resulting in 20 368 elderly participants. The flowchart of included Lifelines respondents is shown in Figure 2.

Prevalence

Out of the 56 089 respondents, a total of 1161 HS cases were identified. Patients who exhibited only one inflammation and those not experiencing HS symptoms at the time of the questionnaire were excluded ($N=142$); in addition, patients with missing information regarding HS activity and one identified familial case were removed ($N=17$), resulting in 1002 total HS cases with active HS. Among these, 305 participants reported a diagnosis of HS (diagnosed HS), and 697 answered positively to the two diagnostic questions (self-diagnosed HS). Furthermore, of the 1002 active cases of HS 209 patients were aged 60 years or older. Therefore, the prevalence of elderly patients with HS in the total population was 0.4% (95% CI 0.3–0.4), and the prevalence of HS in the total elderly population was 1.0% (95% CI 0.9–1.2). The prevalence of persistent HS in the elderly ($n=163$) and late-onset HS in the elderly ($n=46$) were, respectively 0.8% (95% CI 0.70–0.90) and 0.2% (95% CI 0.2–0.3). The bootstrapping analysis yielded similar results, with 0.4% (95% CI 0.2–0.5) in the total bootstrap analysis population and 0.8% (95% CI 0.4–1.2) in the elderly bootstrap analysis population. Bootstrapping analysis revealed 0.6% (95% CI 0.30–1.0) for persistent HS in the elderly and 0.2% (95% CI 0.0–0.4) for late-onset HS in the elderly.

Patient characteristics

The patient characteristics of the elderly HS group ($n=209$) were compared with those of the adult HS group ($n=793$) and non-HS age- and sex-matched controls ($n=810$). The proportion of elderly male patients with HS was higher than for adult male patients with HS (35.9% vs. 22.8%), with a female : male ratio of 1.7 : 1.0 in the elderly HS group and 3.4 : 1.0 in the adult HS group (OR 1.892, 95% CI 1.36–2.63). Compared with the adult HS cases, the elderly HS cases were more likely to be ex-smokers (47.7% vs. 26.3%; OR 2.035, 95% CI 1.36–3.04), while the adult HS cases were more likely to be active smokers (38.4% vs. 20.9; OR 0.613, 95% CI 0.39–0.97). The BMI of the elderly HS group did not differ significantly from the adult HS group. However, the BMI in the elderly HS group was significantly higher than in the elderly control group (OR 1.072, 95% CI 1.03–1.11) (Table 1).

Clinical characteristics

Table 2 shows the clinical characteristics of the Lifelines HS cohort. The elderly HS group had a higher age of onset compared with the adult HS group, with a median age of 40.0 years (20.00–58.75) vs. 23.0 years (16.00–35.00), respectively (OR 1.056, 95% CI 1.05–1.07). Regarding the affected HS areas, elderly patients with HS were less likely to have HS in the armpits (OR 0.595, 95% CI 0.39–0.91), groins (OR 0.643, 95% CI 0.44–0.93) and buttocks (OR 0.563, 95% CI 0.36–0.87). In contrast, elderly patients with HS were more likely to have HS in other areas of the body (OR 1.887, 95% CI 1.25–2.84). There were no significant differences between elderly patients with HS and adult

