Received: 4 May 2023 | Accepted: 14 November 2023

DOI: 10.1111/jdv.19726

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

ORIGINAL ARTICLE

Diet and physical activity as risk-reducing factors for hidradenitis suppurativa

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Funding information
Ministerie van Economische Zaken en Klimaat; Ministerie van Volksgezondheid, Welzijn en Sport; Novartis, Grant/Award Number: CAIN457ANL01T; Rijksuniversiteit Groningen; The Northern Provinces of the Netherlands; Universitair Medisch Centrum Groningen

Abstract

Background: Hidradenitis suppurativa (HS) is a multifactorial inflammatory skin disease that is considered to be an immune-mediated inflammatory disease (IMID). Up till now, the impact of lifestyle on (the development of) HS has not been thoroughly investigated.

Objectives: To investigate the effect of dietary intake and physical activity (PA) on (the development of) HS.

Materials and Methods: A nested case–control study was performed within the longitudinal Lifelines Cohort Study, that took place in the Northern Netherlands, and identified 1004 adult eligible HS patients and 5000 age-matched controls. Dietary data were collected using a validated food frequency questionnaire, subsequently translated to the Lifelines Diet Score (LLDS), alternate Mediterranean Diet Score (aMED) and Dutch Dietary Guidelines score (DDG), with higher scores reflecting healthier dietary habits. PA was measured by the Short Questionnaire to Assess Health-enhancing PA score. Logistic regression analyses were performed between dietary/PA scores, and the prevalence/development and severity of HS.

Results: Compared to controls, HS patients scored lower on the LLDS [OR = 0.98; 95% CI 0.96–0.99], aMED [0.93; 0.89–0.97] and DDG [0.93; 0.88–0.97] with multivariable regression analysis. Overall, this indicates less adherence to dietary recommendations and consumption of a low-quality diet in the HS population. Lower adherence to the LLDS and DDG was also significantly associated with a higher likelihood to HS development in univariable regression analysis [0.96; 0.94–0.99 and 0.91; 0.84–0.99, respectively], and a trend of decreased adherence to the aMED [0.93; 0.85–1.02] was noted. Besides, PA levels were found significantly lower in HS patients ($p \leq 0.001$).

Conclusions and Relevance: Poor diet quality and lower quantities of PA were associated with HS in the general population. Identifying dietary and PA habits of HS patients can contribute to the development of prevention strategies for HS specifically, and for IMIDs in general.

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INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic skin disease of the terminal hair follicle and is considered an immune-mediated inflammatory disease (IMID).[1] Environmental factors are implicated to be involved in both the development and progression of the disease.[2] HS is associated with diet-related comorbidities like (central) obesity (with a 5.88-fold increased odds), metabolic syndrome and type 2 diabetes (odds ratios of 4.46 and 1.69, respectively).[3,4] As the prevalence of HS is higher in the Western world, where typically a Western diet is consumed, it is conceivable that an unhealthy diet increases the risk of HS.[5]

In other IMIDs, such as inflammatory bowel diseases (IBD), the Western diet is already recognized as an important risk factor for the development of disease.[5] However, the effect of diet on the risk of developing HS remains inconclusive. Contrarily, the effect of diet on HS severity is better characterized, with two cross-sectional studies concluding that a higher consumption of the Mediterranean diet (MED) in HS patients might contribute to a decrease in HS severity.[6,7]

Another indication of a potential connection between diet and HS could be the pro-inflammatory effects of obesity, where an excess of visceral fat can initiate and sustain an inflammatory state.[8] Additionally, dietary components from, for example the MED contain intrinsic anti-inflammatory properties themselves.[9] Moreover, ongoing research into the effectiveness of anti-hyperglycaemic drugs as therapeutical agents for HS further underscore the association between diet-related comorbidities and HS.[10] In this context, it can be hypothesized that incorporating a healthy diet along with sufficient levels of physical activity (PA), as main components of a healthy lifestyle, may reduce the likelihood of developing and/or worsening HS.[9,11,12] By the present population-based nested case–control study, using the Lifelines Cohort Study,[13] the association between both diet and PA, and the prevalence, development and severity of HS was investigated.

METHODS

Design, study population and characteristics

A population-based nested case–control study was conducted within the framework of the Lifelines Cohort Study.[13] Lifelines is a multidisciplinary prospective population-based cohort study examining in a unique three-generation design 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 which contribute to the health and disease of the general population, with a special focus on multi-morbidity and complex genetics, and is contributing to health and disease of the general population. All participants provided written informed consent, and the Lifelines Cohort Study was approved by the Medical Ethics Committee of the University Medical Center Groningen, The Netherlands.

