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5 **Title: Outcome Measures for the Evaluation of Treatment Response in Hidradenitis Suppurativa for**
6 **Clinical Practice: A HiSTORIC Consensus Statement**

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193
 194 **Abbreviations:**
 195 HS: Hidradenitis Suppurativa
 196 HiSTORIC: Hidradenitis Suppurativa Core Outcomes Set International Collaboration

197	PRP: Patient Research Partners
198	COS: Core Outcome Set
199	C3: CHORD COUSIN Collaboration
200	ClinRO: Clinician-reported outcome measure
201	PRO: Patient-reported outcome measure
202	CREDES: Conducting and Reporting of Delphi Studies
203	SQUIRE: Standards for Quality Improvement Reporting Excellence
204	HS-IGA: Hidradenitis Suppurativa Investigator Global Assessment
205	HS-PGA: Hidradenitis Suppurativa Physician Global Assessment
206	IHS-4: International HS Severity Score System
207	HiSCR: Hidradenitis Suppurativa Clinical Response
208	HiSQOL: Hidradenitis Suppurativa Quality of Life
209	HSIA: Hidradenitis Suppurativa Impact Assessment
210	HSSA: Hidradenitis Suppurativa Severity Assessment
211	

212 **Abstract**

213 **Importance:** Although several clinician and patient-reported outcome measures have been developed for
214 trials in hidradenitis suppurativa (HS), there is currently no consensus on which are best suited for use in
215 clinical practice. Identifying validated and feasible measures applicable to the practice setting has the
216 potential to optimize treatment strategies and generate real-world evidence that may inform treatment
217 guidelines.

218 **Objective:** To establish consensus on a core set of clinician and patient reported measures recommended
219 for use in clinical practice, and to establish the appropriate interval within which these measures should
220 be applied.

221 **Evidence Review:** Clinician and patient-reported HS measures and studies describing their psychometric
222 properties were identified through literature reviews. Identified measures comprised an item-reduction
223 survey and subsequent e-Delphi consensus rounds. In each consensus round, a summary of outcome
224 measure components and scoring methods was provided to participants. Experts were provided with
225 feasibility characteristics of clinician measures to aid selection. Consensus was achieved if at least 67% of
226 respondents agreed with use of a measure in clinical practice.

227 **Findings:** Among all stakeholders, response rates for item-reduction, e-Delphi I, and e-Delphi II survey
228 rounds were 74.6% (59/79), 93.2% (55/59), and 89.8% (53/59), respectively. In the final e-Delphi round,
229 HS experts and patient research partners (PRPs) agreed with use of the HS Investigator Global
230 Assessment (71.8%) and HS Quality of Life score (92.9%), respectively. The most preferred assessment
231 interval in which to apply these measures was 3-months (69.2%).

232
233 **Conclusions and Relevance:** An international group of HS experts and PRPs from HiSTORIC achieved
234 consensus on a core set of HS measures suitable for use in clinical practice. Consistent use of these
235 measures may lead to more accurate assessments of HS disease activity and life impact, facilitating shared
236 treatment decision making in the practice setting.

237 Introduction:

238 Among inflammatory skin diseases, hidradenitis suppurativa (HS) may be the most
239 heterogeneous in its presentation and disease course. There are several distinct morphologic lesions in
240 HS, including nodules, abscesses and tunnels. Patients experience a broad range of symptoms including
241 fatigue, drainage, odor, itch and most notably, pain. Disease course is rather unpredictable, as patients
242 experience flares in addition to chronic activity. Response to treatment is also highly variable, and few
243 therapies demonstrate consistently high and sustained efficacy.¹ Nearly half of HS patients express
244 dissatisfaction with their medical treatments.^{2,3}