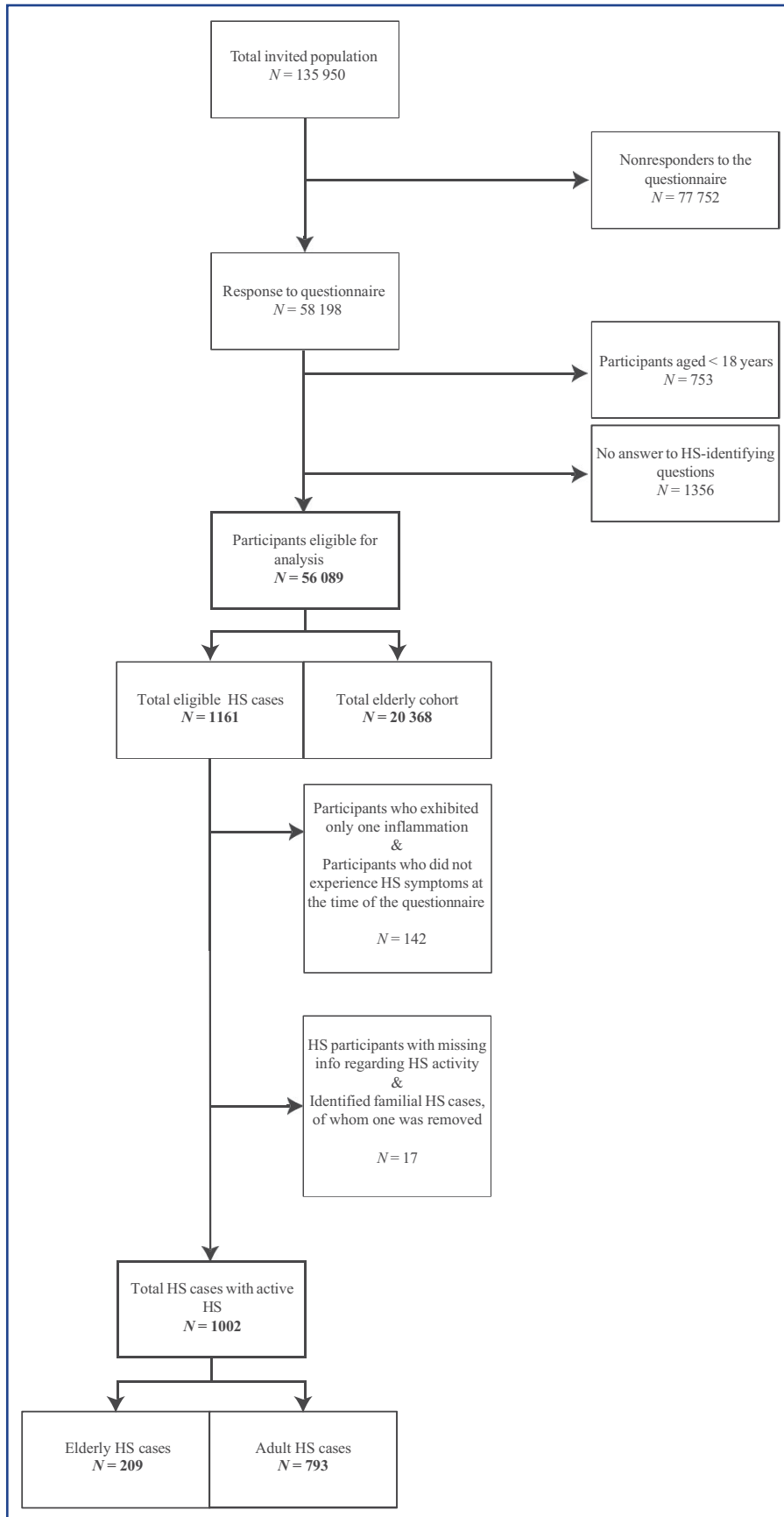


Figure 2 Flowchart demonstrating which participants were eligible for analysis.

Table 1 Patient characteristics of the Lifelines HS cohort

	HS groups			Univariable regression			Univariable regression		
	Total n = 1002	Adults (< 60 years) n = 793	Elderly (≥ 60 years) n = 209	P-value ^a	OR (95% CI)	Control group			
						Elderly (≥ 60 years) n = 810	P-value ^b	OR (95% CI)	
Sex ^c									
Female, n (%)	746 (74.5)	612 (77.2)	134 (64.1)	< 0.001	1.892 (1.36–2.63)	501 (61.9)	0.547	0.907 (0.66–1.25)	
Male, n (%)	256 (25.5)	181 (22.8)	75 (35.9)			309 (38.1)			
Age ^e (years), median (IQR)	52.0 (44.00–59.00)	49.0 (41.00–54.00)	66.00 (62.00–71.00)	NR	NR	67.0 (62.00–72.00)	0.497	0.992 (0.97–1.02)	
BMI, median (IQR)	26.7 (23.70–30.00)	26.7 (23.7–30.1)	26.9 (24.20–30.30)	0.777	1.004 (0.98–1.04)	26.00 (24.10–28.50)	< 0.001	1.072 (1.03–1.11)	
Missing, n	106	96	10						
Smoking status ^d									
Nonsmoker, n (%)	259 (34.4)	205 (35.3)	54 (31.4)	< 0.001	2.035 (1.36–3.04)	297 (41.9)	0.095	1.319 (0.90–1.92)	
Ex-smoker, n (%)	235 (31.2)	153 (26.3)	82 (47.7)	0.038	0.613 (0.39–0.97)	342 (48.3)	< 0.001	2.870 (1.75–4.71)	
Current smoker, n (%)	259 (34.4)	223 (38.4)	36 (20.9)			69 (9.7)			
Missing, n	249	212	37			102			