Between February and May 2020, we conducted an add-on study on Lifelines study participants that identified 1156 non-familial adult patients with HS.[14] From the pool of non-HS participants of Lifelines, 5000 randomly selected age-group matched adults were included as control group (case–control ratio 1:5). Participants who had a unplausible estimated energy intake of less than 500 kcal per day for females and 800 kcal per day for males were excluded, leaving an analysis set of 1004 HS patients and 4436 controls (see flow diagram Figure 1). Of the Lifelines participants with HS, 233 patients developed the disease during the follow-up period between 2007 and 2020 (hereon called 'HS developers'), whereas the total group of HS patients including patients with HS at time of inclusion in the Lifelines study, will be referred to as the 'HS patients' group. Disease characteristics were extracted from the add-on study in 2020: disease severity was assessed using the Hurley stage scoring system, and disease duration was measured in years.[14]

From the Lifelines baseline assessment (from 2007 to 2013), the following information was extracted: sex, age, height, weight, waist circumference, body mass index (BMI), smoking status and socioeconomic status (SES). SES was calculated by the Statistics Netherlands, where lower scores of SES represent a lower SES (minimum of −8, and maximum of +3).

Dietary intake assessment

Dietary data were collected from the Lifelines baseline assessment via a validated self-administered semi-quantitative Food Frequency Questionnaire (FFQ), that quantifies individual dietary intake over the previous month as proxy for habitual intake.[15] Food items were divided into 23 food groups (Table S1). For the calculation of the individual mean intake of food items in g/day and the macronutrient content of the diet, the Dutch food composition table (NEVO table) was used. Dietary supplement intake was not used due to missing data.

Dietary quality scores

Three dietary scores were used to quantify dietary quality per individual: the Dutch Dietary Guidelines (DDG) Index, the Lifelines Diet Score (LLDS) and alternate Mediterranean diet (aMED) score.[16–18] First, the DDG is based on the impact of different food groups and dietary habits in the development of 10 diet-related chronic diseases in The Netherlands, such as type 2 diabetes and depression.[18] Secondly, the LLDS is a score that can be used to assess relative diet quality, where a higher score represents

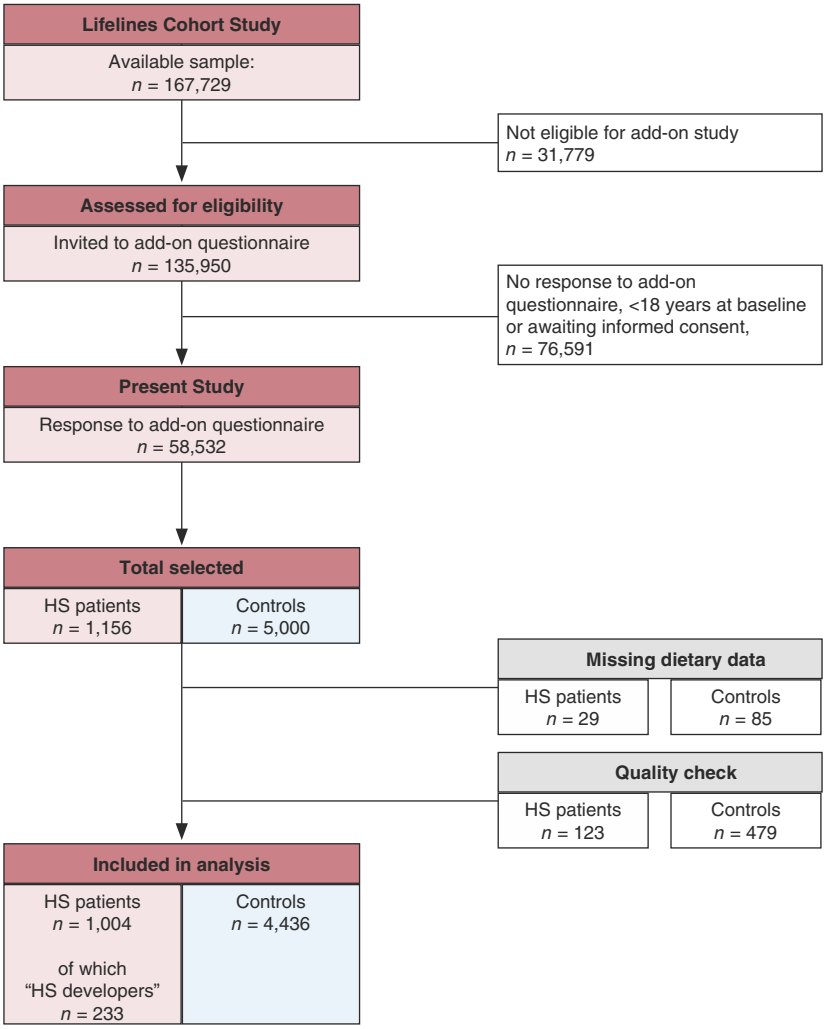

FIGURE 1 Flowchart of inclusion study population.

a diet to be expected to be most beneficial in light of the prevention of nutrition-related chronic diseases.[17] Lastly, the aMED is based on the original Mediterranean diet score, but the scoring was partly altered to better account for the association of diet with several chronic diseases.[16] Dietary scores were selected based on if the content of the scores fitted the available data. Calculations were performed as explained elsewhere.[16–18] By the three scoring systems, higher scores represent higher diet quality and all three scores provide a ranking of how well individuals adhere to the recommendations given by the specific dietary score, see Tables S1–S4.

