



GHISA

Global Hidradenitis Suppurativa Atlas

Global Report on

Hidradenitis Suppurativa

2023

The bottom of the page features large, abstract, overlapping shapes in various shades of blue and teal, creating a dynamic, organic feel.



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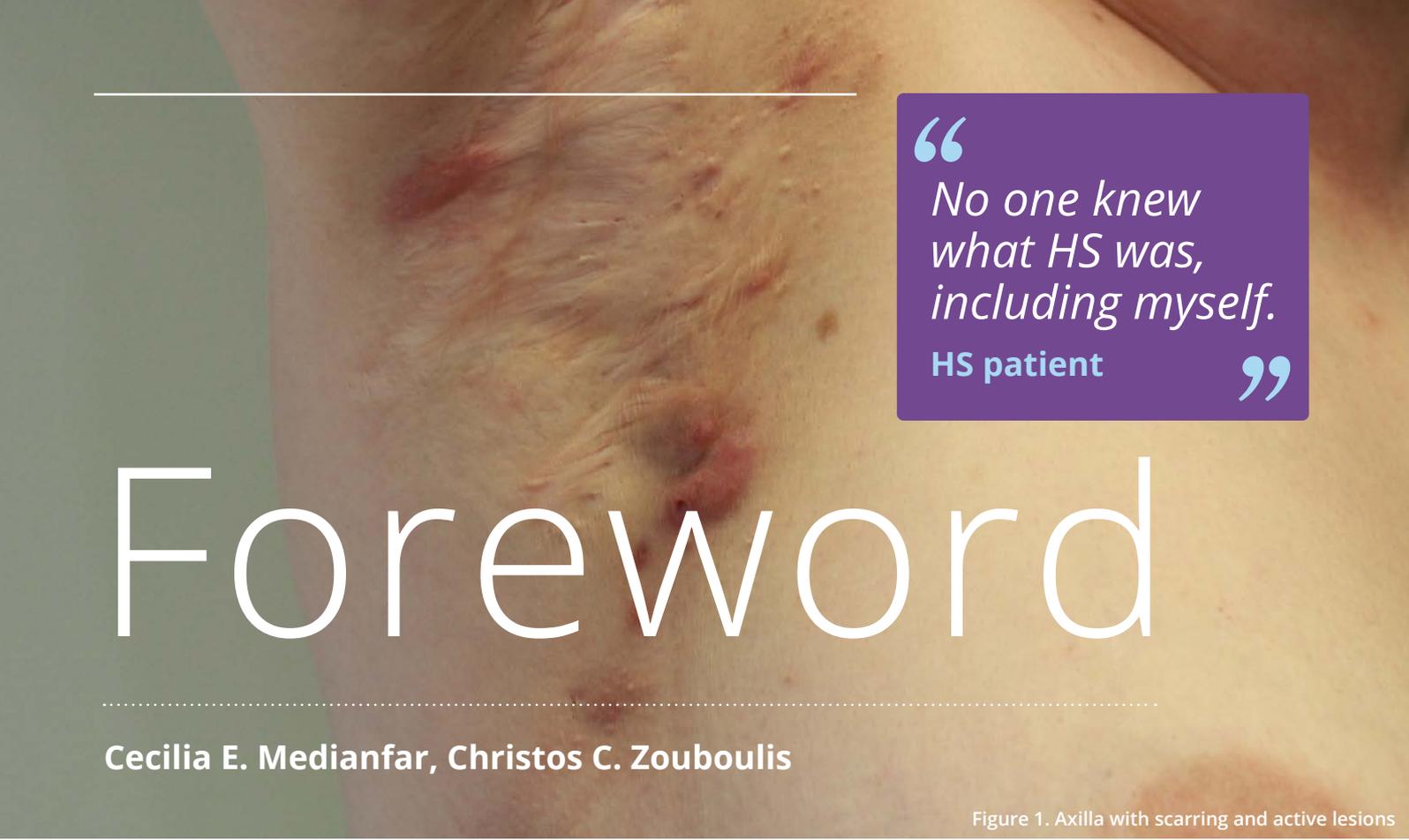
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“
No one knew
what HS was,
including myself.
HS patient”

Foreword

Cecilia E. Medianfar, Christos C. Zouboulis

Figure 1. Axilla with scarring and active lesions

Hidradenitis suppurativa (HS) is an inflammatory skin disease characterized by the formation of painful skin nodules and abscesses in intertriginous areas.

The further development of draining tunnels and the subsequent scarring can be profoundly debilitating, leading to a significant reduction in the patient's quality of life. The patients endure a prolonged delay from disease onset to diagnosis, poor response to treatment, and severe comorbidity load. Unfortunately, neither a clear cause or cure is readily available.

Despite its grave impact on the patients, HS has notoriously been misdiagnosed and overlooked. However, awareness is on the rise, highlighting the critical need

for global recognition and shared knowledge among experts. While it is estimated that 0.40% of the global population suffer, this figure might be inaccurate due to a presumed considerable number of undiagnosed patients silently living with the condition and to missing data from large parts of the world.

This Global Report has been a collaborative effort between the International League of Dermatological Societies (ILDS) and the Global Hidradenitis Suppurativa Atlas (GHISA). GHISA, dedicated to advancing global HS knowledge, awareness, and education about HS, has produced this report to offer a comprehensive overview of HS. It covers extensive aspects on HS, including diagnosis, emerging treatments, and global efforts. By highlighting the severe impact of HS, our aim is to guide policy makers, encouraging resource allocation and health care improvement for the patients.

In the words of HS patients facing barriers in accessing quality care, “No one knew what HS was, including myself”, this Global Report is therefore a pivotal step towards breaking down these barriers and paving the way for a brighter future in HS management.

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GHISA: Connecting Global Networks, Creating Global Impact, Fostering HS Unity Across Continents.

Acronyms and Abbreviations

- **BMI:** Body Mass Index
 - **DALY:** Disability Adjusted Life Years
 - **DLQI:** Dermatology Life Quality Index
 - **EADV:** European Academy of Dermatology and Venereology
 - **EMA:** European Medicines Agency
 - **FDA:** Food and Drug Administration
 - **GBD:** Global Burden of Disease
 - **GHISA:** Global Hidradenitis Suppurativa Atlas
 - **HiSCR:** Hidradenitis Suppurativa Clinical Response
 - **HISTORIC:** Hidradenitis Suppurativa cORe outcomes set International Collaboration
 - **HS:** Hidradenitis Suppurativa
 - **IBD:** Inflammatory Bowel Disease
 - **IHS:** International Hidradenitis Suppurativa Severity Score System
 - **IL:** Interleukin
 - **NIH:** National Institutes of Health
 - **PAPASH:** Pyogenic Arthritis, Pyoderma gangrenosum, Acne, and Suppurative Hidradenitis
 - **PASH:** Pyoderma gangrenosum, Acne and Suppurative Hidradenitis
 - **QoL:** Quality of Life
 - **RCT:** Randomized Control Trial
 - **SAPHO:** Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis
 - **SES:** Socioeconomic Status
 - **VOICE:** Global Survey of Impact and Healthcare Needs
 - **WHO:** World Health Organization
-

Chapter 1:

Introduction

Prof. Gregor B. E. Jemec, Dr. Perpetua Ibekwe

What is Hidradenitis Suppurativa?

Hidradenitis suppurativa (HS) is a chronic inflammatory disease characterized by recurrent episodes of painful deep-seated nodules, abscesses, or tunnels. These elements must appear in axilla, under the breasts or in the anogenital region at least twice every six months for the diagnosis to be made. Furthermore, secondary positive diagnostic features are a positive family history of HS, a negative bacterial swab or the presence of normal skin microbiota. The differential diagnoses include: staphylococcal infection, cutaneous Crohn's disease, neoplasms, lymphogranuloma venereum and scrofuloderma.(8)

In contrast to most skin diseases, it causes significant scarring leading to permanent damage of the skin (1-3). It is a disfiguring, noncommunicable disease that is associated with pain, embarrassment, increased suicide risk and significant decrease in quality of life (3,4). HS typically begins at the end of puberty and is rare for those over the age of 60. (5). The previously reported prevalence ranges <0.1% to 4.1% (6,7). HS is also associated with multiple comorbidities. HS is a global disease with severe consequences, and it burdens patients with disability, impairment and handicap. The precise etiology of HS remains unknown; but includes genetic predisposition, immune dysregulation, microbiome imbalance, and possibly mechanical stress.

Figure 2: Distribution of locations commonly affected in HS

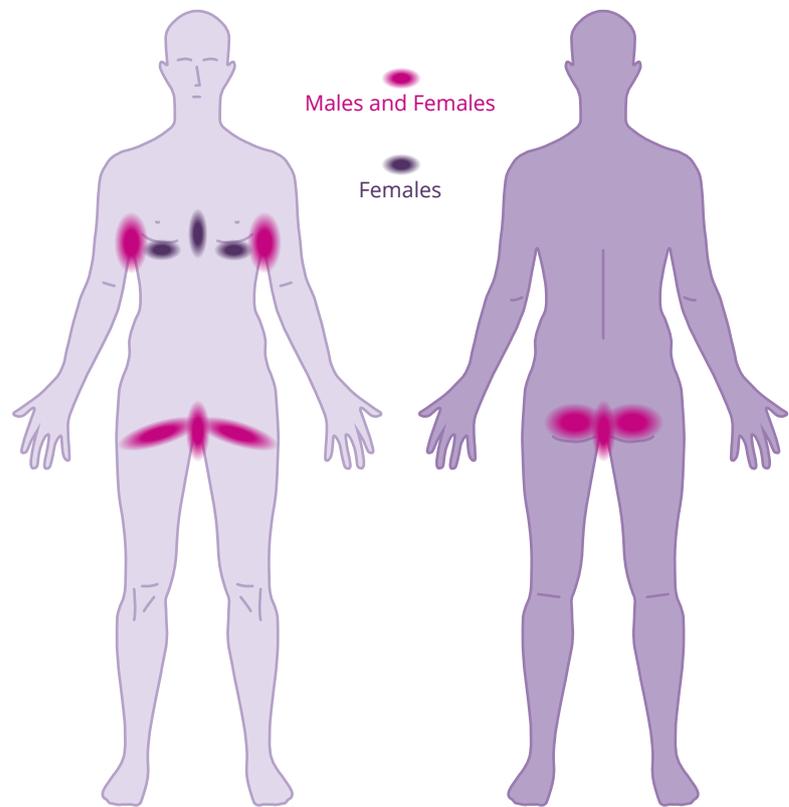


Figure 3. Axillary Lesions



Figure 4. Femoral lesions (Groin)

Treatment of Hidradenitis Suppurativa

Lack of recognition leads to many ineffective treatments, but even when the diagnosis is made, there is a shortage of effective and approved treatment. Generally, it is recommended that patients are seen by dermatologists, and multiple mutually supporting treatments are initiated simultaneously. These include surgery of any fibrotic lesions, medical treatment of inflammation and super-infection, and supportive care.

Treatment is generally unsatisfactory for many patients, and HS specialty clinics there is a real and strong need for the development of safe and effective treatments that can be made available globally. Adding to the unmet need for treatment is the lack of disease recognition in the non-dermatological medical community.

Why a global report on Hidradenitis Suppurativa?