^aComparisons between the adult HS group and the elderly HS group, analysed via univariable regression analysis (the adult group was used as a reference). ^bComparisons between the elderly control group and the elderly HS group, analysed via univariable regression analysis (the elderly control group was used as a reference). ^cThe elderly control group has been sex- and age-matched to the elderly HS group and, thus, does not have significantly different ages. ^dThe nonsmoking group was used as a reference for the analysis. BMI, body mass index; CI, confidence interval; HS, hidradenitis suppurativa; IQR, interquartile range; OR, odds ratio. **Bold** indicates significance.

patients with HS in the Hurley classification. Nevertheless, elderly patients with HS were more likely to have a positive family history of HS (33.8%) compared with adult HS cases (21.3%) (OR 2.530, 95% CI 1.27–5.04). There were no significant differences in clinical characteristics between the late-onset and persistent HS groups.

Comorbidities

The comorbidities associated with HS in comparison with a sex- and age-matched control elderly group were analysed. The results revealed that elderly patients with HS were at a higher risk of having several comorbidities (Table 3, Figure 3). Specifically, they had a higher risk of having history of acne (16.7% vs. 4.8%; OR 3.971, 95% CI 2.45–6.45), psoriasis (20.1% vs. 7.9%; OR 2.928, 95% CI 1.92–4.47), diabetes (9.2% vs. 4.8%; OR 1.945, 95% CI 1.10–3.44), COPD (14.1% vs. 8.1%; OR 1.881, 95% CI 1.18–3.00), asthma (12.6% vs. 6.3%; OR 2.138, 95% CI 1.30–3.52), irritable bowel syndrome (71.4% vs. 56.0%; OR 2.120, 95% CI 1.01–4.46), fibromyalgia (45.1% vs. 27.2%; OR 2.201, 95% CI 1.16–4.18), PCOS (OR 3.491, 95% CI 1.25–9.74) and kidney disease or dysfunction (8.8% vs. 4.5%; OR 2.064, 95% CI 1.15–3.72).

Discussion

There is limited information regarding the prevalence of HS among the elderly population. Our study showed that HS among the elderly is significantly more common than hitherto estimated, with a prevalence of 0.8% in the general elderly population.

Here we propose the name HS tarda for HS presenting in the elderly population, analogous to acne tarda. We suggest the subdivision of HS tarda into patients who develop their first symptoms before 60 years of age, the so-called persistent HS tarda group, and patients who develop initial symptoms after 60 years of age, the late-onset HS tarda group.

Our study suggests that HS tarda may be associated with male sex. HS in the general population appears to be significantly more common among females.^{1–5} With a female : male ratio of 3.4 : 1.0, our adult HS population displayed findings consistent with female : male ratios as presented in the literature.^{1–5} In contrast, in the HS tarda cohort, we observed a female : male ratio of 1.7 : 1.0. This relatively higher prevalence of males among elderly patients with HS supports the findings of Blum *et al.*, who reported a female : male ratio of 1.6 : 1.0 in the elderly HS group compared with a female : male ratio of 3.8 : 1.0 in the adult HS group.¹⁰ The shift in the female : male ratio in HS tarda might be due to the influence of the menopause on HS progression in women.

