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Global consensus process to establish a core data set for hidradenitis suppurativa registries

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AM is a member of the EHSF. AM has acted as a 16 consultant, advisory board member, and investigator and has received honoraria from Novartis, 17 AbbVie, Janssen Cilag, UCB, Lilly, LEO Pharma, L´Oreal, Sanofi, Sandoz, Galderma and Amgen

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HHO has received speaker's honorarium from AbbVie, Eli Lilly, Galderma, Janssen, LEO Pharma and Novartis, advisory board membership from Boehringer Ingleheim, and has been a researcher for Novartis and Pfizer.

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Key words: hidradenitis suppurativa, registry, core set

Plain language summary

Hidradenitis suppurativa (HS) is a condition that causes painful, red swellings in the skin folds (armpits, groin, under the bust and buttocks). It occurs in about 1% of people globally.

A registry is a collection of information focused on a specific disease which follows people over time. Registries for HS already exist in some countries around the world. This study looks to identify the key items of information that should be included when creating a registry of patients with HS. This includes covering data about age and sex, other diseases that can occur at the same time as HS, changes to the skin on examination, patient-reported outcome measures and the effects of treatment.

Online surveys were sent to 20 participants from eight countries, including both doctors and patient representatives. Four rounds of surveys were conducted until consensus was reached on which items were essential to include. Initially, 47 items were included and participants were given the option to suggest additional items in the first round.

The final set of 48 items reached agreement with at least 70% of participants voting for them to be included.

This work is important because unless registries agree on core items to include then the data from different registries cannot be combined, which is needed to answer research questions that require a lot of participants.

Abstract

Background

Several registries for hidradenitis suppurativa (HS) already exist in Europe and USA. There is currently no global consensus on a core dataset (CDS) for these registries.

Creating a global HS registry is challenging due to logistical and regulatory constraints, which could limit opportunities for global collaboration due to differences in the dataset collected. The solution is to encourage all HS registries collect the same CDS of information, allowing the registries to collaborate.

Objectives

To establish a core set of items to be collected by all HS registries globally. The core set will cover demographic details, comorbidities, clinical examination findings, patient-reported outcome measures and treatments.

Methods

Beginning in September 2022 twenty participants including both clinicians with expertise in HS and patient advocates in eight countries across three continents participated in a Delphi process consisting of four rounds of voting, with all participants completing each round. A list of potential items for inclusion in the core set was generated from the relevant published literature, including systematic reviews into co-morbidities in HS, clinical and examination findings, and epidemiology. For disease severity and progression items, the HIdradentitis SuppuraTiva Core outcome set International Collaboration (HISTORIC) core set and other relevant instruments were considered for inclusion. This resulted in 47 initial items. Participants were invited to suggest additional items to include during the first round.

Anonymous feedback was provided to inform each subsequent round of voting to encourage consensus.

Results

The eDelphi process established a CDS of 48 items recommended for inclusion in all HS registries globally.

Conclusions

The routine adoption of this CDS in current and future HS registries should allow registries in different parts of the world to collaborate, enabling research requiring very large numbers of participants.

Bulleted statements

What is already known about this topic?

- Several registries for hidradenitis suppurativa (HS) already exist but there is no consensus on a core dataset (CDS)
- Creating a global HS registry is challenging due to logistical and regulatory constraints.
- Heterogeneity in recording of outcomes in a disease has been shown to hinder the comparison of results and pooling of data.

What does this study add?

- Our study provides a global consensus on a CDS to include in all HS registries worldwide, including demographic details, comorbidities, clinical examination findings, patient-reported outcome measures and treatments.

What are the clinical implications of this work?

- The routine adoption of the CDS in current and future HS registries will allow collaborative pooling of results on a project-by-project basis, enabling research requiring large sample sizes.

Global consensus process to establish a core data set for hidradenitis suppurativa registries.

Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition presenting with recurrent painful nodules, abscesses, and tunnelling predominantly in flexural sites.[1] The disease burden can be very high and can profoundly affect the quality of life of patients and their families.[2-4] It has a prevalence of approximately 1% globally.[5-9]

Many medical and surgical interventions have been tried for HS including topical treatments, systemic antibiotics, retinoids, systemic immunosuppressive agents, and biologics. Non-medical interventions include laser therapy, deroofing procedures and regional excisions of the affected areas. There are limited data to support many of these treatment modalities and more research is required in this area.[10]

Registries for a disease allow prospective collection of real-world data, providing a larger dataset and longer-term follow up when compared with relatively short randomised controlled trials with an explanatory rather than pragmatic design.[11] A pragmatic trial is defined as one which evaluates efficacy of a treatment in routine clinical practice compared to an explanatory trial where a treatment is evaluated in ideal conditions. Registries provide a database of individuals containing clearly defined sets of health and demographic data collected for a specific public health purpose.[12] Registries were initially created to collect epidemiological data but have now been applied diversely in disease prevention, pharmacovigilance, treatment efficacy, screening and healthcare planning.[11]

Several registries for HS already exist in Europe and the USA. [13-16]Creating a global HS registry is challenging due to logistical and regulatory constraints, which could limit opportunities for global collaboration due to differences in the dataset collected. One solution is to encourage all HS registries to collect the same core dataset (CDS) of information allowing the registries to collaborate. Heterogeneity in recording of outcomes in a disease has been shown to hinder the comparison of results and pooling of data, which may be needed to provide the large datasets for projects such as genetic studies and to investigate rare adverse effects of treatments.[17] The development of an internationally agreed core set of variables is essential as indicated by the guideline of the European Commission-funded PAtient REgistries iNiTiative joint action (PARENT JA).[18] Within HS, a core

domain set exists for clinical trial outcomes from the Hidradenitis Suppurativa Core Outcomes Set International Collaboration (HISTORIC) initiative.[19] There may be crossover between the core set for trials and the CDS for a registry, however the registry needs to consider data beyond clinical outcomes, such as comorbidities, and some outcome instruments may be too time consuming for use in a registry setting.

The CDS does not seek to control the information collected by each individual registry; it simply defines the subset of essential items recommended for collection in HS registries. To be successful, minimising the burden on registry participants and study staff, the CDS should be as concise as possible, while not omitting information that is essential. Our goal was to establish a CDS of items to be collected by all HS registries globally which covers demographic details, comorbidities, clinical examination findings, disease severity, progression, and treatments.

Methods

Study design

To establish a CDS an online Delphi exercise (subsequently referred to as eDelphi) was conducted.

The technique for an eDelphi comprises sequential questionnaires that are answered anonymously by participants with relevant expertise. After each questionnaire, the group responses are fed back to participants. Bias is minimised as responses are anonymised and there is no issue with participants being influenced by other members of the group who may dominate an in-person meeting setting. In subsequent rounds, participants have the option to keep or change their opinion and gradually a consensus evolves as the range of answers decreases and the group's opinions converge.[20]

Information sources

A list of potential items for inclusion in the core set was generated from the relevant published literature, including systematic reviews of co-morbidities in HS, clinical and examination findings, and epidemiology.[3,7,21,22] For disease severity and progression items, the HIdradentitis SuppuraTiva Core outcome set International Collaboration (HISTORIC) core set and other relevant instruments were considered for inclusion. [7,19,22-27]

Ethics

No ethical approval was required because participants were either clinicians or patient advocates, providing their opinions only.

Participants

For a CDS to have validity it is recommended that multiple stakeholder groups are included, and that patient participation is pivotal. [28] [29] Participants were invited from two stakeholder groups: healthcare professionals (HCPs) and patient advocates.

Patient representatives were identified through patient associations and via dermatologists with a specialist interest in HS in countries where no formal patient association existed.

HCPs were identified as dermatologists with a special interest in HS. They all had at least five years of experience in managing patients with HS and had multiple publications in the field.

All participants who were invited to participate agreed to take part in the process and are listed as authors on this paper.

Methods to reach consensus on the core domain set

The eDelphi questionnaire was created using surveys.ac.uk and was distributed via email in September 2022. The questionnaire was piloted prior to distribution by being sent to two dermatologists with an interest in HS research, who had previously taken part in multiple eDelphi processes, who were invited to provide feedback. No changes were recommended by this pilot.