245 In this context, assessment of disease activity and treatment response is also complex.
246 Standardized and regular application of outcome measures in clinical practice may facilitate bidirectional
247 discussion between the dermatologist and patient on whether treatment goals are being met and whether
248 timely adjustments to the overall therapeutic strategy may be warranted.⁴ This approach has led to
249 improved outcomes for patients with a number of chronic inflammatory diseases including rheumatoid
250 arthritis and psoriatic arthritis.⁵⁻⁷ Longitudinal recording of clinical outcomes may also support analyses
251 of real-world treatment effectiveness, which provides insights into treatment impact in the broader HS
252 population that clinical trial data cannot.⁸ Further integration of patient-reported measures allows capture
253 of treatment effect on symptoms and life quality, which patients may hesitate to discuss due to fear of
254 stigmatization⁹, and which may otherwise be underestimated by clinicians.¹⁰⁻¹² The objective of this study
255 was to provide expert and patient consensus-based recommendations on the application of validated, HS-
256 specific outcome measures that are feasible for clinical practice.

257 Methods

258 The Hidradenitis Suppurativa Core Outcomes Set International Collaboration (HiSTORIC) is an
259 international multi-stakeholder group comprised of experts, patient research partners (PRP),
260 methodologists, and industry partners with a background in health outcomes whose objective is to
261 develop a core outcome set (COS) for interventional trials in HS, and for clinical practice.¹³ Along with
262 approximately 20 COS groups, HiSTORIC operates under the CHORD COUSIN Collaboration (C3), an

263 umbrella research organization whose mission is to develop, disseminate and implement COS for clinical
264 trials and routine practice for dermatologic conditions with the goal of standardizing valid and reliable
265 measurement of disease activity and treatment response, and of comparing effectiveness.¹⁴ In 2018,
266 HiSTORIC established consensus on the Core Domain Set (‘what to measure’) for interventional clinical
267 trials in HS which included the following: 1) Pain, 2) Physical signs, 3) HS-specific Quality of Life, 4)
268 Global assessment, 5) Progression of course (flare and recurrence after surgery), and 6) Symptoms.¹⁵ To
269 date, HiSTORIC has developed and/or validated a number of clinician-reported outcome measures
270 (ClinROMs) and patient-reported outcome measures (PROMs) mapped to these core domains.¹⁶⁻²²

271 A total of 55 HS Experts (consisting of dermatologists, internists, surgeons, and nurses) and 24
272 PRPs from the HiSTORIC group were invited to participate in the present study which was comprised of
273 the following three phases: 1) literature search to identify candidate outcome measures in HS; 2) an online
274 item reduction survey; and 3) an e-Delphi to establish consensus on a set of HS measures that should be
275 applied to clinical practice. **(Figure 1)** Consensus surveys pertaining to the most suitable clinician and
276 patient-reported outcome measures for practice were completed separately by HS Experts and PRPs,
277 respectively, between September, 2022 and February, 2023. To prioritize feasibility for application to
278 clinical practice, it was determined *a priori* that no more than one ClinROM and one PROM could be
279 recommended at the conclusion of the consensus process. This project was conducted in compliance with
280 the Conducting and Reporting of Delphi Studies (CREDES) standards²³ and the Standards for Quality
281 Improvement Reporting Excellence (SQUIRE) reporting guideline.²⁴

282 *Identification of Candidate Treat to Target Measures*

283 A literature search was performed to identify HS outcome measures that have been evaluated for
284 psychometric properties including convergent validity, inter-rater reliability, intra-rater reliability, and
285 responsiveness. This resulted in a total of 10 ClinROMs and 13 PROMs. Following initial review, two
286 ClinROMs and eight PROMs were removed from consideration due to lack of specificity to HS,
287 insufficient psychometric properties, or inadequate feasibility for the practice setting **(Supplementary**
288 **eTable 1)**. We restricted outcome measurement instruments to those that were disease-specific, as these

289 measures capture disease impact with depth and tend to be more sensitive in detecting changes in the
290 patient's condition compared to general measures.²⁵

291 *Item Reduction survey*

292 A single-round item reduction survey was conducted among HS experts and among PRPs
293 separately to eliminate measures that were unlikely to achieve consensus due to low feasibility or limited
294 relevance to patients' perception of treatment response. Information provided to participants included the
295 following: 1) rationale for the application of HS measures to clinical practice; 2) summary of the
296 components and scoring methodology of candidate measures;^{16,18,19, 26-33} and 3) feasibility characteristics
297 of measures for clinical practice. **(Supplementary eTables 2 and 3)**

298 Experts were asked to select four of eight candidate ClinROMs that were most feasible for use in
299 clinical practice. In addition, experts were asked to select the most appropriate assessment interval within
300 which to apply the measures. The PRPs were asked to rank each of the five PROMs according to their
301 ability to capture information most relevant to determining whether a treatment is working adequately.
302 The four ClinROMs with the highest number of votes and the three PROMs receiving the highest
303 aggregate ratings (based on a weighted scale) were selected for consideration in consensus rounds.