Physical activity scores

Physical activity was measured at baseline through the Short questionnaire to Assess Health-enhancing physical activity (SQUASH) score, and scored habitual PA levels based on an average week in the last months, with higher scores standing for higher levels of PA.[19] Scores were divided in three categories: light intensity PA, moderate PA and vigorous intensity PA in minutes/week (for details, see Appendix S1). For the analysis, we included only moderate and vigorous intensity PA scores, as light intensity PA scores entail an elevated risk of imprecise estimates of total minutes of PA. Subsequently, moderate to vigorous PA measured in minutes/week was combined into one variable, as it is considered the best variable to rank individuals by level of PA.[20]

Data analysis

Characteristics of participants were presented as number (percentage, %) for categorical variables and as mean ± standard deviation (SD) or median [interquartile range, IQR] where appropriate for continuous variables. Continuous data between the distinctive groups were analysed using the ANOVA test for normally distributed data,

and using the Mann–Whitney U test for non-normally distributed data. For categorical data, the chi-square test was used.

Logistic regression analysis

To evaluate the association of the dietary scores with HS, HS patients were compared to the control group using univariable and multivariable regression analyses, while adjusting for the main confounders (sex and age) and using odds ratios (OR), 95% confidence intervals (CI) and backward selection procedure ($p < 0.2$ and $p > 0.05$). To determine whether diet is associated with increased likelihood of the development of HS during the follow-up period, the 'HS developers' were compared to controls. Similar analyses were performed for the different Hurley stages. All statistical tests were two-sided while a p-value of ≤0.05 was considered as statistically significant. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 23 (IBM Corp., Armonk, NY, USA).

RESULTS

Participants characteristics

Of the 1004 included HS patients, the mean age was 55.2 ± 12.3 years compared to 55.9 ± 12.2 years in the control group ($n = 4436$; $p < 0.001$; Table 1). HS patients had a significantly ($p < 0.001$) higher median BMI of 26.1 [IQR 23.6–29.8] kg/m^2 compared to 25.3 [23.1–28.1] kg/m^2; and a higher median waist circumference of 90.5 [82.0–100.0] cm compared to 89.0 [81.0–97.0] cm in controls.

TABLE 1 Demographical and clinical characteristics of study population.

	Total sample $n = 5440$	HS patients $n = 1004$	Control group $n = 4436$	p-value[a]	HS developers $n = 233$	p-value[b]
Sex				**<0.001**		0.092
Female, *n* (%)	3415 (62.8)	748 (74.5)	2667 (60.1)		153 (65.7)	
Male, *n* (%)	2025 (37.2)	256 (25.5)	1769 (39.9)		80 (34.3)	
Age (years), mean (SD)	55.2 (12.3)	51.9 (11.9)	55.9 (12.2)	**<0.001**	52.7 (13.5)	**<0.001**
Height (cm), median [IQR]	173.5 [167.5–181.0]	172.5 [167.0–178.5]	174.0 [168.0–181.0]	**<0.001**	173.0 [168.0–186.3]	0.454
Missing, *n*	0	0	0		0	
Weight (kg), median [IQR]	78.0 [69.0–89.0]	79.0 [69.0–91.0]	78.0 [68.5–88.5]	**0.003**	77.0 [69.5–99.8]	0.503
Missing, *n*	0	0	0		0	
Waist circumference (cm), median [IQR]	89.3 [81.5–98.0]	90.5 [82.0–100.0]	89.0 [81.0–97.0]	**<0.001**	90.0 [82.0–98.0]	0.333
Missing, *n*	0	0	0		0	
BMI (kg/m^2), median [IQR]	25.5 [23.2–28.4]	26.1 [23.6–29.8]	25.3 [23.1–28.1]	**<0.001**	25.5 [23.5–28.7]	0.206
Missing, *n*	0	0	0		0	
Smoking status[c]				**<0.001**		**<0.001**
Active smoker, *n* (%)	738 (13.6)	230 (22.9)	508 (11.5)		49 (21.0)	
Former smoker, *n* (%)	1491 (34.2)	258 (36.6)	1233 (34.3)		56 (24.0)	
Non-smoker, *n* (%)	2137 (48.9)	287 (40.7)	1850 (51.5)		81 (34.8)	
Missing, *n*	1074	229	845		47	
Socioeconomic status, median [IQR]	−0.58 [−1.23 to +0.12]	−0.64 [−1.34 to +0.07]	−0.58 [−1.22 to +0.13]	**0.032**	−0.57 [−1.27 to +0.14]	0.675
Missing, *n*	569	86	483		25	
Hurley stage[c]				N/A		
I, *n* (%)	N/A	717 (71.4)	N/A		170 (73.0)	
II, *n* (%)		212 (21.1)			40 (17.2)	
III, *n* (%)		60 (6.0)			10 (4.3)	
Missing, *n*		15			13	

Note: Bold values indicate significant p-values.