Each respondent was given a unique identifier number to avoid submission of personal information, while ensuring only one submission was received from each participant. During the first round the details of the study and key objectives were outlined. Subsequent rounds reiterated the key objectives and explained the items that had already reached consensus in previous rounds. Participants were provided with histograms summarising the spread of results for each item from the previous round, allowing them to compare their answer with the rest of the group to encourage consensus. The full consensus process is illustrated in figure 1. Provision was made for a potential in-person consensus meeting if items proved contentious and consensus by eDelphi was not possible, however this option was not required.

Item scoring

Participants were asked to use a 9 point Likert scale for each item where one was “strongly disagree with inclusion” in the core set for HS registries and nine was “strongly agree with inclusion”. A score of zero was also available for those that were unsure. Responses of unsure were excluded from the summary of results provided to participants in subsequent eDelphi rounds.

Definition of consensus

The definitions of consensus were defined *a priori*. The pre-defined criterion for inclusion was for at least 70% of respondents to score at least seven for the item. The pre-defined criterion for exclusion was for at least 70% of respondents to score one to three. Any other results were defined as no consensus being reached.

To reduce the risk of attrition bias, all participants were reminded in each round of the importance of completing all rounds of the eDelphi process. Reminder emails were sent to any non-responders.

E-Delphi round one

The items in round one covered demographics, comorbidities, clinical examination findings and disease severity/ progression. 47 items were included in this round. A glossary of terms was provided to all patient representatives (Supplementary table 1). The glossary was created using a review of the literature.

In round one, participants were given the option of suggesting additional items to be included in the dataset. These items were reviewed by the project steering committee to ensure they represented new items, and all unique suggested items were put forward for consideration in round two.

E-Delphi round two

In round two, all items that reached consensus in round one were omitted from further voting and a list of these items was provided at the end of the survey. For existing items that did not reach consensus in round one a histogram depicting the anonymous distribution of scores in round one was provided. For items receiving predominantly low scores, the option to exclude the item was provided with a yes/no/don't know option. The new items suggested at the end of round one were explained in the introduction to round two and included for consideration. Where items were similar or overlapping, for example measurement of current pain or worst pain in the last 24 hours, the option was given to use one instead of the other.

E-Delphi rounds three and four

In rounds three and four participants were asked to review items that were close to consensus in conjunction with a histogram showing the distribution of results from the previous round. For items further from consensus the option to remove the item was provided.

Results

Participants

In total four patients and 16 clinicians, the latter including experience with paediatric patients and use of surgery, were included in eight countries across three continents (Table 1). All 20 participants contributed to each of the four rounds of the eDelphi process, achieving a 0% attrition rate.

Outcome scoring and feedback

A list of the 47 items initially included in the eDelphi exercise is shown in Table 2. Eight novel items were suggested by participants and were all considered valid items for consideration (Table 3). Seven items were excluded via the process(table 4 and table 5).

The final core domain set

The eDelphi process established a core set of 48 items recommended for inclusion in all HS registries. The core set is illustrated by eDelphi round in Table 4 and the final core item set broken down into subdomains is shown in Table 5.

Changes to original plan

Provision was made for a consensus meeting at the European HS Foundation annual conference in 2023, however consensus was reached on all items without a face-to-face meeting by the addition of a fourth round of eDelphi.

No items reached the predefined criteria of 'consensus out'. To ensure that the core set was as concise as possible, items with low levels of support in the previous survey round were highlighted for potential omission with use of a yes/no question for exclusion.

Discussion

We used a rigorous, iterative, and inclusive approach to achieve consensus among an international group of HCPs and patients with expertise in HS. While keeping participants engaged with an eDelphi process can be challenging, all 20 participants provided comprehensive answers across all four eDelphi rounds, hence avoiding attrition bias. All stakeholders were in close agreement with the final CDS. The 0% for attrition illustrates the willingness of both HCPs and patients to support research in HS to improve health outcomes despite no incentives being offered.

Adopting a minimum CDS for all global HS registries allows collaboration between registries for projects such as genome-wide associated studies, phenotype-genotype correlation, and biomarker studies, where large patient numbers may be needed. Table 4 lists the final global core dataset for

HS registries divided into six subdomains: demographics, comorbidities, associated diseases, clinical examination, patient-reported outcomes, and treatment.