It is a noncommunicable skin disease that is associated with prominent skin symptoms, which lead to significant disability, that results in multifaceted impairments for the patient, and ultimately to lasting handicap unique to skin diseases. This report justifies the immediate necessity for improved global healthcare of HS, offering detailed insights to enhance understanding and effective interventions.



Chapter 2:

The Burden of Hidradenitis Suppurativa

Dr. John R. Ingram, Dr. Redina Bardhi, Dr. Iltefat Hamzavi

The prevalence of Hidradenitis Suppurativa

There is wide variation in incidence and prevalence figures available from HS epidemiology studies performed prior to the Global Hidradenitis Suppurativa Atlas (*GHiSA*) initiative (8), which was one of the drivers for conducting a unified global prevalence study. Prevalence estimates have varied from 0.05% to 4.1% (9,10), representing an 82-fold difference (Table 1). Estimates at the lower end of the range tend to be provided by insurance-based routinely collected data sources. Insurance data from USA provided the prevalence figure of 0.05% in a study from 2007 (9). The figure is likely to underestimate true HS prevalence, due to intrinsic issues with insurance data, including exclusion of uninsured patients. This should be seen in the context that HS tends to have a higher prevalence in people in lower socioeconomic, groups who are less likely to have medical insurance (11).



Figure 5. Typical HS lesion

All routinely collected data sources rely on accurate disease recognition and clinical coding. As a result, undiagnosed cases of HS are missed, and this is very relevant in the context of the 7-10-year average diagnostic delay (12,13). A primary care database study from the UK found a HS prevalence of 0.54% in diagnosed patients, which increased to 0.77% with inclusion of validated undiagnosed cases with a history of multiple attendances for flexural skin boils (14). So, one third of the estimated prevalence was undiagnosed cases. With inclusion of probable cases with a documented history of 1-4 flexural skin boils the UK prevalence was 1.19%(14).

Questionnaire-based studies from mainland Europe tend to produce higher prevalence figures. A cross-sectional study of 10,000 members of the French population, with a 69% response rate, provided a one-year period prevalence of 0.97% based on responses to a survey question

about painful flexural boils (15). A Danish survey of more than 30,000 adults aged 30 years and older in the general population made use of two validated survey questions about skin boils and found a prevalence of 2.1% (16).

The highest prevalence estimates have been obtained from in-person review of predominantly young adults, for example a study of those undergoing screening for sexually transmitted diseases provided a figure of 4.1% (10). While the demographics of the study population may increase the prevalence estimate, in-person examination by a dermatologist is the gold standard method for HS diagnosis in the context that it remains a clinical diagnosis.

While much of the difference in prevalence figures may reflect the differing methodologies employed, it remains uncertain to what extent are they underpinned by the ethnicities of the populations studied. Prevalence is three times higher in African Americans compared to White individuals from USA (5), which means that the lower overall prevalence figures in USA compared to Europe is more likely due to the sampling method rather than ethnicity. Nevertheless, reversal of the female: male ratio in Asian HS populations, with higher prevalence in Asian males, suggests that ethnic differences may produce different prevalence figures in different parts of the world. Insurance data from South Korea gave a 10-year prevalence of 0.06% (17), while a validated screening questionnaire gave a prevalence of 0.67% in the Australian population (18).

Is Hidradenitis Suppurativa becoming more or less common?

Studies providing incidence figures over time tend to use large, routinely collected datasets because other methodologies are harder to reproduce in the same population over time. As such, they will miss undiagnosed cases, and therefore will be affected by changes in disease recognition and coding. Population-based data from the USA found that comparing 2006-2016 with 2015-16, HS incidence increased from 8.6 to 11.4 cases per 100,000 population, an increase of one-third (19). This could be a true increase, possibly influenced by changes in HS risk factors such as obesity, or an artefact of increased disease recognition. In contrast, UK primary care data found that the incidence was relatively static during the two decades from 1993 until 2013, with an average annual incidence of approximately 28 cases per 100,000 population (14).

Global disability burden Hidradenitis Suppurativa

The Global Burden of Disease (GBD) Study in 2010 was a systematic effort to measure the extent of disability or loss of health due to diseases (20–22). Disability-adjusted life years (DALY) was utilized to quantify the number of years of life lost due to disability and premature death (20–22). One DALY equals one lost year of healthy life (21,22). With the exception of

dermatitis, the category “other skin and subcutaneous diseases”, that included HS along with 10 other diseases, had the highest burden of all dermatological conditions (0.29% of total US DALYs) (20).

However, despite its high disease prevalence and disability, federal funding for HS research has been lagging. In the USA, HS only received 0.1% of the total skin funding by the National Institute of Arthritis and Musculoskeletal and Skin Diseases in 2013, lower than less common diseases such as immunobullous disorders and vitiligo within the same “other skin and subcutaneous diseases” category (20). In comparison, psoriasis received 6.2% of total skin funding, which far exceeded its burden of less than 0.10% of total US DALYs (20).

In 2022, total NIH funds for HS increased to 6 million dollars according to the NIH reporter database. Although this is a great step forward to improve our medical knowledge of HS pathogenesis and develop life-changing therapies, HS funding continues to struggle when compared to the 1.4 billion dollars awarded for psoriasis research in 2019 (23). While psoriasis is more prevalent than HS, the impact on quality of life with HS is greater (24–26). The disproportionate funding has directly contributed to the limited advances in awareness and treatment. There remains a great need for research. This limited funding can be seen in annual HS-related publications, which continue to lag behind the number of publications for other common and rare dermatological conditions (23).

Results from Global Prevalence Studies

The GHiSA initiative aims to provide the first globally comparable data on epidemiology in HS (27). Definitive global epidemiological data for HS are still relatively lacking. The race-specific prevalence of HS has not been well documented in literature (28). The GHiSA initiative is rapidly filling the evidence gaps, and as an example, a GHiSA study of 506 participants in Greenland found a high HS prevalence of 3.2% (29). Moreover, the same study found that prevalence was higher among patients with Greenlandic Inuit origin than among other origins, suggesting HS may be unevenly distributed between the various races (29).

Currently, few studies have investigated the population prevalence of HS in Africa (30). A GHiSA study in Nigeria (30) revealed a prevalence of 2.2%, higher than the 0.54-0.67% prevalence observed in predominantly white population samples in UK (14) and Australia (18), supporting the previous findings that patients of African descent may be more likely to have HS (5). However, a previous study in Denmark found a similar prevalence of 2.1% in a predominantly white population (16). In contrast, a GHiSA study performed in Ghana (31) showed a prevalence of 0.67%, similar to previous studies where the majority of participants were White (14,18).

Studies of HS prevalence in South-east Asia are also limited. One recent study found the prevalence

of HS in Singapore (32) to be 0.585%, comparable to Western populations. However, another study using insurance data showed a low prevalence of 0.06 % in Korea (17). More studies are required to accurately measure HS prevalence across racial and ethnic groups. It is important to learn if patients of colour are disproportionately affected because of healthcare inequalities and racial bias or if a genetic component exists (28).

Significant gender differences in HS have been well documented. Both GHISA studies performed in Greenland and Ghana (29,31) revealed HS disproportionately affects women, similar to previous studies in the UK, USA, and Australia (5,14,18). However, this trend may vary across different ethnicities. For example, studies in Asia have shown a male predominance (17,32). In addition, there was a lack of gender predominance seen in Nigeria that the authors could not explain (30). Studies are needed to fully characterize gender differences in HS, including underlying mechanisms and clinical characteristics (33).

HS risk factors are currently being investigated in multiple studies throughout the world. BMI and smoking are frequently reported to be associated with HS in Europe, Australia, Greenland, South America, Turkey, and USA (14,15,18,29,34–36). The GHISA studies in Nigeria and Ghana (30,31), however, did not reveal a relationship between BMI and HS, and they did not explore smoking as a risk factor as it is not common practice in those regions,

although nicotine exposure may occur in ways other than tobacco smoking (37).

The US and Canadian Hidradenitis Suppurativa Foundations recommend screening for multiple comorbidities that are associated with HS including pyoderma gangrenosum, depression, generalized anxiety disorder, substance use disorder, suicide, inflammatory bowel disease, diabetes mellitus, cardiovascular disease, obesity and polycystic ovary syndrome among others (36). It is essential to identify comorbidities that affect HS patients globally so that appropriate screening may be implemented to improve the health of patients.

Gaps in data

Global knowledge gaps exist as most of the prevalence data available for HS originate from countries such as USA, Europe or Australia with predominant White participants (8,14,18,38).

Although many of these studies report a predominance of White patients among those affected (38), these findings may be a reflection of the demographics of these regions (39). Multiple studies in the USA have reported that the prevalence of HS is higher among African Americans than White patients (5,39). Studies must be conducted in other parts of the world including Africa, Latin America and Asia (8) to accurately measure HS prevalence across the full spectrum of racial and ethnic groups. As mentioned previously, GHISA is currently

engaged in collecting consistent and comparative HS prevalence data to fill the global knowledge gap. A detailed discussion of their initiative and progress will be presented later in this report.

As discussed previously, it is likely studies are underestimating the true impact of HS by missing undiagnosed cases as patients experience an average diagnostic delay of 7–10 years globally (12,13). In addition, insurance-based routinely collected data sources often miss patients from low socioeconomic backgrounds that are more likely to have severe disease (9). As a result, they may underestimate the number of ethnic and racial groups afflicted by HS, as these groups are more likely to face inequalities in health insurance coverage. In addition, HS clinical trials struggle with disease severity scoring in non-White participants and there is a need to improve the diversity of HS participants in clinical trials, to confirm treatment efficacy in all groups of HS patients (40).

Table 1

Methodology, population and data source used for hidradenitis suppurativa prevalence estimate in North America and Europe

Methodology	Population	Data source	Prevalence estimate (%) and 95% confidence interval	Reference
Population-based, diagnostic codes	Diagnosed cases from 15 million individuals in USA	Insurance claims	Period prevalence in 2007 = 0.053 (0.051-0.054)	Cosmatos et al 20132
Population-based, diagnostic code	Diagnosed cases from 48 million individuals in USA	Insurance claims and self-pay records	0.10 (0.097-0.099)	Garg et al 2017 (5)
Population-based, diagnostic codes	Diagnosed cases from 144,000 individuals in Olmsted County, USA	Rochester Epidemiology Project, centralised database for most healthcare providers	0.13 (0.11-0.15)	Shahi et al 2014 (38)
Population-based, diagnostic code and algorithm for multiple flexural skin boils	Diagnosed and undiagnosed cases from 4.3 million individuals in UK	Routinely-collected primary care CPRD database	0.77 (0.76-0.78)	Ingram et al 20186
Cross-sectional study: positive responses to survey question about painful flexural boils	10,000 members of general French population	6,887 questionnaire responses in those aged 15 years or older	Period prevalence in previous 12 months = 0.97	Revuz et al 2008 (15)
Cross-sectional study: positive responses to 2 survey questions about skin boils	Members of general Danish population	16,404 questionnaire responses (49% response rate) in those aged 30 years or older	2.10 (1.88-2.32)	Vinding et al 2014 (16)
In-person examination by dermatologists	507 patients, male: female ratio 1.2:1, mean age 27 years, undergoing screening for sexually transmitted diseases	History and examination findings	4.1 (3.0-6.0)	Jemec et al 1996 (10)

Legend: References are examples, rather than an exhaustive list.
 CPRD = Clinical Practice Research Datalink.
 HS = hidradenitis suppurativa. Reproduced with permission. (8)

Chapter 3:

How does Hidradenitis Suppurativa affect peoples' lives?