Abbreviations: BMI, body mass index; HS, hidradenitis suppurativa; IQR, interquartile range; SD, standard deviation.

[a]Comparisons between total group of HS patients and controls. For continuous variables, the one-way ANOVA test was used if the data were normally distributed. If not, the Mann–Whitney U test was used. For categorical variables, the chi-squared test was used.

[b]Comparisons between HS developers and controls.

[c]First variable was used as reference for analysis.

Demographical and clinical characteristics of the 'HS developers' ($n = 233$) were comparable to those of the control group (Table 1).

Macronutrient intake

Hidradenitis suppurativa patients had a significantly lower median kilocalorie intake (1896.5; 1555.9–2302.2 kcal) compared to the control group (1965.2; 1633.7–2360.0 kcal) ($p < 0.001$), see Table 2. Also, they had a significantly lower total protein intake (70.9; 59.1–84.2 vs. 73.2; 61.8–85.9 g/day), lower plant protein intake (28.1; 22.9–35.1 vs. 30.0; 24.6–36.8 g/day) and lower carbohydrate intake (209.3; 167.7–256.2 vs. 219.5; 179.7–266.8 g/day) compared to controls.

'Hidradenitis suppurativa-developers' showed no significant differences in macronutrient intake compared to controls (Table 2).

No significant differences between macronutrient intake of the total group of HS patients and mild compared to severe, and mild compared to moderate disease were found (data not shown).

Food group intake

Hidradenitis suppurativa patients consumed significantly less natural unprocessed products such as butter and hard margarines (17.9; 7.2–33.3 vs. 19.7; 8.9–36.6 g/day), fish (10.6; 4.4–16.9 vs. 11.1; 4.8–17.1 g/day), fruit (84.6; 42.3–220.2 vs. 110.1; 42.3–220.2 g/day), legumes and nuts (15.3; 6.9–28.8 vs. 17.0; 8.0–30.3 g/day), unsweetened dairy (137.5; 45.3–251.6 vs. 152.7; 60.8–278.7 g/day) and whole grain products (94.2; 62.8–125.6 vs. 125.6; 62.8–157.0 g/day) compared to the control group. Also, they consumed significantly lower sugary products (65.7; 39.2–98.6 vs. 70.2; 44.9–104.0 g/day), sweetened dairy (80.0; 32.8–137.2 vs. 92.1; 43.8–142.7 g/day) and alcohol (37.3; 7.2–128.6 vs. 53.5; 9.0–128.6 g/day). On the other hand, HS patients had a higher intake of some processed products such as artificially sweetened products (28.7; 0.0–129.1 vs. 17.8; 0.0–96.4 g/day) and savoury products (88.1; 55.2–125.3 vs. 80.3; 48.1–118.9 g/day). Moreover, they consumed higher quantities of white unprocessed meat (10.7; 6.7–15.1 vs. 9.6; 5.6–13.9 g/day) compared to controls (Table 2).

Similar, 'HS developers' had a significantly lower intake of natural unprocessed products such as fruit (84.6; 42.3–220.2 vs. 110.1; 42.3–220.2 g/day) and unsweetened diary (126.2; 42.7–278.1 vs. 152.7; 60.8–278.7 g/day) in comparison with controls. Furthermore, they had a higher intake of savoury products as well (91.3; 55.0–131.1 vs. 80.3; 48.1–118.9 g/day) (Table 2).

No significant differences for macronutrient intake between mild and severe, and mild and moderate disease in the complete group of HS patients was found (data not shown).

Dietary scores

Significantly lower scores of the LLDS with multivariable regression analyses were found in HS patients (23.8 ± 6.0) compared to controls (24.8 ± 5.9), yielding a small but significant increased risk of 1.02 (1.01–1.04) per one standard unit increase in LLDS (Table 3). HS patients, compared to controls, had a lower adherence to the aMED and DDG leading to an 1.07 [1.12–1.03] and 1.07 [1.11–1.03] increased risk per one standard unit increase in both the aMED and DDG, respectively.

'Hidradenitis suppurativa developers' (compared to the controls) scored slightly less (23.6 ± 6.1 vs. 24.8 ± 5.9) on the LLDS yielding a 1.03 [1.05–1.01] fold significantly increased risk for the development of HS during the follow-up period as demonstrated by multivariable analyses. Likewise, 'HS developers' showed a trend of lower scores on the DDG and aMED, leading to respectively 1.04 [1.12–0.95] and 1.06 [1.13–0.98] fold increased risk of the onset of HS per one standard unit increases of aMED and DDG (Table 3).