The Eumelanin Human Skin Colour Scale, a new five point standard nomenclature for physicians to describe human constitutive skin colour, published in 2022, achieved consensus in the first round. The rapid consensus for this item highlighted the increased understanding and recognition of better representation of patients with skin of colour in research projects.[31,32]This is important because HS is thought to be particularly prevalent in African American and other non-White populations based on epidemiological studies.[33] These studies have not been reproduced comprehensively in data from the global South as yet and questions regarding genetic and environmental factors remains, however the Global Hidradenitis Suppurativa Atlas (GHISA) project is coordinating a worldwide prevalence study.[34,35]

HS is established as a multi-system disease and the inclusion of multiple co-morbidities in the CDS shows recognition of this.[3,36] By collecting data on these co-morbidities and especially those disease associations relevant to phenotyping we can better understand the disease and its subtypes in the future. The ultimate aim is to identify patients who will respond best to a particular intervention, providing personalised therapy, and to identify those patients whose disease may rapidly progress and so require early intervention with the most effective therapies.

Clinical examination findings included in the CDS highlight that some features of the disease, such as cribriform scarring, might be indicators of disease severity and rapid progression and further data collected through registries on these elements will aid prognosis predictions in the future.[37]

Fatigue as a symptom in HS has not been widely investigated, however it is included along with drainage in the HiSTORIC symptom domain for HS trials.[19] Incorporating it in the CDS as a patient reported outcome both recognises its importance to patients with HS and also allows data to be collected to research the impact of fatigue in HS.[38]

Whilst we lacked representation from Africa and South America we did have representation from eight countries in three continents and we included participants from all regions with an existing registry. This wide representation strengthens our recommendations and importantly patients were actively involved throughout the process. All stakeholders have been encouraged to endorse the recommendations of the CDS as it will only be impactful if consistently implemented.

Future work includes creation of a UK and Ireland HS registry which will incorporate the CDS. This will allow piloting of the dataset to ensure it is feasible from a patient perspective and does not overburden colleagues working in busy clinical settings.

In conclusion, we present a global CDS for HS with the intention to be adopted by all registries worldwide to allow pooling of registry data globally to help answer important research questions which remain in HS that require very large sample sizes.

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Tables and figures

Figure 1: Study summary illustrating the eDelphi process

Table 1: Participant demographics

Variable	**Frequency n=20**	**Percentage**
Gender		
Male	11	55%
Female	9	45%
Dermatologist	16	80%
Patient advocate	4	20%
Geographical origin		
USA	5	35%
Netherlands	3	15%
Denmark	3	15%
UK	2	10%
Ireland	2	10%
Spain	1	5%
Singapore	2	10%
Australia	1	5%

Table 2:Initial items included in round 1

Area	***Items included***
Demographics	*Sex*
	Age
	Race (Eumelanin human skin colour scale)
	Smoking status
	Body mass index
	Waist circumference (part of metabolic syndrome)
	Family History of HS in 1st degree relative
	Socioeconomic status
	Date of onset
	Date when diagnosed with HS
Comorbidities	*Type 2 diabetes mellitus*
	Hypertension

	Dyslipidaemia
	Cardiovascular disease (ischaemic heart disease and/or cerebrovascular disease)
	Depression
	Anxiety
	Crohn disease
	Ulcerative colitis
	Psoriasis (including chronic plaque, flexural, paradoxical secondary to biologic therapy)
	Inflammatory arthritis (ankylosing spondylosis, rheumatoid arthritis, psoriatic arthritis)
	Polycystic ovarian syndrome
	Down syndrome
	Obstructive sleep apnoea
	Cutaneous squamous cell carcinoma linked to HS
	Pyoderma gangrenosum