Dr. Hessel H. van der Zee, Dr. Barry McGrath

Introduction

Pain and foul-smelling suppuration emerging from the lesions associated with HS lead to a significant reduced quality of life. Patients furthermore experience shame and stigmatization (41). The disease has an impact on all aspects of quality of life, inability to go to school or work, social isolation, and depression (41).

Assessing disease severity

In 1989 the Hurley system was the first introduced severity score for HS (41). Stage 1 presents as inflammatory nodule or abscess formation, single or multiple, without sinus tracts and scarring. Stage 2 presents as recurrent abscesses and nodules with sinus tract formation or scarring: single or multiple widely separated lesions, and stage 3 presents as diffuse

or near-diffuse involvement with multiple interconnected sinus tracts, scarring, and abscesses across the entire area. Although it is an easy to use and quick severity assessment, it is static and not sensitive enough in the clinical trial setting and treatment follow-up. The refined Hurley staging subdivided Hurley stage 1 and 2 into an additional A, B and C in order to guide treatments, especially surgery (42). Other severity systems have been proposed, including the Sartorius score that is a detailed and dynamic score, but difficult to use (42). The HiSCR has been especially developed for clinical trials and is defined as an at least 50% reduction of inflammatory nodules and abscesses without an increase in draining tunnels (42). Recently, the international Hidradenitis Suppurativa Severity Score System (IHS4) has been developed by an internal consortium of HS experts (43). The IHS4 is a composite score

based on counts of inflammatory nodules, abscesses and draining tunnels. Inflammatory nodule 1 point, abscess 2 points and draining tunnel 4 points. The IHS4 score also allows HS to be subdivided into 'mild' ($3 \leq$ points), 'moderate' (4-10 points) or 'severe' ($11 \geq$ points). Furthermore, based in the continuous IHS4 score a dichotomous cutoff has been validated at 55% reduction of the score compared to baseline, The IHS4-55 (43). The HS-IGA (HS Investigator Global Assessment) has been developed as a response to the difficulty and variation in measuring disease activity and treatment responsiveness in clinical trials. Severity scoring in HS-IGA is based on objective lesion count and has been validated in a subset of patients (44). Still new severity assessment and classification tools emerge, aiming to heighten interrater reliability, simplify use in clinical settings, and identifying HS subtypes.



Figure 6. Non-inflamed nodules in axilla, transient elements (Hurley I)



Figure 7. Inflamed lesions mixed with chronic lesions. (Hurley II)



Figure 8. Pronounced inflammation and scarring with tunneling. (Hurley III)

Associated diseases

HS is part of the follicular occlusion tetrad consisting of HS, acne conglobata, dissecting cellulitis of the scalp and pilonidal disease (41). These clinical entities all share follicular occlusion as a primary pathogenetic event. These diseases can occur in conjunction with each other or alone. HS has a significant comorbidity burden beyond the skin, including metabolic, cardiovascular, endocrine, gastrointestinal, rheumatologic, psychiatric disorders, and auto-inflammatory syndromes.

Metabolic and cardiovascular comorbidities are the most commonly associated with HS.

Increased prevalence of metabolic syndrome (in up to 50% of patients), based on concomitant obesity, dyslipidemia, hyperglycemia and hypertension, has been reported in patients with HS, contributing to an increased risk of cardiovascular-associated death (8).

The prevalence of inflammatory bowel disease (IBD) among patients with HS is 2.8–3.3% (0.8–2.5% for Crohn's disease; 0.8–1.3% for ulcerative colitis) meaning that patients with HS have a higher risk of developing IBD compared with the general population, who show a prevalence of up to 0.3% and 0.5% for Crohn's disease and ulcerative colitis, respectively (8). Conversely, the prevalence of HS in patients with Crohn's disease or ulcerative colitis has been reported to be up to 25% (8). HS has also been reported to occur in several auto-inflammatory syndromes such as PASH (pyoderma gangrenosum, acne and suppurative hidradenitis) and PAPASH (pyogenic arthritis, pyoderma gangrenosum, acne, and suppurative hidradenitis) (45)

An association between HS and spondyloarthritis has been widely considered. A single-center cross-sectional study found that 28.2% of patients had spondyloarthritis, compared to 2.6% of patients in the control group (46). In another cross-sectional study in a cohort of patients with axial spondyloarthritis, the prevalence of HS was 9.1% (47).

It is well known that HS results in reduced quality of life due to factors such as pain, pronounced impairment of sex life, absenteeism from work, increasing unemployment, and increased feelings of stigmatization and loneliness (48–50). A registry study from Finland identified diseases of the circulatory system, and accidents and violence (including suicides), as major contributors

to the shortened (~ 15 years) life expectancy in HS patients (51). Studies have highlighted the higher risk of all-cause mortality in HS patients versus unaffected controls (52–56).

Psychological and mental health

Increased anxiety and depression in the HS patient population when compared to the general population have been widely reported, although the rates vary widely. A diagnosis of depression has been reported in 42.9% of HS sufferers (38). Moreover, a cross-sectional study demonstrated a significant increased risk for completing suicide and suicidality even after adjusting for confounding variables (57)

Elevated depression among children and younger people with HS has also been noted (58,59). International HS treatment guidelines recommend routine depression and anxiety screening (60). Bipolar disorder and schizophrenia have also been associated with HS, though such reports are limited (61,62).

Substance abuse (specifically cannabis, opioids, and alcohol) have also been reported to be higher amongst people with HS than controls (63,64). These substances have analgesic properties, possibly accounting for their increased use in some people with HS, given the debilitating pain experienced by many with HS (4,50,55,63,64).

Influences from the workplace

Disease onset is usually between the second and third decade of life, a critical period for employment choices, opportunities, and career trajectories. Analyses on HS populations from several European countries highlight that HS can profoundly impact professional activity. Unemployment rates in Denmark within the working-age HS population were more than six times higher than the general population (65). Unemployment among HS patients in Ireland was reported at several times higher than the general population (66). An analysis of the HS population in Germany showed unemployment rates at twice the general population (67). Furthermore, higher work presenteeism and absenteeism rates in the HS population relative to the general population were also reported (65,67).

Work productivity and at-work productivity loss (absenteeism plus presenteeism) have also been shown to be considerably affected by HS in reports from Canada (68), Denmark (65), Hungary (69), and the Netherlands (49).

International studies report similar trends. Results from the Global Survey of Impact and Healthcare Needs (VOICE) project showed that 14.5% of HS patients were disabled due to their disease. Furthermore, HS symptom severity strongly correlated with negative impact on work or schooling (13). The 'UNITE' international HS registry reported that only 60% of adults with HS were

employed and some 64% of those employed reported some degree of work impairment due to HS (70).

Social participation

Social isolation is used by some HS patients as a way of coping with the pain (71–73). Daily wound care management concerns many patients and can have a tremendous personal impact (74,75). In some cases, self-isolation has been reported as a coping strategy (76).

People with HS can often go to extreme lengths to hide their diseased sites (active signs and scars), avoiding participation in sports. Furthermore, active HS lesions that are painful, discharging, and purulent can make physical activity intolerable, while chronic scarring may limit the range of motion of certain exercises (77).

Moreover, HS has been shown to profoundly impact sexual activity (48,78–80)). Males experience higher sexual dysfunction and a reduced quality-of-sexual-life, while females report higher sexual distress when compared with control groups (81). Notably, sexual desire appears to be largely unaffected in people with HS (82). The QoL and sexuality of the partners of people with HS has also been shown to be impacted (83).

Socioeconomic and societal burden

HS can impose a substantial financial burden on the affected individual, healthcare, and society. Many HS patients (84) face considerable out-of-pocket

expenses, especially with regard to wound care products (74,75). Frustration with ineffective treatment options prompts some to explore complementary and alternative medicines, at considerable personal expense (85,86).

High levels of healthcare resource utilization in HS patients have been reported. Analysis of claims costs from US databases found that all-cause and HS-specific healthcare resource utilization and costs are high in adults and adolescents with HS (87). A study from Germany found that the hospital care of HS patients is cost-intensive (88). A report from Hungary indicates that HS imposes a substantial socioeconomic burden, fuelled by work presenteeism and absenteeism, treatments, and informal care (69). A recent study from Germany highlighted a considerable annual loss of gross value (~ EUR 12 billion) due to the unemployment, presenteeism, and absenteeism attributed to HS (67).



Figure 9. Chronic axillary scarring

Measuring the impact of HS on quality of life (QoL)

HS can cause substantial impairment on QoL in terms of physical, psychological, and social wellbeing. Disease severity, impact of surgery, and unpredictability of HS can exacerbate this impact. A recent pan-European study found that among the most common dermatological disease, QoL was particularly impaired in people with HS (89). Among dermatoses, QoL is typically assessed using generic measurement tools such as the Dermatology Life Quality Index (DLQI). The mean DLQI scores for HS (8.3–12.7) are typical for severe dermatoses (90). In a global study (involving almost 1300 HS patients from five continents), 14.5% reported disability due to the disease, while 81% reported at least one comorbidity (with anxiety and depression at 33% and 36%, respectively), further exacerbating impact on QoL (13). In cohabiting HS patients, their cohabitants' QoL can also be impacted, including partners (91–93) and parents (94).

The physical symptoms of HS, including pain, pruritus, fatigue, suppuration, and malodour (95) have traditionally been measured using some of these generic measurement tools. However, HS QoL assessment can be problematic as many generic QoL tools do not capture some HS-specific symptoms. In response, some HS-specific outcome measures have been developed (96). The Hidradenitis Suppurativa cORE outcomes set International Collaboration (HISTORIC) have developed both patient-reported outcomes and physician-reported measures (97). (49)(50–54)

Chapter 4:

Improving the quality of care for people with Hidradenitis Suppurativa

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Understanding triggers

The primary defect in HS pathophysiology involves hair follicles. The cascade of follicular occlusion, followed by follicular rupture, and a foreign body-type immune response provide milieu for the development of clinical HS. The triggers for development of HS are multifactorial, including endogenous factors (such as genetic, endocrine factors, microbiological factors) and exogenous factors (such as lifestyle factors, diet) (Table 2) (98)

Researchers have observed that approximately one third of HS patients have at least one family member also suffering from HS (hence suggesting a genetic predilection), and several gene mutations involving the γ -secretase complex: nicastrin (NCSTN), presenilin 1 (PSEN1), presenilin enhancer 2 (PSENEN) and APH1B (99) have been implicated in HS (100). Further, a genome wide association study (GWAS) of 720 patients has identified variants in two loci near the SOX9 and KLF5 genes associated with the risk of HS, underlining a genetic risk of disease (101). Yet, as not all individuals with HS have a family history of disease, the excessive inflammatory response that is common to all individuals with HS can be attributed to other factors listed above.

Hormones have been implicated in the occurrence of HS; however, the actual role of hormones remains to be fully elucidated. Researchers have observed patterns of peripubertal onset of HS and perimenstrual flares, improvement of HS during pregnancy, post-partum flares, and association of

HS with contraceptive pills with low estrogen/progesterone ratio (102). Premenstrual flares tend to occur in the luteal phase of the cycle where androgen levels are higher (103), suggesting a possible role of androgens in HS.