No significant differences in dietary scores between patients with mild compared to severe, and mild compared to moderate for the whole group of HS patients were found (data not shown).

Physical activity scores

Hidradenitis suppurativa patients (compared to controls) had a significantly ($p < 0.001$) lower moderate PA score (60.0; 0.0–480.0 vs. 120.0; 0.0–600.0), moderate to vigorous PA score (300.0; 91.3–750.0 vs. 360.0; 150.0–946.3) and vigorous PA score (120.0; 10.0–270.0 vs. 150.0; 60.0–310.0; Table 4).

Likewise, 'HS developers' had a significantly lower vigorous PA score (105.0; 0.0–272.5 vs. 150.0; 60.0–310.0; $p = 0.001$), compared to controls.

No significant differences in PA between mild and severe, and mild and moderate HS were found within the total group of HS patients (data not shown).

DISCUSSION

For the first time, the effect of dietary intake on the risk of HS in a large population-based study was investigated. Significant differences in (macro)nutrient intake in HS patients compared to controls were reported. Lower dietary scores, reflecting lower diet quality, were associated with a higher likelihood (on the development) of HS, and HS patients were less physically active.

Similar to the findings of earlier literature, HS patients (= total group of assessed HS patients) had a higher BMI and waist circumference, but consumed less kilocalories and carbohydrates than the control group.[21] It is previously described that losing weight is more complex than solely lowering kilocalorie intake, which might contribute to the difference in the HS patients' low kilocalorie intake and inversely high BMI.[22,23] Other explanations for the

TABLE 2 Habitual dietary intake.