In our study, we found that the HS tarda group had a significantly higher age of onset of HS symptoms compared with the adult HS group (40 years vs. 23 years). In the general population, a median age of onset of 21.8 years has been reported.¹⁴ These findings are supported by the research of Blum *et al.*, who identified similar differences in the age at symptom onset of the elderly group as well as the adult HS group to our findings.¹⁰ Naik *et al.* proposed a bi-model distribution of the age of onset of HS, with most patients reporting the onset of symptoms in late adolescence and some

Table 2 Clinical characteristics of the Lifelines HS cohort

	HS groups		Elderly (>= 60 years) n=209			Univariable regression			Multivariable regression ^a			Elderly HS groups			Univariable regression			Multivariable regression ^a		
	Total n=1002	Adults (< 60 years) n=793	Adults (>= 60 years) n=209	P-value ^b	OR (95% CI)	P-value	OR (95% CI)	P-value ^c	Late-onset n=46	Persistent n=163	Late-onset n=46	P-value ^c	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)			
Age of onset of HS (years), median (IQR)	25.0 (18.00–40.00)	23.0 (16.00–35.00)	40.0 (20.00–58.75)	< 0.001	1.056 (1.05–1.07)	< 0.001	1.049 (1.04–1.06)	NR	65.0 (60.75–69.00)	29.0 (18.00–45.25)	65.0 (60.75–69.00)	NR	NR	NR	NR	NR	NR			
Affected areas																				
Armpit(s), n (%)	29 (30.8)	16 (33.3)	13 (21.5)	0.001	0.550 (0.38–0.79)	0.016	0.595 (0.39–0.91)	NR	< 10 (< 21.7) ^d	40 (24.5)	< 10 (< 21.7) ^d	0.053	0.262 (0.10–0.67)	NR	NR	NR	NR			
Under the breasts, n (%)	66 (6.6)	54 (6.8)	12 (5.7)	0.580	0.834 (0.44–1.59)	NR	NR	NR	11 (6.7)	< 10 (< 21.7) ^d	0.265	0.307 (0.04–2.44)	NR	NR	NR	NR	NR			
Groins, n (%)	544 (54.3)	458 (57.8)	86 (41.1)	< 0.001	0.511 (0.38–0.70)	0.019	0.643 (0.44–0.93)	NR	73 (44.8)	13 (28.3)	0.047	0.486 (0.24–0.99)	0.176	0.500 (1.18–1.36)	NR	NR	NR			
Sexual organs, n (%)	318 (31.7)	271 (34.2)	47 (22.5)	0.001	0.559 (0.39–0.80)	0.185	0.755 (0.50–1.14)	NR	40 (24.5)	< 10 (< 21.7) ^d	0.186	0.552 (0.23–1.33)	NR	NR	NR	NR	NR			
Buttocks, n (%)	270 (26.9)	233 (29.4)	37 (17.7)	< 0.001	0.517 (0.35–0.76)	0.010	0.563 (0.36–0.87)	NR	30 (18.4)	< 10 (< 21.7) ^d	0.796	0.325 (0.33–1.95)	NR	NR	NR	NR	NR			
Other, n (%)	225 (22.5)	149 (18.8)	76 (36.4)	< 0.001	2.470 (1.77–3.45)	0.002	1.887 (1.25–2.84)	NR	55 (33.7)	21 (45.7)	0.140	1.649 (0.85–3.21)	NR	NR	NR	NR	NR			
Self-reported Hurley stage ^e																				
I, n (%)	710 (> 70.8)	565 (> 71.2)	145 (> 69.4)	0.626	1.095 (0.76–1.57)	NR	NR	NR	110 (> 67.5)	35 (> 76.1)	0.550	0.786 (0.36–1.73)	NR	NR	NR	NR	NR			
II, n (%)	228 (> 22.8)	178 (> 22.4)	50 (> 23.9)	0.403	0.731 (0.35–1.52)	NR	NR	NR	40 (24.5)	10 (21.7)	0.999	0.000 (0.00–0.00)	NR	NR	NR	NR	NR			
III, n (%)	57 (> 5.7)	48 (> 6.1)	< 10 (< 4.8) ^d						< 10 (6.1) ^d	< 10 (< 21.7) ^d										
Missing, n	NR ^d	NR ^d	NR ^d						NR ^d	NR ^d										
Family members with HS ^f																				
No, n (%)	107 (35.2)	84 (39.0)	35 (26.3)	0.016	1.950 (1.13–3.35)	0.008	2.530 (1.27–5.04)	NR	16 (23.4) ^g	< 10 (21.7) ^d	0.063	0.245 (0.55–1.08)	NR	NR	NR	NR	NR			
Yes, n (%)	84 (27.6)	53 (21.3)	45 (33.8)						28 (38.3) ^g	< 10 (21.7) ^d										
Don't know, n (%)	113 (37.2)	86 (39.7)	51 (38.3)						NR	NR										
Missing, n	698	570	136						NR	NR										