Smoking and obesity are well established triggers for development and exacerbation of HS (104,105). The chemicals in tobacco smoke are thought to have the potential to act to several receptors that trigger the action of immune cells and skin cells such keratinocytes, fibroblasts (106). When activated, keratinocytes cause infundibular epithelial hyperplasia, acanthosis and excessive outermost skin barrier formation (a process known as cornification) (106). Both tobacco smoke and obesity may trigger the release of pro-inflammatory molecules (106). Inflammatory cells which are present in the hypertrophic adipose tissue (found in obese patients) may produce proinflammatory cytokines and induce dysregulated release of adipokines (107). These adipokines further propagate the inflammatory cascade by recruitment of macrophages to adipose tissue, contributing to more release of proinflammatory mediators. It has been reported that the adipokines resistin and leptin were found to be increased in HS patients' serum and adiponectin levels reduced (102). Obesity further worsens existing HS through increased skin-to-clothing and skin-to-skin friction. Such mechanical stress has been shown to promote hair follicle occlusion and rupture (108).

Once HS has developed, many factors can cause flare-ups of HS. In a patient-centric survey study,

stress was the most reported trigger (81.3%), alongside high carbohydrate/glycemic index diet (32.3%), exercise (31.9%), weight gain (28.4%), friction and tight clothing (1.3%) (109). Other triggers identified were tobacco exposure (smoking or secondhand smoke), hormonal fluctuations (including menstruation) and lifestyle-related (trauma, poor sleep, prolonged sitting, shaving, exposure to cleaning chemicals) (109). These triggers can cause acute flares which dramatically and negatively impact a person's quality of life.

Barriers to quality care for people with Hidradenitis Suppurativa

Challenges in HS management include the presence of barriers to optimal treatment and delivering quality health care. These barriers can be divided into individual factors and healthcare organizational factors. Under individual factors: presence of multiple physical impairments arising from disease states, perceptions of self and others with HS, the ability of individuals and/or their caregiver's for (self) management. Some patients report a distrust in the medical field, that can result in them turning to social media for advice rather than their medical practitioner (110). Under healthcare organizational factors: Deficient knowledge and awareness of HS amongst practitioners, the organization of the country's healthcare infrastructure including available healthcare resources.

Individual factors

Presence of multiple physical impairments arising from HS

Individuals with HS may experience significant physical and quality of life (QoL) impairments due to their disease including the constellation of disfiguring lesions, foul-smelling discharge, scarring, and pain. Studies have shown that patients who experienced more pain tended to experience also more work productivity loss, poorer QoL, anxiety, and depression (111,112). A recent qualitative study assessing patients' perspectives of barriers to care demonstrated that disease activity directly influenced employment – that patients avoided jobs with activities that might induce flares, like long-term sitting, frequent walking, or on-site attendance (113). Patients have described that making career choices based on their skill-set alone makes it difficult to accommodate their symptoms or control disease activity (113). Work productivity loss further affects income which directly affects patients' financial capacity to support their treatments (114).



Figure 10. Extensive separate lesions of right axilla

Lastly, significant comorbidities of anxiety and depression arising from HS may also drastically affect the ability of individuals to self-care or seek help, further entrapping HS patients in a vicious cycle of psychological impairments and downstream harms to self (115).

Perceptions of self and others with HS

Studies demonstrate that most young individuals with dermatological conditions do not seek professional help (116). These studies cite reasons of patient embarrassment or patient belief that their condition does not warrant visiting the doctor (117,118). Furthermore, the general public may have misconceptions of HS such as HS being contagious or a product of poor hygiene. Such misconceptions could compound the avoidance of seeking treatment and self-care of HS patients (119). Conversely, as Ng et al had reflected - individuals who had previously heard of HS, and have knowledge of its pathophysiology, might be more open to interpersonal and social interactions with HS patients (119).



Figure 11. Diffuse anogenital involvement with suppuration

In the Asian context, one study has found that despite a relative male predilection for HS disease, females exhibited significantly higher social attitude-and-perception scores (higher scores meaning more positive perception, less stigmatization and higher social acceptance) than males. This indicates that females stigmatize HS less than males, with males especially having lower scores in the workplace (e.g. they perceive that HS patients have difficulty finding a job) and social contexts (e.g. they perceive that HS patient are embarrassed in public) (119).

Ability for self-management

HS patients may face difficulty with recommendations put forth by their attending physicians. Although weight loss through exercise is often recommended by physicians to decrease metabolic risk and risk of flares in HS patients, authors have found this recommendation to be challenging in practice for many patients (77). HS patients may take measures to visually conceal their diseased sites (both active signs and scars), with short-sleeved shirts, and avoid swim wear. Active lesions that are painful, purulent and discharging make many exercises intolerable, while chronic scarring may limit the range of motion of certain exercises (77). Warmer, humid climates in parts of Asia further compound issues of heat, sweat and friction faced by HS patients (120). Patients may thus be conflicted by the desire to lose weight with the fear of triggering the disease. Summative literature on qualitative research on the experiences of HS patients reflect that patients often feel that healthcare professionals

advise treatment changes “without understanding the challenges for the individual, leaving people feeling stigmatized and ‘dehumanized’” (121). Hence, generic instructions by attending physician to “exercise more”, without consideration of the difficulties faced by HS patients, may be perceived by patients as un-empathetic or uncaring, and does not improve patient outcomes (77).

As aforementioned, psychological impairments and mood issues may also pose as significant barriers to self-care for HS patients.

Healthcare organizational factors

Deficient knowledge and awareness of HS amongst practitioners

HS is often underdiagnosed, partly owing to lack of knowledge of HS among primary care physicians (122). HS may also be under-recognized by patients themselves. Studies have reflected that physicians themselves may not have the ability to recognize HS and distinguish it from other



Figure 12. Chronic inflammatory axillary nodule

dermatological conditions like acne, contributing to under-diagnosis and delays in treatment of HS patients (110). The diagnosis of HS after initial presentation of symptoms has been reported to range from 3 to 10 years with most studies finding a delay of 6 to 10 years (123). Miscommunication, or use of unscientific terminologies amongst physicians when they use colloquial terms like ‘boils’ to explain HS to patients, may further contribute to poor awareness amongst the general public (116,119).

Although HS is most often primarily managed by dermatologists once the diagnosis has been established, the lack of familiarity with this condition and its comorbidities pose a challenge for non-dermatologic providers to confidently make a diagnosis, and/or make appropriate referrals to dermatology for further assessment. In many regions of the world, access to dermatology could be limited by the scarcity of providers, long wait times, and limitations by patient insurance (124). Hence, patients may tend to present first to providers in other specialties, including family medicine, internal medicine, obstetrics and gynecology, pediatrics, and emergency medicine (123). In a 2021 survey of 211 family medicine physicians in Turkey, only 23.7% reported feeling confident in diagnosing HS. Of the 211 physicians, up to 63% erroneously believed HS to be an infectious process of the apocrine glands (125). Addressing gaps in physicians’ knowledge is critical.

Organization of a country’s healthcare infrastructure including available healthcare resources

The pathophysiology of HS is regarded to be complicated due to a myriad of causative factors. Current clinical trials have managed to investigate critical immunity-related pathways; however, many of these trials also exclude patients who have new onset or acute disease within the past 6 to 12 months. The average patient in HS clinical trials would have disease durations greater than 5 years. Present tendency to exclude patients exhibiting earlier disease limits available therapeutics for this group.

Timely and early initiation of appropriate treatment for HS is limited by various factors.

To date, Adalimumab and Secukinumab are the only approved biologic therapies in the European Union, UK, and USA for patients with moderate-to-severe HS (126–128). Studies reveal that delays in initiating biologic therapy in patients with moderate to severe HS could be related to lack of HS providers willing to prescribe these drugs, their hesitancy arising from unclear treat-to-target paradigms, high prior authorization burden, and limited access to specialists with expertise in HS. Patient related factors may include hesitancy regarding injections or side effects, lack of trust in medical providers, delayed diagnosis, and previous experience with ineffective treatments.

A survey study of HS patients revealed that 46% reported dissatisfaction with their current treatment (129). The most common reason for dissatisfaction was perceived lack of efficacy (43%). Only 21% were prescribed biologic therapy, while 86% had been prescribed more traditional therapeutic options such as oral antibiotics, and 70% having received incision and drainages. Other researchers reported a mean of 15 years from time of first systemic therapy to first biologic therapy, with 21% of patients having received 5 different treatments prior to starting a biologic (130).

Barnes et al emphasize, that health care coverages associated with the country's existing healthcare infrastructure, can affect the level of care received by HS patients. Health system characteristics influence patient-centered care, associated costs, perceived access to care and disease activity (113). Financial burden has been recognized as a barrier to biologic exposure and prescription willingness amongst physicians, as insurance may not cover the use of these expensive treatments, even though effective management of HS to minimize or prevent flares may in the long run decrease the need to treat HS in high-cost acute care settings (131).

In the USA, analysis of databases including patients with privately funded health insurance (US Commercial Claims and Encounters with Medicare Supplemental and Coordination of Benefits [CCAE+MDCR] database) and those who receive publicly funded health insurance (IBM US Medicaid database) reveal differences in dermatologist visits and treatment

exposures between the two groups of patients with the former privately funded group tending to reflect more visits to dermatologists, more exposure to biologic treatment and the latter publicly funded group reflecting less dedicated dermatological care (visiting acute care hospitals instead), and comparably less exposure to biologic treatments. This highlights the influence of socioeconomic status (SES) on management practices – unfortunately, the populations which are of increased risk of HS also have lower SES (cite?). Those with a low SES are also more likely to have Medicaid or other public health insurance (64.3%), and tend to receive poor-quality health care, with reduced access to healthcare overall (131,132).

What can be done?

Improving access through digital health innovations and tele-dermatology

Digital health care innovations can be a simultaneously boon and barrier towards the management of HS patients. During the COVID-19 pandemic, tele-dermatology was adopted rapidly globally. Despite the relative success of tele-dermatologic management of chronic, debilitating dermatological conditions - such as acne and atopic dermatitis - during the COVID-19 pandemic, authors have reflected relatively less enthusiasm amongst physicians in employing tele-dermatology for HS patients (133). A survey study highlighted that a significant proportion of physicians were reluctant to have tele-dermatology completely replace their routine face-to-face visits and

were ambivalent toward perceived willingness of HS patients to be managed over tele-dermatology (133). This reluctance was even more apparent amongst older physicians who perceived more difficulties with accurate assessment of disease severity, reflecting concerns that patients with HS may not be familiar with the technology (133).

To improve the acceptability of tele-dermatology amongst patients and physicians, authors suggest that physicians should streamline tele-dermatology services to be offered to patients with quiescent or mild HS (i.e. Hurley stage I, International Hidradenitis Suppurativa Severity Score system score 1-3). Patients with less HS involvement in intimate body areas and those who were more willing to share documentation of their HS condition (if required, including affected intimate body areas) could be more strongly considered for telemedicine services, if they had already established strong physician-patient relationships with their HS providers. To maintain patient privacy as far as possible, Patel et al suggests requesting images of HS-affected skin only when 'essential', such as prior to urgent commencement of biologic therapy (134). Sensible triaging of HS patients who may require urgent biologic commencement, and conversion to face-to-face consultations to assess flare symptoms, non-responders and patients who have tried multiple lines of treatment could be directions forward (133).