304 *Consensus on HS Measures For Clinical Practice*

305 Consensus rounds were conducted separately among experts and PRPs on the most preferred
306 ClinROMs and PROMs applicable to practice. Participants who completed the item reduction survey
307 were eligible to participate in consensus rounds. Information provided to participants included the
308 following: 1) summary of the components and scoring methodology of candidate measures; 2) feasibility
309 characteristics of measures for routine practice; and 3) psychometric properties of the measures.^{16-18, 26-28,}

310 ³⁴⁻⁴² Background materials provided to participants are provided in **Supplementary eTables 2-4.**

311 Experts were asked to rate level of agreement with the following standardized statement for
312 ClinROMs included in the consensus exercise: “‘Measure Name’ *is a feasible measure that I am willing*
313 *to utilize in my routine clinical practice to assess treatment response.*” We use the term “treatment
314 response” to refer to a change in the value of a particular outcome measure after the initiation of a

315 treatment. In addition, experts were asked to select the most appropriate assessment interval within which
316 to apply the measure. The PRPs were asked to rate level of agreement with the following standardized
317 statement for PROMs included in the consensus exercise: “‘Measure Name’ *captures aspects of HS*
318 *impact that are relevant to me, and it should be used routinely to evaluate response to treatment.*”

319 Experts and PRPs were asked to score each standardized statement using a 5-point Likert scale,
320 which allowed participants to specify their level of agreement (strongly agree to strongly disagree). In
321 accordance with the Delphi method, experts and PRPs were provided with aggregate data and
322 anonymized comments from the previous Delphi round prior to making selections in the subsequent
323 round.

324 Thresholds and definitions of consensus were based on previously cited values and were
325 designated a priori.⁴³ Consensus In was defined as at least 67% of total participants agreeing or strongly
326 agreeing with use of the measure in clinical practice. Consensus Out was defined as at least 67% of total
327 participants disagreeing or strongly disagreeing with use of the measure. Instruments that did not meet
328 either of these definitions were deemed to have no consensus. Prior to survey distribution, we specified
329 that if multiple measures reached consensus, the measure with the highest percent agreement would be
330 recommended.

331 Descriptive statistics were calculated to evaluate the demographic characteristics of clinicians and
332 patients responding to each survey round. All statistical analysis was performed using Excel, version
333 16.70. This study was approved by the human subjects research committee of the Feinstein Institutes for
334 Medical Research at Northwell Health.

335 **Results**

336 Demographic characteristics of experts and PRPs participating in item reduction and e-Delphi
337 rounds are shown in **Tables 1 and 2**, respectively. Across these rounds, the majority of experts were
338 practicing dermatologists (92.9 to 94.9%) with a median of 18 to 19 years of clinical experience following
339 training. Most PRPs were female (76.5 to 85.7%), between the ages of 30-49 years (74.3 to 80.6%) and
340 had moderate disease (52.9 to 57.1%). Response rates were 42/55 (76.4%), 38/42 (90.5%), and 39/42

341 (92.9%) in the item-reduction, e-Delphi I, and e-Delphi II rounds, respectively, among experts. Among
342 PRPs, response rates were 17/24 (70.8%), 17/17 (100%), and 14/17 (82.4%) in the item reduction, e-
343 Delphi I, and e-Delphi II rounds, respectively.