	Syndromes: PASH (PG, acne conglobata and HS); PAPASH (pyogenic arthritis, acne, PG and HS); PASS (PG, acne vulgaris, HS and ankylosing spondylitis)
	Thyroid disease
	Renal amyloidosis
	Non-alcoholic fatty liver disease
Comorbidities relevant to phenotyping	*Pilonidal sinus*
	Acne conglobate
	Acne vulgaris
	Scalp folliculitis/ Folliculitis decalvans
Clinical examination findings	*Skin regions affected – Left/ right: axilla, breast/ chest, buttock, peri-anal/ perineal, groin/ medial thigh, genital, other (posterior neck, trunk, non-medial thighs)*
	Presence and location of folliculitis

	Presence and location of epidermoid cysts
	Presence and location of pyogenic granuloma type lesions
	Presence and location of open comedones
	Hurley stage in each affected region
	Refined Hurley staging
	Investigators global assessment
	Patient global assessment
	HiSQOL – 17
	HiSQOL – mini
	Dermatology Life Quality Index (DLQI)
	Current pain Numerical Rating Scale (NRS) 0-10
	Total drainage Numerical Rating Scale (NRS) 0-10

Table 3: Additional items added in round 2

Additional items suggested by participants
Worst pain in the last 24 hours
Inflammatory nodule and abscess count
Inflamed tunnels count
Cribriform scarring
Current medical and surgical treatment
Previous medical and surgical treatment (recorded at baseline)
Odour Numerical Rating Scale (NRS) 0-10
Fatigue (instrument to be decided)

Table 4: Items that reached consensus in or were excluded by eDelphi round

Round	Items reaching consensus	Items excluded
1	• Sex • Age • Race (include Eumelanin human skin colour scale) • Smoking status • Body mass index • Family history of HS in a 1st degree relative • Date of onset • Date when diagnosed with HS • Type 2 diabetes mellitus • Hypertension • Dyslipidaemia • Cardiovascular disease (ischaemic heart disease and/or cerebrovascular disease) • Depression • Anxiety • Crohn Disease • Ulcerative colitis • Psoriasis (including chronic plaque, flexural, paradoxical secondary to biologic therapy) • Inflammatory arthritis (ankylosing spondylosis, rheumatoid arthritis, psoriatic arthritis) • Polycystic ovary syndrome • Cutaneous squamous cell carcinoma linked to HS • Pyoderma gangrenosum • Syndromes: PASH (PG, acne conglobata and HS); PAPASH (pyogenic arthritis, acne, PG and HS); PASS (PG, acne vulgaris, HS and ankylosing spondylitis) • Pilonidal sinus • Acne conglobata • Acne vulgaris • Scalp folliculitis / folliculitis decalvans • Skin region affected – Left/ right: axilla, breast/ chest, buttock, peri-anal/ perineal, groin/ medial thigh, genital, other (posterior neck, trunk, non-medial thighs) • Presence and location of open comedones (pores) • Hurley stage in each affected region • Investigator global assessment (HS-IGA) (ref=24) • HiSQOL-17 • Dermatology Life Quality Index (DLQI) • Current pain Numerical Rating Scale (NRS) 0-10 • Total drainage Numerical Rating Scale (NRS) 0-10	

2	• Down syndrome • Anaemia • Patient global quality of life assessment (ref=25) • HiSQOL-Mini • Inflammatory nodule and abscess count • Tunnel count • Current medical and surgical treatment • Previous medical and surgical treatment (recorded at baseline) • Presence and location of folliculitis • Epidermoid cysts	• Amyloidosis
3	• Metabolic syndrome • Fatigue • Worst pain in last 24 hours Numerical rating scale 0-10	• Current pain Numerical Rating Scale (NRS) 0-10
4	• Non-alcoholic fatty liver disease • Refined Hurley staging • Cribriform scarring	• Socioeconomic status • Thyroid disease • Odour Numerical Rating Scale 0-10 • Pyogenic granulomas • Obstructive sleep apnoea