Improving awareness through education and research

Within the dermatology realm, the past decade has seen a massive increase in HS research including existing work to expand available biologic treatment for moderate-to-severe HS (123). Emphasis should be placed on educating other specialties on recognition and diagnosis of HS, providing them the ability and confidence to make appropriate referrals to dermatology and/or commence initial treatment, and manage subsequent flares. Guidance on medical and surgical management of HS can be reinforced through large annual dermatology meetings (123). Foundations focused on HS advocacy, education and research have also developed internationally through the years - including the Hidradenitis Suppurativa Foundation. These foundations play critical roles in educating patients

and advanced practice providers through patient sharing sessions and dedicated meetings such as the Symposium on Hidradenitis Suppurativa Advances and the European Hidradenitis Suppurativa Foundation (EHSF) conference (123).

Providing opportunities through social media

Social media platforms, such as Facebook, Twitter, Instagram, and TikTok can provide HS patients opportunities to expose themselves to large HS communities from which they may seek education related to their disease (135). A study revealed that based on observations from the largest HS support group in 2017–2018, consisting of almost 13,000 members, over half of the posts were requests for information, predominantly about lifestyle changes, symptom management, and experiences with medications (135). Unfortunately,

social media may also be tainted by misinformation. Authors suggest that although dermatologists cannot “suppress” the opinions and voices of others on social media platforms, the active engagement of trained dermatologists can improve patients’ access to reliable information (136). Over time, continued accurate engagement may increase awareness, reduce stigma, and ultimately lead to faster diagnosis and treatment of HS (135).

Principles of HS management

Few chronic skin conditions encompass impairments in such multifaceted areas of human health including physical, occupational, interpersonal and psychological domains of functioning. Despite the huge burden, there is a lack of uniformly effective therapies for HS patients. In order to optimize the management outcome and mitigate the high healthcare utilization cost, the timely treatment is critical (137).

The current approach to cases with HS is a multifaceted approach combining lifestyle modifications, addressing associated comorbidities and combined medical and surgical therapy (138). The goal of medical therapy is the control of existing inflammation and prevention of flares and new lesions, while the goal of surgical therapy is removal of irreversible damaged tissue and scarring (139). Medical therapy is often the first line of treatment particularly for high inflammatory and migratory lesions. Surgical therapy would be more effective for the lesions not responding to

Table 2
Triggers associated with HS

Triggers related to personal factors (endogenous)	Triggers related to environment (exogenous)
<ol style="list-style-type: none"> 1. Genetic 2. Dysregulated microbiome 3. Hormonal 	<ol style="list-style-type: none"> 1. Obesity 2. Smoking 3. Stress 4. Diet (high carbohydrate, high glycemic diet) 5. Exercise 6. Skin occlusion and friction eg. shaving 7. Increased friction with tighter clothing, prolonged sitting 8. Trauma Poor sleep 9. Exposure to chemicals

medical therapy, residual scars, tunnels and abscesses. This chapter delves into the fundamental principals in HS management by looking at the treatment of a person as a whole and not only skin manifestations.

Treating skin manifestations

The limited understanding of the pathologic mechanisms of HS has led to a critical lack of effective therapeutic interventions. HS is a multifactorial disease, encompassing genetic and environmental factors, lifestyle, hormonal status

and microbiota. The treatment options are multifaceted including behavioral change, topical therapy, systemic therapy, surgical interventions, laser and light-based therapy (140). Table 3 summarizes commonly used treatment options.

Table 3
Treatments for HS

Treatment options for HS	Mechanism of action	Contraindications
Clindamycin 1%	Antimicrobial effects against anaerobic, staphylococcal, and streptococcal species, reduced skin inflammation and prevention of biofilm formation (141)	Hypersensitivity to clindamycin (142)
Resorcinol 15%	Anti-microbial, anti-inflammatory, and keratolytic effects (141)	Hypersensitivity to resorcinol, skin type > 5, pregnancy, active HSV (143)
<i>Systemic Therapy</i>		
Oral antibiotics <ul style="list-style-type: none"> • Tetracyclines • Trimethoprim-Sulfamethoxazole (TMP-SMX) • Clindamycin/rifampin 	<p>Tetracyclines: bind 30S subunit of bacterial ribosome to inhibit protein synthesis (144)</p> <p>TMP-SMX: synergistic inhibition of folic acid synthesis, reducing purine synthesis required for DNA/protein production (145)</p> <p>Clindamycin: anti-staphylococcal, anti-streptococcal properties; decreases bacterial protein synthesis and neutrophil chemotaxis(146); binds 50S subunit of bacterial ribosome to inhibit protein synthesis, suppresses inflammation (147)</p> <p>Rifampin: broad-spectrum antibiotic with antimicrobial and immunomodulatory properties (146); inhibits DNA-dependent RNA polymerase (148)</p>	<p>Tetracyclines: pregnancy (maternal hepatotoxicity risk/fetal tooth discoloration and diminished growth of long bones), pediatric patients <8 years (tooth discoloration), renal failure (144)</p> <p>TMP-SMX: sulfa allergy, pregnancy, liver damage/jaundice/hepatic failure, blood disorders, renal impairment, neonates <6 weeks of age (145)</p> <p>Clindamycin: history of pseudomembranous colitis or ulcerative colitis; hypersensitivity to clindamycin or lincomycin (147)</p> <p>Rifampin: rifampin/rifamycin allergy, use of drugs metabolized by CYP 3A4 and hepatic P-glycoprotein, hepatic impairment (148)</p>

Table 3 continued

Treatments for HS

Treatment options for HS	Mechanism of action	Contraindications
Dapsone	Competes with para-aminobenzoic acid to inhibit dihydropteroate synthase (149); has antimicrobial, bacteriostatic, and inflammatory properties (146)	Prior hypersensitivity, agranulocytosis, sulfa allergy, significant cardiopulmonary disease, liver/renal function impairment, peripheral neuropathy; caution in pregnancy (149)
Antiandrogens	Block mineralocorticoid receptors and exert antiandrogen properties(146)	Renal impairment (spironolactone), pregnancy (finasteride) (150)
<i>Biologics and small molecules</i>		
Anti-TNF-α • Adalimumab • Infliximab	Adalimumab: human recombinant IgG1 monoclonal antibody that binds TNF- α to prevent binding of TNFR cell receptors; reduces leukocyte recruitment, C-reactive protein, erythrocyte sedimentation rate, IL-6, and serum metalloproteinases (151) Infliximab: chimeric (mouse/human) antibody to TNF- α that binds TNF- α to prevent binding of TNFR cell receptors(151)	Moderate to severe heart failure (NYHA class III/IV), severe liver diseases, demyelinating diseases, pregnancy, lactation, hypersensitivity to mouse proteins (infliximab) other severe infections (151)
Anti-IL-17 • Secukinumab	Human monoclonal antibody that binds IL-17A to reduce production of proinflammatory cytokines by neutrophils and lymphocytes (151)	
JAK inhibitors	Target Janus kinase proteins that cause cytokine release via intracytoplasmic transcription factors signal transducer and activator of transcription (STAT) (152)	
<i>Laser and light therapies</i>		
Neodymium-Doped Yttrium Aluminium Garnet (Nd:YAG) laser	Laser used for hair removal targeting inflammation, abscess formation, and tunnel development in primary follicular hyperkeratosis (153)	Hypopigmentation with laser use (154)
CO2 laser	Ablative laser used for excisions, marsupializations, and vaporizations of HS lesions to vaporize skin until reaching healthy tissue (151)	Adnexal disease, iatrogenic conditions, recent treatment with isotretinoin, use after extensive surgical procedures (155)

The first line of treatment in early stage of the disease include topical therapy and systemic antibiotics. The application of biologics and small molecules is an evolving area in management of HS. However; despite the increasing diverse therapeutic armamentarium, a substantial number of patients do not achieve or maintain disease remission. Surgical intervention has also an important role in management of HS.

Treating the whole person beyond the skin

HS is a dynamic disease, and various clinical scores are used to assess the severity of HS skin alterations. The chronic inflammatory state in HS is associated with upregulation of tissue and circulating cytokines. HS is associated with a huge burden and unsurprisingly multiple systemic conditions, whether skin alterations or extracutaneous inflammatory

alterations occur first is currently unknown. The chronic pain and disfigurement from this disease is debilitating. Given the low QoL outcomes, it is not surprising that HS patients also suffer more frequently from psychological disorders, and engage in negative thought patterns (e.g., feeling unworthy) that potentiate existing vulnerabilities to mental health challenges (36,158). Comprehensive care strategies coordinated among multiple disciplines and particularly in a timely manner are critical in improving the care of patients with HS. Table 4 lists common comorbidities associated with HS.

Horizon scanning of new drugs in the pipeline and phase 2/3 trials

Information on clinical trials in this section can be found via NCT number on www.clinicaltrials.gov

There are currently many therapeutic strategies for HS under development targeting varying components of HS pathogenesis. With the EMA and FDA approval of secukinumab, the IL-17 pathway has attracted prominent attention with several different drugs currently under investigation that target IL-17. Preliminary pooled results from two phase 3 RCTS (NCT04242446 and NCT04242498) evaluating the efficacy of bimekizumab, a humanized monoclonal trispecific antibody targeting both IL-17A and IL-17F, demonstrated significantly higher response rates over placebo (159). Recently announced results from a phase 2a study with sonelokimab (an anti-IL-17A/F nanobody; NCT05322473) showed superiority over placebo. An open label phase 2 study assessing

Table 4

Common comorbidities associated with hidradenitis suppurativa

Associations	Examples
Mental health disorders	<ul style="list-style-type: none"> • Depression • Anxiety • Bipolar disorder
Gastrointestinal disorders	<ul style="list-style-type: none"> • Crohn's disease • Ulcerative colitis
Genetic disorders	<ul style="list-style-type: none"> • PASH syndrom (pyoderma gangrenosum, acne, suppurative hidradenitis) • PAPASH syndrom (pyogenic arthritis, pyoderma gangrenosum, acne, suppurative hidradenitis) • SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis) • Dowling–Degos disease • Down syndrome • Keratitis–ichthyosis–deafness • Pachyonychia congenita syndrome
Inflammatory dermatoses	<ul style="list-style-type: none"> • Acne • Psoriasis • Pyoderma gangrenosum
Cardiovascular disorders	<ul style="list-style-type: none"> • Metabolic syndrome
Joint/Musculoskeletal disorders	<ul style="list-style-type: none"> • Spondyloarthritis and/or spondyloarthropathy
Malignancy	<ul style="list-style-type: none"> • Squamous cell carcinomas • Lymphomas

Izokibep (a small protein inhibitor of IL-17A (NCT05355805)) has recently been completed with positive results, and a phase 3 study (NCT05905783) is currently ongoing. In contrast, two phase II studies targeting IL-23 upstream of IL17, using guselkumab (160) or risankizumab (161) were prematurely terminated as the primary end point was not met and the overall findings do not support the efficacy of either drug in the treatment of HS. Other potential upstream mechanisms have been postulated including IL-1 (162), with lutikizumab, a dual IL-1 α / β inhibitor, currently under investigation in a phase 2 trial (NCT05139602). A phase 2 trial with bermekimab (a IL-1a monoclonal antibody) was terminated for futility. Studies targeting the IL1 receptor or IL-1 receptor-associated kinases (IRAK) have so far not demonstrated superiority over placebo (MEDI8968, an anti-IL-1 receptor antibody in NCT01838499, and zimlovisertib, an IRAK inhibitor in NCT04092452).