344 *Item-reduction survey*

345 The four ClinROMs that received the highest number of votes among experts were the following:
346 HS-Investigator Global Assessment (HS-IGA) (63%), HS-Physician Global Assessment (HS-PGA)
347 (63%), International HS Severity Score System (IHS-4) (56.5%), and HS Clinical Response (HiSCR)
348 (54.3%). Among PROMs, the HS Quality of Life score (HiSQOL) (weighted ranks=60), HS Impact
349 Assessment (HSIA) (51), and HS Severity Assessment (HSSA) (50) were scored by PRPs as most
350 relevant to capturing therapeutic response. The remaining ClinROMs and PROMs were not selected for
351 consideration in consensus rounds due to low agreement among experts and PRPs, respectively. Results
352 of the item reduction survey round are shown in **Supplementary eTable 5**.

353 *Consensus on Outcome Measures and Assessment Interval*

354 Results for expert consensus rounds are shown in **Figure 2**. After the second round, the HS-IGA
355 met criteria for Consensus In, with 71.8% of experts agreeing to its utility in clinical practice. None of the
356 remaining ClinROMs achieved $\geq 67\%$ agreement after e-Delphi II. Use of the IHS-4, HS-PGA, and
357 HiSCR in clinical practice was supported by 56.4%, 51.3%, and 30.7% of experts, respectively, after e-
358 Delphi II. More than half (53.8%) of experts disagreed with the use of HiSCR in clinical practice. Most
359 experts agreed to apply the selected measures at 3-month (69.2%) or 4-month (17.9%) intervals.

360 Results for PRP consensus rounds are shown in **Figure 3**. After the second round, the HiSQOL
361 met criteria for Consensus In, with 92.9% of PRPs agreeing to its application in clinical practice. No other
362 PROMs achieved $\geq 67\%$ agreement. Use of the HSSA and HSIA in clinical practice was agreed upon by
363 an equal percentage (50.0%) of PRPs.

364 **Discussion**

365 An objective framework within which to evaluate disease status and response to treatment, both medical
366 and procedural, is a necessary component to determining whether timely changes to the treatment strategy

367 during the ‘window of opportunity’ in HS may be warranted.⁴⁴ In this study, HiSTORIC achieved
368 consensus on outcome measures in HS that are recommended to be applied in clinical practice. These
369 included the HS-IGA, a ClinROM selected by HS experts, and the HiSQOL, a PROM selected by
370 patients. Most respondents endorsed a 3-month assessment interval. The HS-IGA was developed
371 using a Phase 3 clinical trial dataset [PIONEER I (NCT01468207), AbbVie] with input from experts,
372 PRPs, and methodologists within HiSTORIC.¹⁶ The measure was validated using a replicate Phase 3
373 clinical trial dataset [PIONEER II (NCT01468233), AbbVie] as well as a separate more recent Phase 2
374 clinical trial dataset [HS0001, UCB].^{16,17} As a global assessment, the HS-IGA is a simple-to-use measure
375 which demonstrates very strong test-retest reliability, good convergent validity with known disease
376 activity anchors, and responsiveness to change (**Supplementary eTable 6**).^{16,17} The HS-IGA utilizes the
377 familiar construct of a 6-point ordinal scale with response defined as 2-point improvement from baseline.
378 (**Supplementary eTable 7**) The HS-IGA is scored as a number between 0 and 5 based on the sum of
379 abscess, nodule (inflammatory and non-inflammatory), and tunnel (draining and non-draining), in either
380 the upper or lower body regions. Specification of qualifying lesion types and distinction among difficult-
381 to-discern lesion types (i.e., inflammatory nodule vs abscess, or draining abscess vs draining tunnel) are
382 not required by the clinician, which may support measurement accuracy. Papules, plaques, pustules,
383 comedones, and scars are not counted in the score. The score limits counting to 21 qualifying lesions.
384 These features of the HS-IGA may allow for feasibility and ease of use in clinical practice.