^aCorrected for sex, body mass index, smoking status. ^bComparisons between the adult HS cases (reference group) and the elderly HS cases, analysed via univariable and multivariable regression analysis. ^cComparisons between the persistent HS cases (reference group) and the late-onset HS cases, analysed via univariable and multivariable regression analysis. ^dAs the number of identified cases is below 10, < (x = 10 as the numerator) is given as the percentage to sustain the anonymity of the Lifelines participants. Additionally, the missing cases are not reported (NR_A) in variable comparison groups where one group has n < 10. ^eHurley stage I was used as the reference for the analysis. ^fNo family members with HS was used as the reference for the analysis. ^gDue to Lifeline anonymity rules, missing values cannot be provided; therefore, the percentages shown are estimated. CI, confidence interval; HS, hidradenitis suppurativa; IQR, interquartile range; NR, not reported; NR_A, not reported to maintain anonymity (in instances where n > 10); OR, odds ratio. **Bold** indicates significance.

Table 3 Prevalence of the comorbidities in the Lifelines cohort

	Elderly cohorts			Univariable regression	
	All elderly, n = 1019	With HS n = 209	Non-HS controls n = 810	P-value ^a	OR (95% CI)
Skin disorders					
Acne (history of), n (%)	74 (7.3)	35 (16.7)	39 (4.8)	< 0.001	3.971 (2.45–6.45)
Missing, n	2	0	2		
Psoriasis, n (%)	106 (10.4)	42 (20.1)	64 (7.9)	< 0.001	2.928 (1.92–4.47)
Missing, n	1	0	1		
Metabolic diseases					
Diabetes, n (%)	58 (5.7)	19 (9.2)	39 (4.8)	0.022	1.945 (1.10–3.44)
Missing, n	3	3	0		
Cardiovascular diseases					
Heart attack/failure/valve dysfunction, n (%)	59 (5.8)	14 (6.9)	45 (5.6)	0.472	1.256 (0.68–2.34)
Missing, n	8	6	2		
Hypertension, n (%)	349 (35.1)	74 (37.0)	275 (34.6)	0.524	1.111 (0.81–1.53)
Missing, n	26	9	17		
Lung diseases					
COPD, n (%)	94 (9.3)	29 (14.1)	65 (8.1)	0.008	1.881 (1.18–3.00)
Missing, n	7	4	4		
Asthma, n (%)	77 (7.6)	26 (12.6)	51 (6.3)	0.003	2.138 (1.30–3.52)
Missing, n	2	2	0		
Gastrointestinal disorders					
Crohn disease, n (%)	< 10 (< 1.0) ^b	< 10 (< 4.8) ^b	< 10 (< 1.2) ^b	0.209	3.296 (0.51–21.16)
Missing, n	NR _A	NR _A	NR _A		
Irritable bowel syndrome, n (%)	109 (59.6)	30 (71.4)	79 (56.0)	0.048	2.120 (1.01–4.46)
Missing, n	836	167	669		
Musculoskeletal disorders					
Arthrosis, n (%)	257 (75.1)	63 (80.8)	194 (73.5)	0.193	1.515 (0.81–2.83)
Missing, n	677	131	546		
Rheumatoid arthritis, n (%)	56 (25.0)	15 (31.3)	41 (23.3)	0.185	1.608 (0.80–3.24)
Missing, n	795	161	634		
Fibromyalgia, n (%)	73 (31.1)	23 (45.1)	50 (27.2)	0.016	2.201 (1.16–4.18)
Missing, n	784	158	626		
Gynaecological disorders					
PCOS (history of), n (%)	15 (1.5)	< 10 (< 4.8) ^b	< 10 (< 1.2) ^b	0.017	3.491 (1.25–9.74)
Missing, n	NR _A	NR _A	NR _A		
Kidney disease or dysfunction, n (%)					
Kidney disease or dysfunction, n (%)	54 (5.3)	18 (8.8)	36 (4.5)	0.016	2.064 (1.15–3.72)
Missing, n	6	4	2		