In addition, there is a strong theoretical basis for targeting JAK-STAT signaling in HS given its associations with Th17 cells, neutrophil chemotaxis, and B cell migration and activation. Several oral and topical Janus kinase (JAK) inhibitors are currently under investigation for HS. Upadacitinib, an oral JAK inhibitor, demonstrated superiority over placebo in a phase 2 trial (163) (NCT04430855) and is now undergoing evaluation in a phase 3 study (NCT05889182). Povorcitinib, a specific JAK1 inhibitor, showed good tolerance in two small open-label phase 2 studies (164),

and phase 3 studies are currently in progress (NCT05620836, NCT05620823). Ruxolitinib, a JAK1/2 inhibitor, is being tested topically compared to vehicle (NCT05635838) in a phase 2 trial. Additionally, a phase 2 study indicated that Brepocitinib (a JAK1/TYK2 inhibitor) was found to be superior to placebo, while PF-06826647, which blocks only TYK2, did not demonstrate clinical efficacy (NCT04092452).

Directing treatment at neutrophil recruitment and activation fits well in the pathogenic concept of HS. Eltrekibart, a humanized monoclonal antibody which neutralises chemokines that bind to the CXCR1 or CXCR2 receptors, showed good clinical response in a phase 2 clinical trial (NCT04493502) with a larger phase 2b trial underway (NCT06046729). However, another small phase 2 RCT investigating RIST4721 (a CXCR2 inhibitor, NCT05348681) was discontinued following safety findings. Spesolimab and imsidolimab, two anti-IL-36 monoclonal antibodies employed in generalized pustular psoriasis are being evaluated in phase 2 clinical trials (NCT04762277; spesolimab and NCT04856930; imsidolimab).

An alternative approach involves targeting B cells. A phase 2 randomized, double-blind clinical trial is in progress to assess the efficacy of iscalimab, an anti-CD-40 monoclonal antibody (NCT03827798). Additionally, the investigation of remibrutinib, an oral BTK inhibitor that inhibits B cells and other myeloid cells, is also underway in phase 2 clinical trials (NCT03827798).

While the involvement of the complement pathway in the pathogenesis of HS has been demonstrated, phase 2 studies with vilobelimab (IFX-1, an anti-C5a monoclonal antibody, NCT03487276) and avacopan (an oral C5a inhibitor, NCT03852472) were recently terminated as they both failed to meet their primary endpoint. A phase 2 study with BDB-001, another anti-C5 antibody is still ongoing (NCT05103423).

Overall, while many promising phase 2 and 3 RCTs are currently ongoing, a large amount of trials have failed to meet their primary endpoint resulting in premature termination. This demonstrates the highly heterogeneous pathophysiology of HS, involving a multitude of inflammatory pathways and cell types as well as raise questions about currently used clinical endpoints.

Chapter 5:

Addressing the gaps, barriers and needs

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Gaps in global hidradenitis suppurativa epidemiologic data

Despite multiple country-specific and region-specific efforts, a definitive global consensus on the prevalence of hidradenitis suppurativa (HS) remains unclear. Existing studies exhibit significant variability in their design, ranging from the use of screening questionnaires to clinical diagnoses by dermatologists, as well as variations in sampling locations. This diversity in approaches poses substantial challenges for achieving a comprehensive global epidemiological understanding of the condition (3,5,8,165–169). Herein, we outline major gaps in our understanding of the global epidemiology of HS.

- Diagnostic delay has been reported, approximating 7-10 years from symptom onset to time of diagnosis (12). This is likely due to difficulties accessing care from providers familiar with HS, resulting in underdiagnosis, misdiagnosis, implementation of ineffective therapeutic options, and stigmatization of affected individuals (12,113,166,170–177).
- HS prevalence by sex, race and ethnicity remains understudied. For example, compared to Western European and Australian populations, distinct differences in sex predominance, influence of tobacco use on disease severity, and anatomical disease presentation is reported in Asian populations. Additionally,

although HS is reported to disproportionately impact African Americans in the United States, these results have not been reproduced in HS prevalence studies conducted in Australia, the United Kingdom, Nigeria, and Ghana (5,17,28,30,31,39,178–185). These findings suggest population-specific drivers, including environment and genetics, may play a role in HS onset.

- HS has been associated with substantial cardiovascular, metabolic, and psychiatric comorbidities (7,13,17,170,186). However, incomplete HS prevalence estimates have hindered evaluation of the true impact and direction of these associations.
- Global epidemiological HS data are scant. The current studies reporting the HS epidemiology are inconsistent, incomparable, and most of them originate from Europe, Australia, or North America (7,13,17,165,170,172,180,181,184,186,187).
- Few studies have examined HS incidence and prevalence in pediatric patients and older adults (188). Limited understanding of HS epidemiology in these populations have hindered studies examining associated comorbidities and effective treatments.
- Although HS disproportionately affects women of child-bearing age and fluctuations in the condition have been reported during pregnancy, little is known about characteristics and care of pregnant women with HS (189–192).

The Global Hidradenitis Suppurativa Atlas (GHISA) Initiative

There is an urgent need for a robust and systematic approach to assess HS epidemiology globally. The Global Hidradenitis Suppurativa Atlas (GHISA) project was initiated to address gaps in knowledge about HS epidemiology (27). GHISA is an international non-profit organization launched to promote awareness and information in support of improved management of HS globally (27). The primary objective of GHISA is to tackle the challenges associated with HS through global collaboration, research, and disease awareness.

GHISA is governed by a president, secretary-general, honorary secretary, steering committee, and treasurer. The governance committee oversees national investigators, ensuring coordination at a national level. Moreover, GHISA comprises separate sub-committees dedicated to advancing research methods, fundraising, marketing, and collaborative expansion.

The overall aim of the GHISA Global Prevalence Study is to present reference data for global HS epidemiology, and thereby provide the first estimate of HS burden globally (Phase 1). To that end, systematic and prospective HS prevalence data are currently being collected from approximately 50 countries across 6 continents. Data resulting from the GHISA Global Prevalence Study will be used to develop core criteria for future epidemiological studies (Phase 2). Ultimately, GHISA aims to conduct

Addressing the healthcare needs of people living with Hidradenitis Suppurativa

Healthcare systems and associated barriers to care differ geographically. In Europe, HS may be primarily managed by general practitioners (GPs) (175,193). In the US, healthcare insurance carriers may dictate access to specialist care (113). In continental Africa, there is less than 1 dermatologist per 1 million people compared to 10, 36, 65 dermatologists per 1 million people in western countries like the UK, the USA, and Germany respectively (194,195). Accordingly, these factors shape access to care and the resultant needs of diverse populations. The following needs regarding HS care have been identified by investigators and patients:

Limited Therapeutic Options

- There is limited provider and public knowledge of HS diagnosis and appropriate medical and surgical treatments (113,166,173,174,176,177,196).
- There are limited therapeutic options for acute HS flare management (72,113).
- There are limited therapeutic options to control symptoms such as pain (13,72,170,171,173).
- There are limited therapeutic options to treat mild HS (171).

Poor Healthcare Access and High Healthcare Costs

- There is a lack of timely access to HS specialists and multidisciplinary specialized hospital-based centers (72,113,158,171,196).
- There is minimal wound care education and cost coverage for HS patients (113,171).
- In the US context of multi-payer insurance models, cost of care can be high (113,158,171).

Decreased School Attendance and Work Productivity due to HS Management

- Managing HS requires time for doctor visits and ongoing treatment regimens, resulting in reduced availability and energy for school- or work-related activities (113).
- HS has been associated with low socioeconomic status as the condition impacts ability to attend school and work due to pain and discomfort. Some people with HS require disability compensation (113,158,196).
- HS lesions can limit mobility and hinder physical activities, making physically demanding tasks or prolonged positions at work or school challenging due to pain and discomfort (72).

Limited Support Services to Help Patients Cope with Impaired Quality of Life

- There is limited interdisciplinary supportive care from behavioral health professionals to address psychosocial burdens of HS (72,170,175).
- Patients with HS encounter stigma related to their condition, highlighting the pivotal role of rapport and trust in the patient-doctor relationship influencing patients' willingness to access care and manage their disease (113).
- The constant pain and discomfort associated with HS can affect daily activities, mobility, and sleep, leading to a diminished quality of life (7,197).
- HS can affect social interactions and relationships, with patients often avoiding social situations, intimacy, or physical contact due to concerns about their condition (71,113,198). Research indicates higher levels of loneliness and social isolation among HS patients compared to healthy individuals (71).

Conquering these barriers and improving access to comprehensive care are essential to enhance the well-being and outcomes of individuals diagnosed with HS. To address these needs, a multi-layered approach has been developed to outline the role of stakeholders and institutions in the health care chain.

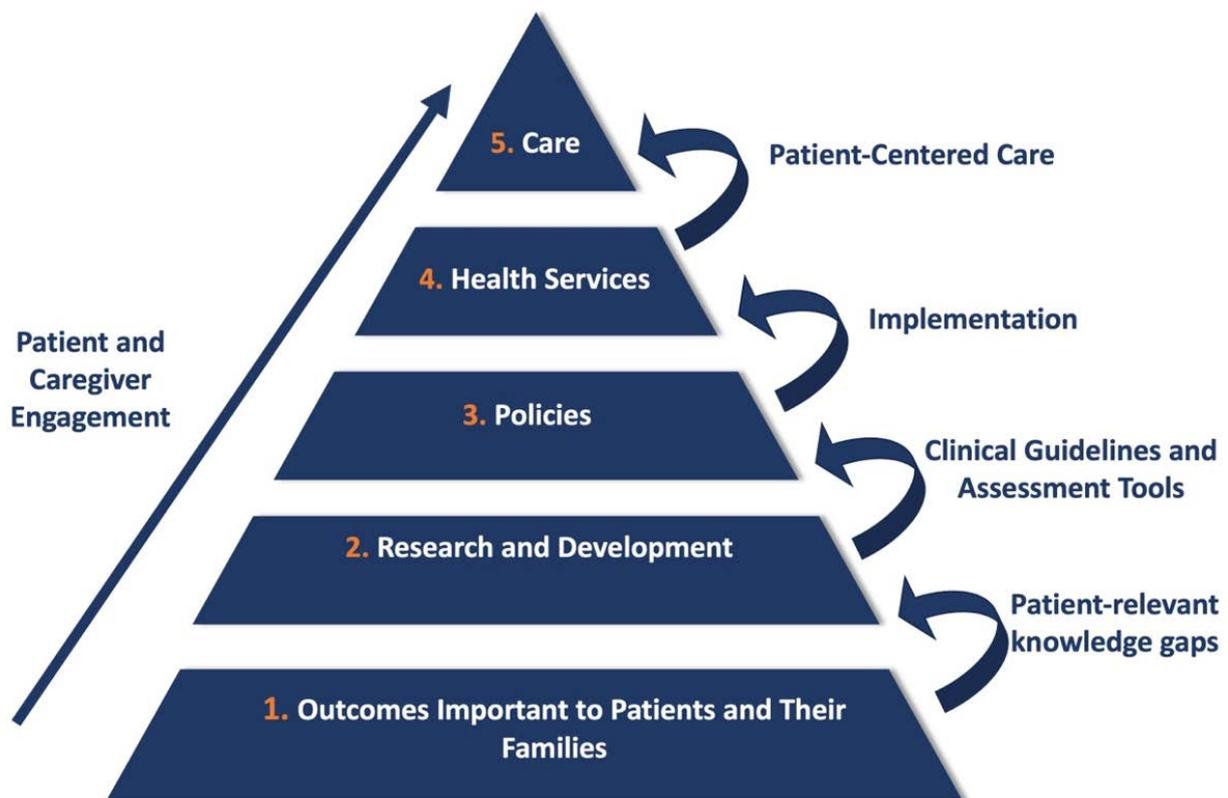
Patient-Centered Healthcare System Model

The Patient-Centered Healthcare System Model proposed by the World Health Organization (WHO)

provides a framework for stakeholder involvement in improving patient care (199). For people with health conditions, this model provides a helpful outline of the individual and systemic factors that contribute to quality health care.