Table 5 : Final global core dataset for HS registries

Core dataset subdomain	
Demographics	Sex
	Age
	Race (Eumelanin human skin colour scale)
	Smoking status
	Body mass index
	Family history of HS in 1st degree relative
	Date of onset
	Date when diagnosed with HS
Comorbidities	Type 2 diabetes mellitus
	Hypertension
	Dyslipidaemia
	Cardiovascular disease
	Depression
	Anxiety
	Crohn Disease
	Ulcerative colitis
	Psoriasis
	Inflammatory arthritis
	Polycystic ovary syndrome
	Cutaneous SCC linked to HS
	Pyoderma gangrenosum
	Syndromes: PASH, PAPASH, PASS
	Non-alcoholic fatty liver disease
	Metabolic syndrome
	Down syndrome
	Anaemia
Comorbidities relevant to phenotyping	Pilonidal sinus
	Acne conglobata
	Acne vulgaris
	Scalp folliculitis / folliculitis decalvans
Clinical examination findings	Skin regions affected
	Hurley stage in each affected region
	Refined Hurley staging
	Inflammatory nodule and abscess count
	Draining tunnel count
	*Non-draining tunnel and non-inflammatory nodule count
	Presence and location of folliculitis
	Cribriform scarring
	Epidermoid cysts
	Presence and location of open comedones
Patient reported outcome measure	HiSQOL-17 (and HiSQOL-Mini subset of item
	Dermatology Life Quality Index (DLQI)

	Fatigue
	Worst pain in last 24 hours numerical rating (NRS) 0-10
	Total drainage NRS 0-10
	Patient global quality of life assessment
Current/ previous treatment	Current medical and surgical treatment
	Previous medical and surgical treatment

SCC = squamous cell carcinoma. PASH = pyoderma gangrenosum (PG), acne conglobata and hidradenitis suppurativa (HS). PAPASH = pyogenic arthritis, acne, PG and HS. PASS = PG, acne vulgaris, HS and ankylosing spondylitis. *Note non-draining tunnel and non-inflammatory nodule count is for HS Investigator Global Assessment (HS-IGA).

Supplementary table 1: Glossary of terms used in eDelphi surveys

Acne conglobata	A severe form of acne associated with lots of deep cysts in the skin
Amyloidosis	A group of rare, serious conditions caused by a build-up of an abnormal protein called amyloid in organs and tissues throughout the body
Anaemia	Low blood count
Ankylosing spondylosis	An inflammatory condition of the spine
Axilla	Armpit
Cerebrovascular disease	The medical term for disease of the brain blood supply for example a stroke
Comedones	Blocked hair follicles
Crohn Disease	An inflammatory disease of the small and large intestines
Cutaneous	Related to the skin
Down syndrome	A genetic disorder due to an extra chromosome 21 associated with developmental delay and multiple other medical problems
Dyslipidaemia	Blood lipid levels that are too high or low. Blood lipids are fatty substances, such as triglycerides and cholesterol
Epidermoid cysts	Cysts occurring on the skin surface
Folliculitis decalvans	Chronic inflammation of the scalp hair follicles
HbA1c	The HbA1c test shows the average level of blood glucose (blood sugar) over the past 3 months
Hurley Stage	A three-point scoring system for HS severity, mild moderate, severe
Inflammatory arthritis	Inflammation of the joints
Ischaemia heart disease	The term is given to heart problems caused by narrowing of the heart arteries
Medial	Towards the middle of the body
Non-alcoholic fatty liver disease	A group of conditions related to the deposition of fat in the liver
Obstructive sleep apnoea	When breathing during sleeping stops and starts due to relaxation and narrowing of the walls of the throat
Phenotype	Observable physical features in an individual
Pilonidal sinus	A small hole or tunnel in the skin at the top of the buttocks
Polycystic ovary syndrome	Multiple small cysts in the ovaries associated with irregular periods, acne and excess hair growth
Posterior	At the back of the body
Psoriasis	Inflammatory skin disease causing raised, scaly areas often on the elbows, knees and scalp

Psoriatic arthritis	An inflammatory condition of the joints linked to psoriasis
Pyoderma gangrenosum	An inflammatory skin disorder causing open skin sores (ulcerations). The size and depth of the ulcerations vary and they are often extremely painful.
Pyogenic arthritis	(Septic arthritis) A painful infection of a joint due to germs circulating in the bloodstream
Pyogenic granulomas	Small raised red bumps on the skin that may have a moist surface and bleed
Squamous cell carcinoma	A type of cancer linked to the overgrowth of squamous cells
Ulcerative colitis	An inflammatory disease of the large intestines