^aComparisons between the persistent HS cases (reference group) and the late-onset HS cases, analysed via univariable regression analysis. ^bAs the number of identified cases is below 10, the x is used as the nominator for the percentage to sustain the anonymity of the Lifelines participants. Additionally, the missing cases are not reported (NR_A) in the variable comparison groups where one group has n < 10. CI, confidence interval; COPD, chronic obstructive pulmonary disease; HS, hidradenitis suppurativa; IQR, interquartile range; NR_A, not reported to maintain anonymity (in instances where n < 0); OR, odds ratio; PCOS, polycystic ovary syndrome. **Bold** indicates significance.

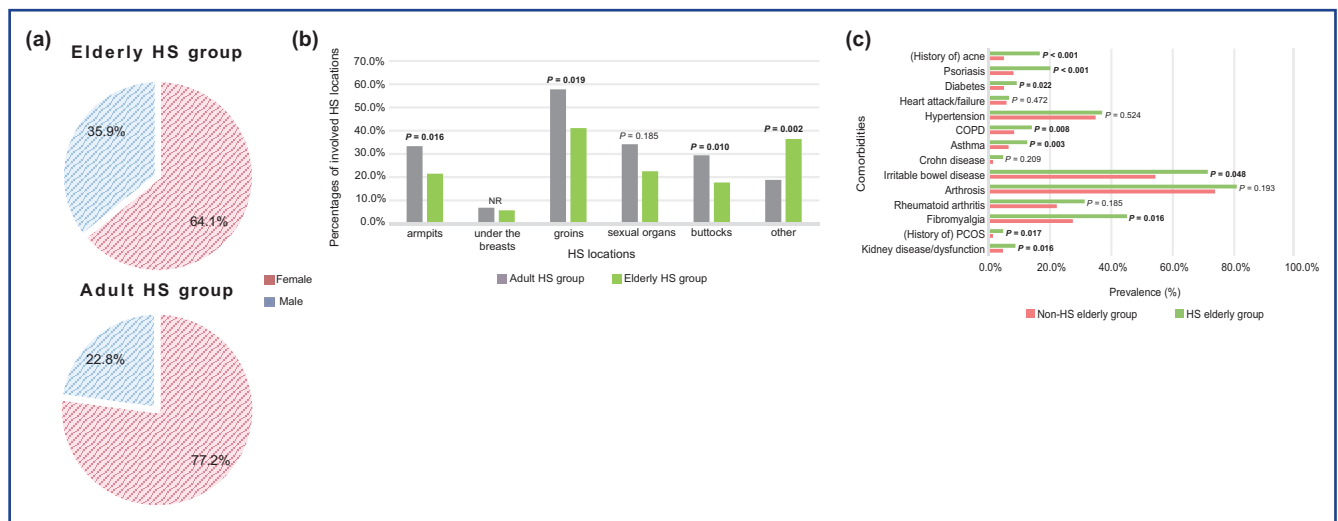


Figure 3 Summary of Lifelines cohort characteristics. (a) Circle diagram depicts the percentages of females and males in both the adult and elderly HS groups. (b) Bar chart showing the prevalence of the involved HS areas within the adult HS group and the HS tarda group. (c) Bar chart representing the percentage prevalences of comorbidities associated with the elderly HS group compared with the age-matched elderly control group (non-HS). P-values were analysed via univariable regression analysis. COPD, chronic obstructive pulmonary disease; HS, hidradenitis suppurativa; PCOS, polycystic ovary syndrome. **Bold** indicates significance.

patients reporting their first symptoms around 40 years of age.¹⁵ Our finding may raise the question of whether the second peak of HS onset is associated with HS persisting into older age. Moreover, we also found patients who developed their first symptoms after the age of 60 years, the so-called late-onset HS tarda. In addition, recent data concluded that age at symptom onset could be an important prognostic factor, as patients with late-onset HS had a significantly higher disease severity than patients with common-onset HS.¹⁶

The frequently required aggressive HS treatment, including the use of biologics or extensive surgery, can be demanding in the elderly HS population as a consequence of a delayed wound-healing process, susceptibility to adverse drug events and the risk of potentially harmful interactions due to a combination of the progressive impairment of the immune system, multi-comorbidities and polypharmacy.^{17–19} Therefore, careful consideration of the potential risks and benefits of aggressive treatments should be made when treating elderly patients with HS.