Figure 14: Patient-Centered Health-care System Model, adapted from the WHO (199)

This figure represents a Patient-Centered Health-care System Model, adapted from the World Health Organization (WHO). The model emphasizes the pivotal role of patients in the healthcare process and underscores the importance of tailoring healthcare services to meet patient needs and preferences. Key components include prioritizing outcomes important to patients, engaging in research and development, implementing supportive policies, enhancing health services, and improving patient care. This approach empowers patients, promotes informed decision-making, and seeks to enhance the quality of care for those diagnosed with HS.



1. Outcomes Important to Patients and Their Families

Research demonstrates that patients with HS report a very large impact of HS on their health-related quality of life (QoL) (71,111,158,197,200,201). Quality of life factors include symptoms and feelings, daily activities, leisure, work/school, personal relationships, and treatment. Addressing these domains for patients could significantly impact the experience of diagnosed with HS. For patients with HS, this specifically includes pain reduction, ability to engage in work activities, and self-confidence.

Patients often describe HS pain as a chronic discomfort, with acute flares exacerbating their distress and diminishing their QoL (72). The chronic pain linked with HS hampers physical mobility, disrupts sleep patterns, and adversely affects psychosocial wellbeing and social relationships (72). Further, an interview-based study exploring the psychosocial burden of HS found that the

condition substantially impacted mood, personal relationships, perceptions of the future, leisure activities, personal appearance, self-confidence, and motivation in patients with moderate and severe forms of HS (113,171,173,174,193,196,202,203). Societal stigma associated with HS also contributes to its psychosocial burden (118,204–206). This is underscored by a study showing that patients deemed that improvement of the visual appearance of lesions and prevention of scarring as the most crucial elements of their surgical management. (171). Overall, patient-centered outcomes include improved quality of life, enhanced pain management options, reduced costs associated with HS management, and timely and accurate diagnosis by medical providers.

Perception of HS also varies among patients, caregivers, and providers. Caregivers play a significant role as stakeholders in defining important outcomes. In a study evaluating

research priorities to patients, caregivers, and healthcare providers regarding top skin conditions, patient-relevant knowledge gaps for HS were identified. These knowledge gaps encompass various aspects, including elucidating the molecular mechanisms of the disease and identifying novel treatment strategies (207).

GHiSA will make a direct and valuable contribution in this regard through its patient-centered research and data collection efforts. By actively involving patients and their families in research initiatives, GHiSA can identify and prioritize outcomes that matter most to patients. This approach ensures that GHiSA's endeavors are aligned with the needs and preferences of those affected by HS, ultimately leading to more meaningful and impactful results.

2. Research and Development

Active patient engagement in HS research is crucial for defining pertinent research areas. Involving patients throughout the clinical research process ensures their perspectives, needs, and knowledge are integrated into study design, aiding in the evaluation, improvement, and applicability of treatments (173). Recent studies highlight key research areas, such as disease mechanisms, effective therapeutics, and ways to measure treatment response (174,207). To enhance patient-centered care, these priorities should guide funding, research, policies, and sponsorship decisions in the field of HS.



Figure 15. Chronic disease with mix of different elements, perpetuating the discomfort for the patient.

By collaborating with leading HS research efforts like C3/HiSTORIC and HS PROGRESS, GHiSA actively works to bridge existing knowledge gaps. Through partnerships with researchers, healthcare providers, and patients, GHiSA fosters innovative studies, exploring new ideas, diagnostic tools, and treatments. Patient organizations like GlobalSkin and Patient Foreningen HS guide GHiSA's activities, ensuring a patient-centered approach in guideline development and research priorities. GHiSA also collaborates with the International League of Dermatological Societies (ILDS), aiming to raise awareness and develop assessment tools globally. Together, these efforts collect worldwide HS data, filling knowledge gaps and comprehensively enhancing patient care (27,208,209).

3. Policies

Several healthcare policy changes could help address the unmet needs of patients diagnosed with HS. These include:

- A. Patient Education and Awareness: Healthcare policies should support initiatives aimed at increasing public and healthcare provider awareness about HS. This can involve educational campaigns, continuing medical education programs, and resources that provide accurate information about the condition, its impact, and available treatments.
- B. Insurance Coverage for HS Treatments: Policies should ensure that necessary HS treatments, including

medications, wound care supplies, and surgical interventions, are covered and reimbursed by healthcare insurance plans. With the advent of biologics as effective therapeutic options, policies should provide access to biosimilars when biologics are expensive regardless of insurance status. This would alleviate the financial burden on patients and facilitate timely access to appropriate care.

- C. Improved Access to Specialized Care: Healthcare policies should prioritize increasing access to healthcare professionals familiar with HS, such as dermatologists or wound care specialists. This can be achieved by ensuring an adequate number of specialists in underserved areas, offering training programs for healthcare providers to recognize and manage HS, and implementing telemedicine services to reach patients in remote locations.
- D. HS Management Guidelines: Developing evidence-based management guidelines for HS can guide healthcare providers in diagnosing and treating the condition effectively. These guidelines can help standardize care practices, reduce misdiagnosis and inappropriate treatments, and improve overall outcomes for patients.
- E. Disability Recognition: HS can significantly impact patients' ability to work or attend school due to pain, mobility issues, and associated comorbidities.^{13,65} Recognizing the impact of HS on work/school productivity

and providing appropriate accommodations, such as medical leaves and workplace adjustments, would help support patients in maintaining employment and education.

- F. Integrated and Interdisciplinary Care: Policies should encourage the establishment of interdisciplinary care teams that include dermatologists, wound care specialists, mental health professionals, and other relevant healthcare providers. This integrated approach can address the complex physical, psychological, and social aspects of HS, leading to improved patient outcomes and quality of life.
- G. Research Funding: Policies should prioritize research funding for HS to advance understanding of the disease, identify novel treatment strategies, and explore the underlying mechanisms. This would contribute to evidence-based care and facilitate the development of more effective therapies for HS.

(67,113)

The lack of comprehensive and consistent epidemiological data on HS poses potential challenges in awareness-building and resource distribution from policymakers. GHiSA's primary objective is to collect vital global prevalence data, a pivotal step expected to enhance public health planning and enable more informed resource allocation. This effort plays a critical role in shaping healthcare policies pertaining to HS, both nationally and internationally.

By advocating for people diagnosed with HS, GHISA also advances initiatives that improve access to care, support patient education, and prioritize HS patient needs in healthcare decision-making. Implementing the proposed healthcare policy changes would enhance the care and support provided to people diagnosed with HS, reducing barriers to access, improving treatment options, and ultimately improving their quality of life.

4. Health Services

The responsibility for enhancing health services for patients diagnosed with HS rests with the healthcare system. While it is true that healthcare systems vary across different geographical regions, the following improvements apply universally.

1. Healthcare professionals require improved education and training programs to enhance their understanding of HS, encompassing diagnosis and management. Access to specialized care, including dermatologists, wound care specialists, and mental health professionals specializing in HS, must be ensured, and can be facilitated through telehealth, enabling remote consultations and providing educational resources for HS patients' self-management. Raising awareness among obstetrician-gynecologists regarding the prevalence of HS in Western women and training advanced practice providers to recognize key clinical signs and diagnostic criteria in regions with limited dermatologist access can significantly reduce misdiagnosis and improve HS care globally (113,210).

2. GHISA is dedicated to improving HS healthcare through a patient centered approach, involving patients in decision making and addressing their unique needs. To achieve this, GHISA promotes integrated care models and collaborates with healthcare providers to establish specialized clinics. Globally, creating standardized guidelines for diagnosis, treatment, and management can help to ensure consistent, evidence-based care, enhancing the overall HS healthcare experience.
3. It is important to establish robust data collection systems and patient registries to gather standardized information about HS, facilitating research and informing policy decisions. One such example is the GHISA project.
4. Comprehensive patient support programs should be offered, including educational resources, self-management tools, and psychosocial support to help patients cope with the challenges of diagnosed with HS.

At its core, advocating for systemic policy changes and increased funding is necessary to support HS research endeavors, awareness campaigns, and the development of specialized HS clinics and services. By implementing these systemic changes, the healthcare system can better address the unmet needs of HS patients, improve access to care, enhance provider knowledge and collaboration, and promote patient-centered approaches in HS management.

5. Clinical Care

Despite their proximity to healthcare facilities, patients residing in urban and suburban areas encounter significant challenges in accessing suitable treatment. This issue is echoed by healthcare providers in both European and American contexts, as revealed in their expressions of dissatisfaction regarding current therapeutics and pain management during semi-structured interviews (171). Additionally, the diagnosis of HS outside dermatological settings remains problematic, with only 51.5% of emergency physicians accurately diagnosing the condition in a sample of 132 Danish physicians, often misidentifying it as bacterial infection/furunculosis (201,202). This highlights the necessity for additional clinical diagnostic tools in non-dermatological settings to increase awareness and improve the diagnosis of HS.

In response, GHISA adopts a patient-centered approach, aiming to enhance HS patients' quality of life by improving condition and comorbidity management. Recognizing the profound impact of HS on patients' lives, including employment, GHISA emphasizes the importance of holistic and comprehensive evidence-based care addressing both physical and mental health burdens (13,170). This approach not only involves providing comprehensive medical support but also focuses on building strong physician-patient relationships, essential for patient trust and willingness to seek care (113).

Addressing the General Perception of Hidradenitis Suppurativa

Destigmatizing HS

Some misconceptions of HS include perceiving HS to be contagious, sexually transmitted, or due to poor hygiene. Surveys of non-HS patients in South Asia revealed social biases related to HS; some participants would not hire, date, or marry someone with the condition (32). The social discrimination experienced by individuals with HS contribute to the psychosocial burdens and impairment of patient's quality of life associated with the condition (111,198,205). Destigmatizing HS begins with improving public awareness about the disease. Helping employers, family, and friends understand the impacts of HS on people's lives may help to reduce negative perceptions towards HS and ameliorate the lives of HS patients. In addition, clinicians can work to limit disfigurement due to disease and surgery and decouple HS from tobacco smoking and obesity in patient education and care. Taken together, these changes will help to minimizing patient shaming.

Increasing Awareness of HS Among General Public

Industry partners, HS foundations, dermatologic societies, and disease-specific nonprofit advocacy groups all work to increase global awareness of the disease and advocate for the needs of patients. For example, the Hidradenitis Suppurativa Foundation gathers

plain language summaries of recent publications in the field to educate patients about HS. Other advocacy groups include the Canadian Hidradenitis Suppurativa Foundation, European Hidradenitis Suppurativa Foundation, Asia Pacific Hidradenitis Suppurativa Foundation, EADV Task Force on HS, and global patient alliances (GlobalSkin, HS Australia, and Association Française pour la Recherche sur l'Hidrosadénite). The HS Awareness week, a global event held annually in June, provides an additional avenue to highlight HS and increase universal recognition of the condition. In addition to these organizations, patient support groups can work with investigators to advance research and provide community and emotional support for patients living with the condition.