385 The HiSQOL, a disease-specific quality of life measure for adults with HS, captures the unique
386 features of HS that are not directly measured with general skin quality of life measures. The measure
387 consists of 17 items, each with a 7-day recall period, that assesses a wide range of symptoms related to
388 HS, including pain, itch, odor, and drainage, as well as psychosocial impact, and activities that may be
389 impacted by HS.¹⁹ Each item is scored using an ordinal scale, ranging from ‘not at all’ to ‘extremely’ with
390 a score ranging from 0 to 4, respectively. Some items have a response option of ‘unable to do, due to HS’
391 that is scored with the highest number of points (4), indicating high impact on quality of life. The total
392 score ranges from 0 to 68, with higher scores indicating worse quality of life. (**Supplementary eFigure**

393 1) The HiSQOL has been translated into approximately 20 languages, which will support its broader
394 application.^{45,46} The HiSQOL has also been converted into an electronic version, which showed
395 acceptability and usability regardless of age, gender, or device familiarity, as well as ease of use.⁴⁷ The
396 HiSQOL was developed by an international steering group that included patients, thereby enhancing its
397 content validity and ability to comprehensively capture the impact of HS on quality of life. As a result, it
398 may be more sensitive to changes in the status of an HS patient with treatment.¹⁰ Previous studies on the
399 HiSQOL have demonstrated excellent reliability, including test-retest and internal consistency, and very
400 strong convergent and known-groups validity.^{19,21} Analysis from a recent phase II trial defined minimal
401 important difference on the HiSQOL as an 18-point or 58% reduction in total score from baseline.⁴⁸
402 Additional studies with the HiSQOL are underway to evaluate responsiveness and application to
403 adolescents with HS, as well as to create a reduced, or ‘mini’, set of items.

404 It is important to underscore that recommendations on use of disease measures for HS in practice
405 represent one component of a comprehensive evaluation strategy. Adherence to recommendations also
406 does not ensure an improved outcome for every patient. Ultimate judgment on assessment and treatment
407 should be made by the physician in partnership with the patient. The intent of these recommendations is
408 to provide an objective framework with both clinician and patient input that can facilitate bidirectional
409 discussion, trust building, and decision-making on the current treatment strategy and the need to adjust or
410 escalate treatment in an appropriate timeframe. Defining feasible HS measures that can be utilized in
411 routine practice provides the foundation on which targets of treatment may be established and treatment
412 outcomes may be assessed. While HiSTORIC has achieved consensus on the HS measures which should
413 be applied in practice, the thresholds that should be achieved on each as an indication of treatment
414 adequacy is not yet defined. For this reason, payers should not require use of this framework for access or
415 continuation of treatments. As additional and more effective treatment options become available, the
416 Treat to Target benchmark will have more meaningful application in practice. Indeed, similar Treat to
417 Target frameworks that guide treatment decisions through shared decision-making have improved

418 outcomes for patients with other chronic diseases including diabetes mellitus, hypertension, rheumatoid
419 arthritis, and psoriatic arthritis.⁴⁹⁻⁵³

420 There are limitations to the present study which merit consideration. While we aimed to optimize
421 global participation, most experts and HS patients represented countries in North America and Europe,
422 where historically HS has been a significant research focus. The HS expert consensus results may have
423 been influenced by differing regional practices in HS management. Neither the HS-IGA nor the HiSQOL
424 have been studied in the practice setting. However, experts and patients have agreed that both validated
425 measures are simple to use and evaluate concepts relevant to the practical care of HS patients. Lastly,
426 while we encourage application of the proposed HS disease activity and impact measures in practice, we
427 recognize the inherent variability in individual practice time, staffing and workflows which may limit
428 implementation. Potential implementation challenges include the need to train clinicians in outcome
429 measure scoring, interpretation, as well as the staff in routine administration and collection of data. Given
430 some challenges to practice implementation, outcome measurement may need to be prioritized for
431 patients with diseases, such as HS, for which treatment outcomes are frequently suboptimal. This study
432 also had several strengths. Experts were primarily dermatologists with approximately 20 years of clinical
433 experience and expertise in medical management of HS patients. In addition, the e-Delphi method had
434 several benefits, including (1) asynchronous survey distribution (2) anonymity of survey responses and
435 (3) presentation of anonymized comments to aid decision making. The PROM was selected by patients
436 with HS and experience in participating in consensus processes on HS measures. We also employed an
437 iterative process of consultation and feedback to ensure development of a high-quality survey instrument
438 for each round.