	Total sample $n = 5440$	HS patients $n = 1004$	Control group $n = 4436$	p-value[a]	HS developers $n = 233$	p-value[b]
Macronutrient intake						
BMR%[c]	127.7 [105.3–151.0]	122.8 [100.7–148.1]	128.3 [106.7–151.7]	**<0.001**	125.7 [106.1–151.0]	0.729
Total protein (g/day)	72.7 [61.3–85.6]	70.9 [59.1–84.2]	73.2 [61.8–85.9]	**0.001**	74.6 [60.2–85.1]	0.750
g/kg	0.93 [0.8–1.1]	0.9 [0.7–1.1]	0.9 [0.8–1.1]	**<0.001**	0.9 [0.8–1.1]	0.626
Plant protein (g/day)	29.7 [24.3–36.5]	28.1 [22.9–35.1]	30.0 [24.6–36.8]	**<0.001**	29.8 [24.0–36.0]	0.451
g/kg	0.4 (0.3–0.5)	0.3 [0.2–0.4]	0.4 [0.3–0.5]	**<0.001**	0.4 [0.3–0.5]	0.216
Animal protein (g/day)	42.2 [34.8–51.3]	41.8 [34.2–51.4]	42.6 [34.9–51.3]	0.275	43.4 [34.5–52.0]	0.478
g/kg	0.5 [0.4–0.7]	0.5 [0.4–0.7]	0.5 [0.4–0.7]	**0.004**	0.5 [0.4–0.7]	0.981
Total fat (g/day)	76.4 [61.3–95.5]	75.8 [58.8–94.8]	76.5 [61.8–95.7]	0.077	79.0 [63.1–97.9]	0.349
En%[d]	35.4 [32.2–38.6]	35.8 [32.5–39.1]	35.4 [32.1–38.4]	**0.018**	35.9 [32.2–39.0]	0.286
Carbohydrates (g/day)	217.6 [177.7–264.7]	209.3 [167.7–256.2]	219.5 [179.7–266.8]	**<0.001**	221.4 [179.6–262.8]	0.862
En%[d]	44.7 [41.2–48.2]	44.6 [40.6–48.0]	44.8 [41.4–48.3]	**0.034**	44.5 [40.9–48.2]	0.497
Alcohol (g/day)	3.9 [0.9–10.2]	3.3 [0.8–10.5]	4.3 [0.9–10.2]	0.124	3.2 [1.1–11.2]	0.685
En%[d]	1.5 [0.4–3.6]	1.4 [0.3–3.7]	1.5 [0.4–3.6]	0.393	1.4 [0.4–3.5]	0.735
Food group intake (g/day)						
Alcoholic beverages	50.9 [8.9–128.6]	37.3 [7.2–128.6]	53.5 [9.0–128.6]	**0.024**	36.1 [13.4–128.4]	0.473
Artificially sweetened products	21.2 [0.0–103.6]	28.7 [0.0–129.1]	17.8 [0.0–96.4]	**<0.001**	18.5 [0.0–99.3]	0.384
Butter and hard margarines	19.3 [8.9–35.9]	17.9 [7.2–33.3]	19.7 [8.9–36.6]	**0.016**	18.8 [7.2–34.4]	0.426
Cheese	24.2 [13.5–41.1]	22.4 [13.0–41.0]	24.6 [13.5–41.1]	0.331	21.7 [11.5–43.1]	0.614
Coffee	464.5 [232.3–580.6]	464.5 [232.25–696.8]	464.5 [232.3–580.6]	0.939	464.5 [160.8–580.6]	0.315
Eggs	8.9 [7.2–17.9]	8.9 [4.5–17.9]	8.9 [7.2–17.9]	**0.027**	8.9 [5.4–17.9]	0.359
Fish	11.0 [4.8–17.0]	10.6 [4.4–16.9]	11.1 [4.8–17.1]	**0.025**	10.5 [4.4–16.8]	0.202
Fruit	110.1 [42.3–220.2]	84.6 [42.3–220.2]	110.1 [42.3–220.2]	**<0.001**	84.6 [42.3–220.2]	**0.003**
Legumes and nuts	16.5 [7.9–30.1]	15.3 [6.9–28.8]	17.0 [8.0–30.3]	**0.007**	16.0 [8.3–31.4]	0.990
Oils and soft margarines	13.8 [3.8–27.7]	12.9 [4.1–26.2]	14.1 [3.7–28.1]	0.359	14.0 [4.3–28.8]	0.500
Potatoes	49.8 [29.9–89.7]	49.8 [24.9–89.7]	49.8 [29.9–89.7]	**<0.001**	49.8 [22.4–89.7]	**0.017**
Red and processed meat	64.6 [45.0–84.5]	64.8 [45.2–85.5]	64.5 [44.9–84.3]	0.589	66.6 [45.0–86.7]	0.391
Refined grain products	65.6 [43.2–98.8]	64.1 [42.5–95.0]	65.9 [43.4–99.2]	0.192	67.6 [44.0–101.6]	0.546
Savoury and ready products	81.3 [49.3–120.3]	88.1 [55.2–125.3]	80.3 [48.1–118.9]	**<0.001**	91.3 [55.0–131.1]	**0.004**
Soups	35.7 [22.3–71.5]	35.8 [22.3–71.5]	35.8 [22.3–71.5]	**0.039**	35.8 [18.0–71.5]	0.139
Sugary products	69.6 [43.8–103.0]	65.7 [39.2–98.6]	70.2 [44.9–104.0]	**0.002**	68.8 [33.5–141.4]	0.488
Sugar-sweetened beverages	83.3 [21.5–185.8]	96.4 [20.8–202.1]	79.1 [21.5–181.1]	0.053	96.5 [26.7–209.2]	0.098
Sweetened dairy	89.9 [41.8–141.1]	80.0 [32.8–137.2]	92.1 [43.8–142.7]	**<0.001**	86.8 [33.5.2–141.4]	0.352
Tea	232.3 [44.6–348.4]	232.3 [35.8–348.4]	232.3 [58.1–348.4]	**0.029**	160.8 [35.8–348.4]	0.140
Unsweetened dairy	146.1 [56.8–278.7]	137.5 [45.3–251.6]	152.7 [60.8–278.7]	**<0.001**	126.2 [42.7–278.1]	**0.012**
Vegetables	108.3 [73.7–149.1]	108.3 [63.5–149.9]	108.3 [73.7–149.1]	0.744	108.3 [63.2–149.2]	0.513
White unprocessed meat	9.6 [6.0–13.9]	10.7 [6.7–15.1]	9.6 [5.6–13.9]	**0.004**	10.8 [6.7–15.0]	0.055
Whole grain products	108.7 [62.8–130.4]	94.2 [62.8–125.6]	125.6 [62.8–157.0]	**<0.001**	94.2 [62.8–125.6]	0.066

Note: Values are reported as median [interquartile range, IQR], as all values were not normally distributed. Analyses were performed using the Mann–Whitney U test.
Bold values indicate significant p-values.

Abbreviation: HS, hidradenitis suppurativa.

[a]Comparisons between total group of HS patients and controls.

[b]Comparisons between HS developers and controls.

[c]BMR% = total kilocalorie intake as percentage of Basal Metabolic Rate (Calculated with Harris benedict Equation: Women: BMR = 655.0955 + (9.5634 × weight) + (1.8496 × Length) − (4.6756 × Age); Men: BMR = 66.4730 + (13.7516 × Weight) + (5.0033 × Length) − (6.7550 × Age)).

[d]En% = macronutrient as percentage of total energy intake (calculated as macronutrient/kilocalories × 100).

TABLE 3 Associations of dietary scores with (the development of) HS.