Educating Medical Professionals about HS

Multiple studies have reported general lack of understanding of HS by medical professionals, resulting in underdiagnosis and misdiagnosis, and inappropriate treatment recommendations (113,171,173–175,202,203,211). To address this, industry partners and HS foundations have launched HS provider awareness campaigns to disseminate knowledge about HS care and management. One example includes the HS Foundation's partnership with leaders in academia to develop continuing medical education program on HS for all healthcare professionals (212). For other healthcare systems across the world, development of accredited continual medical education

programs on HS for healthcare professionals across specialties may help to improve management of HS (213). The American Academy of Dermatology is working on HS guidelines development and the European HS Foundation has developed treatment guidelines for HS, which the aim to improve the likelihood of timely and appropriate HS management (41,138,214).



Figure 16. Single perianal lesion

Conclusion

This chapter discusses the gaps, barriers, and needs in understanding the global epidemiology of HS, a chronic skin condition. Key gaps include the lack of consensus on HS prevalence worldwide, diagnostic delays, limited understanding of prevalence by sex, race, and ethnicity, and insufficient data on comorbidities. To address these gaps, the Global Hidradenitis Suppurativa Atlas (GHISA) project was initiated. GHISA aims to gather systematic and prospective HS prevalence data from approximately 50 countries across 6 continents in the Global Prevalence Study (Phase 1). This data will serve as the basis for developing core criteria for future epidemiological studies (Phase 2). Phase 3 of GHISA involves conducting additional epidemiological studies on HS, investigating phenotype, genotype, environmental factors, lifestyle habits, and comorbidities.

The chapter also emphasizes the importance of a patient-centered approach in addressing the healthcare needs of individuals with HS. It discusses the Patient-Centered Healthcare System Model proposed by the World Health Organization (WHO), which highlights stakeholder involvement in improving patient care. We highlight the importance of research, policy development, and public campaign efforts to increase public awareness and destigmatize HS.

Overall, there is a need for collaborative efforts among researchers, healthcare providers, patients, and advocacy groups to bridge the knowledge gaps, improve care access, and enhance the quality of life for individuals diagnosed with HS.

Chapter 6:

Conclusions and considerations

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Prof. Veronique del Marmol, Bente Villumsen**

Considerations for the World Health Organization

- HS is a chronic skin disease with an important impact on the lives of patients and family members, and substantial financial implications for individuals and societies. The severity of the disease-burden of HS should be recognized.

Considerations for governments and policymakers

- People with HS should have access to affordable professional medical care and individually adapted treatment.
- It is essential that HS patients are diagnosed as early as possible. Early diagnosis and appropriate therapy give the best chance to prevent patients from unnecessary suffering, uncontrolled disease, irreversible scarring and disability, with a positive effect on mental health and societal costs of the disease.
- Current disparities in access to care and access to treatment, (inter)nationally or within national jurisdictions and (sub)populations, should be addressed and resolved.
- Medications on the current WHO Model List of Essential Medicines, including systemic therapies, are the bare minimum of what should be available for the treatment of HS.
- Information and education on HS should be provided to work towards increasing public awareness and reducing stigma, exclusion, and discrimination (e.g., through campaigns and educational programs).
- Patients' organizations should be recognized, enabled, supported and be consulted in policy decision making.
- At a minimum, public and private facilities should provide the drugs included on the WHO Model List

of Essential Medicines, including systemic therapies. Universal health coverage schemes should cover the costs of these treatments.

- For newer biological therapies, more needs to be done to reduce the price of these medicines, if they are to present a sustainable and affordable treatment option for patients with HS. Governments should take cost-effectiveness of treatment options into account when developing national guidelines.
- Optimum treatment of HS, and its comorbidities, require shifting to a model of people-centered and integrated health services, as outlined in the WHO global strategy on people-centered and integrated health services.
- Governments and non-governmental organizations should provide education on HS to health-care professionals, including undergraduate medical and nursing curricula and in-service training for physicians in primary care.
- There is a great need to raise awareness and knowledge about HS among general practitioners to increase early diagnosis and prevent disability.
- Governments also have a role in supporting HS research.
- Governments have a key role in reducing stigma and discrimination.

Considerations for health care systems and health care professionals

- Health care professionals' associations should develop (or adapt/adopt) and maintain clinical practice guidelines, according to the required methodology and in collaboration with patients.
- Health care professionals, especially clinicians working in primary health care, should be aware of HS, its management and its co-morbidities.
- Health care professionals' associations should provide (online) training for physicians from low- and middle-income countries to ensure adequate diagnosis and treatment of HS.
- Health care professionals' associations should collaborate with patients' organizations, (e.g. by serving on their Medical Advisory Boards) to help achieve shared goals.
- Health care professionals' associations should encourage and support the formation of patients' organizations where currently none exists.
- Health care providers should be given the appropriate time, training, and resources to educate people with HS and their carers in lay language about treating and managing the disease.
- Associations of medical specialists have a role in seeking consensus on the classification of HS and

standardization of the collection of epidemiological data using a unified methodology.

- Health care providers should implement health care delivery strategies such as remote and on-demand care, to address issues of capacity and travel distance, preferably in collaboration with patients.
- Every person with HS should be treated as whole, and not just their skin, with consideration of the wider burden of skin disease on everyday life.
- The principle of shared decision-making should be followed (e.g., discussing the patients' beliefs, lifestyle and preferences when deciding on a treatment plan).
- People with HS and their carers should receive adequate information, resources, and support.
- When resources allow, people with HS who have co-morbidities should be treated by multi-disciplinary teams of specialists, including dermatologists, rheumatologists, psychologists, psychiatrists, plastic surgeons, gastrointestinal surgeons, gynecologists, and others.

Considerations for patients' organizations and civil society

- Patients' organizations should continue advocating for the rights of people with HS and their families, addressing issues such as social isolation, discrimination, exclusion, and stigma.
- Patients' organizations should be involved in raising public awareness of HS preferably in collaboration with governments, policymakers, and health care professionals' associations.
- Patients' organizations (especially local) should have a key role in providing (local) support to people with HS and their caregivers and should facilitate (online) platforms for mutual communication and recognition.
- Patients' organizations should have a role in holding governments and policymakers to account regarding their plans and commitments and should be able to challenge policies where appropriate.
- Patients' organizations should be able to collaborate with health care professionals' associations in the development of clinical practice guidelines, health technology assessments, and other formal policies regarding the care and treatment of HS.
- Patients' organizations have a responsibility to encourage the formation of patients' associations where currently none exists.
- Patients' organizations and civil society have a key role in holding governments and policymakers to account on global commitments, and in fighting discrimination of people with HS.

Priority areas for research

- Research should be conducted in partnership with patients, to ensure outcomes are meaningful to the lives of people with HS.
- Research should make use of the defined Core Outcomes for Trials for HS to provide robust evidence that can be compared between trials and enable evidence synthesis in systematic reviews and meta-analyses.
- Researchers should investigate the etiology of HS and therapies to prevent as well as to manage the symptoms of the disease. It is vital to create low-cost effective treatment options that can be made widely available.
- Research on new treatments should focus on options which can be applicable globally, on a large scale.
- Academia and independent funding bodies should address research topics that are of less commercial interest and focus on improving the evidence base on the prevention flares of HS, the development of comorbidities, and benefits and harms of existing therapies.
- When not carried out by the pharmaceutical industry, academia and independent funding bodies should conduct robust clinical trials comparing active treatments and establish the added value of each treatment to position them in treatment algorithms within clinical practice guidelines.
- While clinical trials are intended to show efficacy of an intervention (e.g., compared to placebo or another active treatment) real-world data from patient registries is essential to demonstrate effectiveness and adverse events on a larger scale, with more long-term patient follow up. Therefore, collection of real-world data on HS needs to be supported, encouraged, and ideally internationally harmonized in terms of outcomes measured.
- Academia should ensure the results of fundamental research are implementable within standard care and be of added value to the shared decision-making process around treatments for HS.
- The pharmaceutical industry should acknowledge the importance of including patients in their research and development programs.
- The pharmaceutical industry should also focus on mild-to-moderate HS as there is currently a gap. In doing this, the appropriate products should be marketed, available and affordable.
- A key area of health-care research is the epidemiology of HS and its incidence and prevalence at the global level. Research methods need to be harmonized and reflect cultural as well as geographical

Patients closing words – a global united voice

A crucial role in planning the future of HS management includes listening to those that live with HS. Throughout this report and in the following section we turn our focus to the narratives of the patients. Through their quotes, we aim to highlight the severe implications, profound stigmatization, and the urgent need for global recognition of HS.

Patients with HS suffer from pain, fatigue and the discomfort from drainage and struggle with unpredictable flares.

...constant pain and drainage. Always planning around my HS.

...challenges getting out of bed with muscle aches and fatigue... even driving hurts from flares in the lower are...

...The pain can make showering very challenging – simply because the HS flares under my arms can be so painful to raise my arms...

HS is exhausting. Constant ups and downs.

Just when you think you have mastered your HS – it pops up in a different area...

A negative self-image results from the lesions, and from lack of knowledge, misconceptions, and negative reactions from others – even from some health care professionals.

I struggle to see the beauty in myself every day.

So many are just uninformed. They put us in a box – stds, gross, unhygienic...

People see HS as a nasty condition. People with HS stink and are lazy...

I've faced discrimination in doctor's office... I felt like the surgeon was pushing me off trying his hardest to get me out of his office...

...she thought I was contagious and told me to get out.

Another common misconception about HS is that only people who are overweight can have it.

All aspects of life are impacted. Education, work life, family, relationships, marriage, parenting – planning around having HS and adjusting to it is demanding and reduces possibilities in life.

At my previous employer, I was asked if I actually work, because I was having so many flare-ups. I've been on disability for a few years now.

...having to do everything differently from working jobs to interacting with friends and family, the way I have to clean wounds, what I eat...

...many days I have to cancel plans with friends or family members because the HS flares are too painful, and the fatigue has gotten the best of me.

Sexually, HS has impacted that part of my life. Even my marriage. The physical limitations as a parent seem to be the hardest for me currently.

I was afraid to sit down in front of people because HS flares on my buttocks would constantly leak and leave a wet spot on the chairs.

Access to care and treatment is a challenge, and many patients don't get any treatment.

Can't afford it

Insurance not accepting certain treatments and having to pay out of pocket for wound supplies.

No health insurance, expensive co pays. Never seen a specialist.

Coping strategies often include distracting our minds, adjusting our diet, and eating healthy, reducing stress and activity levels. Support through the HS patients' community is important and makes us feel less alone.

Writing music helps me cope with the anxiety and depression.

I like to play videos to distract my mind from the pain of the HS flares.

I try to "not care about it."

I am overwhelmed with love in the community I have.

Find an online community of fellow HS warriors for emotional support. They will understand what you're truly going through with HS.

Patients with HS request action for recognition of the disease and for better treatment. Across the globe we share the experience of pain, stigmatization, and the struggle for diagnose and treatment.

“

There are too many suffering, when they do not deserve to!

HS Patient

”

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