Patients with HS have a high multimorbidity burden, especially comorbidities which are inflammatory in nature.^{2,20} Our study found that patients with HS tarda were at risk for multimorbidity as they had a four times higher risk of having a history of acne, a three times higher risk of psoriasis and history of PCOS, and a two times higher risk of having fibromyalgia, irritable bowel disease, diabetes, kidney dysfunction/diseases, COPD and asthma than an age- and sex-matched control group. As multimorbidity is strongly associated with frailty, it is recommended to reduce the multimorbidity risks and to encourage multidisciplinary collaboration with general practitioners and geriatrics healthcare practitioners.^{19,21,22} In addition, we determined that patients with HS tarda displayed high levels of smoking and alcohol consumption and a higher BMI, which are associated risk factors of frailty and reduce the patient's resilience to cope with internal and external stressors.¹¹ Comorbidities and risk factors and their impact on frailty should be considered in the treatment of HS in the elderly population.

HS tarda has a variety of specific predictive factors and clinical characteristics, compared with the common HS presentation. This study showed that male sex, a higher age of onset and a positive family history for HS are major predictive risk factors. Additionally, HS tarda appears to be less common in typical HS-affected body sites as patients were less likely to develop HS in common locations such as the armpits, groins or buttocks and more often develop HS in other areas of the body.

Limitations include that the study was retrospective in nature and that some variables consisted of incomplete data. Additionally, the study was limited by the self-reported HS diagnosis, but to minimize the chance of false-positive cases, validated questions and images of HS were used. Moreover, the estimated prevalence of HS tarda might even be an underestimation of the actual prevalence, due to missing data and the online delivery of the HS questionnaire, which may have excluded elderly participants without access to a computer or smartphone, or who lacked the necessary digital skills. Additionally, elderly individuals might have difficulties recalling past events, leading to underreporting and/or overreporting of specific details, such as a comorbidity diagnosis.

This study highlights the need for more, larger-scale and prospective studies to investigate potentially understudied clinical characteristics and comorbidities in elderly patients with HS. Prospective research regarding treatment efficacy is needed to understand the management mechanisms of the elderly HS group. In addition, more elderly HS populations need to be identified to understand the pathophysiology and phenotypic characteristics of this elderly HS subgroup.

In conclusion, this is the first study that revealed the prevalence of HS in an elderly population, and we demonstrate a prevalence of 0.8% of HS in the general elderly population, and, to our knowledge, this is the largest study defining the clinical characteristics and comorbidities of this population. Male sex, an older age of onset and a positive family history for HS were associated with a higher risk of developing HS tarda. Our findings provide new insights into the clinical characteristics and epidemiology concerning HS in the elderly, and can contribute to new steps in diagnostic approaches and clinical management of this specific and fragile population.

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Conflicts of interest

D.v.d.W., N.D.K.K. and B.C.v.M. report no conflicts of interest. H.H.v.d.Z. reports fees (advisory boards, consultations) from AbbVie, InflaRX, Insmed, Novartis Pharma and UCB Pharma. B.H. reports fees (paid to the institution) for the following: advisory boards, consultations, educational grants and investigator initiative studies from AbbVie and Janssen-Cilag; advisory boards, consultations and investigator initiative studies from Novartis Pharma; advisory boards and consultations from UCB Pharma; consultations and investigator initiative studies from Akari Therapeutics and Celgene; consultations from LEO Pharma, Philips, Regeneron, Roche and Sanofi; and investigator initiative studies from Solenne B.V.

Data availability

The data supporting this study's findings are available from Lifelines. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of Lifelines.

Ethics statement

The Lifelines Cohort Study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the University Medical Center Groningen, the Netherlands (reference number: METc 2007/152, reference number for the current add-on study: METc 2019/571).

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