	Dietary scores		
	LLDS	**aMED**	**DDG**
Total sample $n = 5440$	24.6 (5.9)	4.0 (1.5)	4.6 (1.7)
Missing, *n*	41	0	0
HS patients $n = 1004$	23.8 (6.0)	3.8 (1.4)	4.4 (1.7)
Missing, *n*	11	0	0
Control group $n = 4436$	24.8 (5.9)	4.1 (1.5)	4.7 (1.7)
Missing, *n*	30	0	0
Univariable analysis			
p-value[a]	**<0.001**	**<0.001**	**<0.001**
OR [95% CI]	0.97 [0.96–0.98]	0.89 [0.85–0.93]	0.90 [0.87–0.94]
Multivariable analysis[b]			
p-value[a]	**<0.001**	**0.001**	**<0.001**
OR [95% CI]	0.98 [0.96–0.99]	0.93 [0.88–0.97]	0.93 [0.89–0.97]
HS developers $n = 233$	23.6 (6.1)	3.9 (1.4)	4.4 (1.7)
Missing, *n*	1	0	0
Control group $n = 4436$	24.8 (5.9)	4.1 (1.5)	4.7 (1.7)
Missing, *n*	30	0	0
Univariable analysis			
p-value[c]	**<0.001**	0.127	**0.022**
OR [95% CI]	0.96 [0.94–0.99]	0.93 [0.85–1.02]	0.91 [0.84–0.99]
Multivariable analysis[b]			
p-value[c]	**0.011**	0.378	0.114
OR [95% CI]	0.97 [0.95–0.99]	0.96 [0.88–1.05]	0.94 [0.87–1.02]

Note: Values are reported as mean (SD), as all values were normally distributed.

Bold values indicate significant *p*-values.

Abbreviations: aMED, alternate Mediterranean diet score; CI, confidence interval; DDG, Dutch Dietary Guidelines Index (see Appendix S1); HS, hidradenitis suppurativa; LLDS, Lifelines Diet Score; OR, odds ratio; SD, standard deviation.

[a]Associations with HS status, adjusted for age and sex.

[b]Adjusted for age and sex.

[c]Associations with HS development, adjusted for age and sex.

TABLE 4 Physical activity scores.

	Total sample $n = 5106$	**HS patients $n = 940$**	**Control group $n = 4166$**	***p*-value[a]**	**HS developers $n = 217$**	***p*-value[b]**
Physical activity score						
Moderate	90.0 [0.0–585.0]	60.0 [0.0–480.0]	120.0 [0.0–600.0]	**0.001**	60.0 [0.0–820.0]	0.492
Vigorous	150.0 [45.0–300.0]	120.0 [10.0–270.0]	150.0 [60.0–310.0]	**<0.001**	105.0 [0.0–272.5]	**0.001**
Moderate to vigorous	360.0 [130.0–900.0]	300.0 [91.3–750.0]	360 [150.0–946.3]	**<0.001**	320.0 [119.5–1057.5]	0.145
Missing, *n*	334	64	270		16	

Note: Values are reported as median [interquartile range, IQR], as all variables were not normally distributed. Analyses were performed using the Mann–Whitney U test.

Bold values indicate significant *p*-values.

Abbreviations: HS, hidradenitis suppurativa; IQR, interquartile range.

[a]Comparisons between total group of HS patients and controls.

[b]Comparisons between HS developers and controls.

high BMI and lower than expected kilocalorie intake of HS patients could be their higher consumption of artificially sweetened products (that can lead to the development of glucose intolerance),[24] lower levels of PA and possible self-(under)reporting of food intake. In addition, HS patients reported a lower (plant)protein intake in comparison to controls, while a higher protein intake, derived predominantly from plant sources, has been associated with beneficial effects on health outcomes.[25] Collectively, this picture is not uncommon and matches with unhealthier

lifestyles that have been associated with other inflammatory disorders.[26]

Hidradenitis suppurativa patients had a comparably high intake of red processed meat versus controls; however, their intake of fibre-rich food such as whole grains and fruit was significantly lower. Earlier studies of other IMIDs such as Crohn's disease have illustrated a link between a diet high in meat and low in fibre with disease susceptibility.[26] Also, these dietary habits were shown to have a muted effect on tumour necrosis factor (TNF) inhibiting drugs, which are widely used in therapy for HS.[26–28] Other studies have previously shown that processed meat has been associated with increased risk of IBD, whereas a whole food diet has been proven to be connected to healthy weight management and less inflammation.[29,30]

Additional to the known association of Crohn's disease and HS, the auto-inflammatory nature of HS and the anti-inflammatory effects of specific healthy diets, the food group intake of HS patients could influence disease severity, and response to therapy.[14] However, in our study no significant associations between disease severity and diet were identified. An explanation could be that the original Hurley staging system as used in our study can be considered to be less suited to determine disease severity since it does not take inflammation and the extent of disease into account.[31] In line with this, Velluzzi et al. found no correlation of severity of HS and Mediterranean diet adherence, also using the original Hurley stage system.[21] More research is needed to better understand the complex relationship between diet and (the development of) HS, while also focusing on the possible link of diet and disease severity.

Next to investigating differences in food group intake, the association of knowledge based dietary scores built upon these food group intake with HS was assessed. Significantly less adherence to the LLDS, DDG and aMED in HS patients compared to age-matched controls was found in both the univariable and multivariable regression analyses. Moreover, patients who developed HS during the follow-up period, categorized as 'HS developers', demonstrated significantly lower adherence to the LLDS (indicating consumption of more unfavourable foods) at the baseline prior to the development of HS, and also exhibited a reduction in adherence to the aMED and DDG, albeit not significantly. Differences in the strength and significance of associations between high diet quality quantified by the LLDS, DDG and aMED with the risk on (the development of) HS might arise from using different scoring systems for adherence to recommendations. For example, while the LLDS expresses relative diet quality according to the Dutch dietary guidelines, and is comparable to the DDG score, the aMED has been linked to inflammation.[16–18]

Besides diet, the association of PA with the risk of HS was evaluated. HS patients were found to be less physically active than controls. Congruently, one cross-sectional study demonstrated impairment in daily activities in HS patients; however, another cross-sectional study found similar moderate PA levels HS patients compared to controls.[21,32] Despite our findings of a possible beneficial effect of PA in reducing the likelihood of HS, management of PA in HS patients should be well-supervised, especially as the friction of the skin that might occur as a result of exercising, could contribute to the occurrence of new boils or increase pain and thus can lead to HS patients avoiding further exercise. Consequently, the engagement of a specialized physiotherapist in HS treatment or prevention is highly recommended.

Even though our study was the first large population-based nested case–control in HS and used a validated and structured FFQ, it bears also several limitations such as the accuracy of patients self-reporting nutritional intake, possible recall bias in the prevalent patients with HS at the time of filling in the FFQ, and possible selection bias by including healthier subjects in our cohort study, than real-world.[33,34] Furthermore, the macronutrient data challenges the food intake data. For this observation, we do not have a biological explanation, but perhaps it is more a random observation than a scientific meaningful finding. In addition, our study utilized health-related data in the timeframe 2007 to 2013, but these measurements may not accurately reflect the state of patients who developed HS later on, possible introducing a bias. Lastly, most of our found associations between diet and HS are quite modest in strength. However, as diet represents only a small friction in the greater totality of the lifestyle domain, it can be speculated that its attribution in a complex, multifactorial disease as HS is relatively minor.

CONCLUSION

Poor diet quality and lower levels of PA are associated with a higher likelihood of HS in the general population. Our findings suggest modifications of lifestyle factors like diet might reduce the risk of HS in specific, and the risk for IMIDs in general. Future interventional research is firmly needed to elucidate the association of lifestyle and the development and course of HS further.

ACKNOWLEDGEMENTS

None.

FUNDING INFORMATION

(1) Novartis Pharma B.V. Project code: CAIN457ANL01T. (2) The Lifelines Biobank initiative has been made possible by subsidy from the Dutch Ministry of Health, Welfare and Sport, the Dutch Ministry of Economic Affairs, the University Medical Center Groningen (UMCG the Netherlands), University Groningen and the Northern Provinces of the Netherlands.

CONFLICT OF INTEREST STATEMENT

K. Bouwman reports no conflicts of interest. S. Moazzen reports no conflicts of interest regarding this study. M. Kroah-Hartman reports no conflicts of interest. G. Dijkstra reports

no conflicts of interest regarding this study. B. Horváth reports fees from Janssen-Cilag (Advisory Boards, Educational grants, Consultations, Investigator Initiative Studies), AbbVie (Advisory Boards, Educational grants, Consultations, Investigator Initiative Studies), Novartis Pharma (Advisory Boards, Consultations, Investigator Initiative Studies), UCB Pharma (Advisory Boards, Consultations), Leo Pharma (Consultations), Solenne B.V. (Investigator Initiative Studies), Celgene (Consultations, Investigator Initiative Studies), Akari therapeutics (Consultations, Investigator Initiative Studies), Philips (Consultation), Roche (Consultation), Regeneron (Consultation) and Sanofi (Consultation), which fees were payed to the institution. B.Z. Alizadeh reports no conflicts of interest regarding this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Lifelines. Restrictions apply to the availability of these data, which were used under licence for this study. Data are available from the authors with the permission of Lifelines.

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How to cite this article: Bouwman K, Moazzen S, Kroah-Hartman M, Dijkstra G, Horváth B, Alizadeh BZ. Diet and physical activity as risk-reducing factors for hidradenitis suppurativa. J Eur Acad Dermatol Venereol. 2024;38:910–919. https://doi.org/10.1111/jdv.19726