439 In conclusion, HiSTORIC has achieved consensus on the application of HS-IGA and HiSQOL
440 measures to evaluate HS patient outcomes in clinical practice. The measures are recommended to be
441 applied at three-to-four-month intervals during treatment. Application of HS outcome measures in
442 practice may facilitate shared decision making on treatments with the goal of optimizing treatment
443 strategies, controlling symptoms, and slowing disease progression. Use of these measures in practice may

444 also generate real-world evidence that may inform HS treatment guidelines. Future consensus studies will
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- 712
- 713 1. Alikhan A, Sayed C, Alavi A, et al. North American clinical management guidelines for
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- 715 Suppurativa Foundations: Part II: Topical, intralesional, and systemic medical management. *J Am*
- 716 *Acad Dermatol.* 2019;81(1):91-101.
- 717 2. Garg A, Neuren E, Cha D, et al. Evaluating patients' unmet needs in hidradenitis suppurativa:
- 718 Results from the Global Survey Of Impact and Healthcare Needs (VOICE) Project. *J Am Acad*
- 719 *Dermatol.* 2020;82(2):366-376.
- 720 3. Midgette B, Strunk A, Akilov O, et al. Factors associated with treatment satisfaction in patients
- 721 with hidradenitis suppurativa: results from the Global VOICE project. *Br J Dermatol.*
- 722 2022;187(6):927-935.
- 723 4. Leshem YA, Chalmers JR, Apfelbacher C, et al. Measuring Atopic Eczema Control and Itch
- 724 Intensity in Clinical Practice: A Consensus Statement From the Harmonising Outcome Measures
- 725 for Eczema in Clinical Practice (HOME-CP) Initiative. *JAMA Dermatol.* 2022;158(12):1429-
- 726 1435.
- 727 5. Versteeg GA, Steunebrink LMM, Vonkeman HE, Ten Klooster PM, van der Bijl AE, van de Laar
- 728 MAFJ. Long-term disease and patient-reported outcomes of a continuous treat-to-target approach
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- 730 2018;37(5):1189-1197.
- 731 6. Ramiro S, Landewé RB, van der Heijde D, et al. Is treat-to-target really working in rheumatoid
- 732 arthritis? a longitudinal analysis of a cohort of patients treated in daily practice (RA BIODAM)
- 733 [published correction appears in *Ann Rheum Dis.* 2020 Jun;79(6):e77. *Ann Rheum Dis.*
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- 735 7. Coates LC, Moverley AR, McParland L, Brown S, Navarro-Coy N, O'Dwyer JL, Meads DM,
- 736 Emery P, Conaghan PG, Helliwell PS. Effect of tight control of inflammation in early psoriatic

- 737 arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial. *Lancet*.
738 2015;386(10012):2489-98.
- 739 8. James JF, Madray VM, Salame N, et al. Demographic Gaps and Requirements for Participation:
740 A Systematic Review of Clinical Trial Designs in Hidradenitis Suppurativa. *Dermatology*.
741 2023;239(1):45-51.
- 742 9. Orenstein LAV, Salame N, Siira MR, et al. Pain experiences among those living with hidradenitis
743 suppurativa: a qualitative study. *Br J Dermatol*. 2023;188(1):41-51.
- 744 10. Jedrzejczak MJ, Ingram JR, Lowes MA, et al. Expert Knowledge, Attitudes, and Practices in
745 Management of Hidradenitis Suppurativa Pain. *JAMA Dermatol*. 2021;157(4):464-466.
- 746 11. Willems D, Hiligsmann M, van der Zee HH, Sayed CJ, Evers SMAA. Identifying Unmet Care
747 Needs and Important Treatment Attributes in the Management of Hidradenitis Suppurativa: A
748 Qualitative Interview Study. *Patient*. 2022;15(2):207-218.
- 749 12. Shih T, De DR, Rick J, Shi VY, Hsiao JL. Low Rates of Psychosocial Screening and Lifestyle
750 Counseling in Hidradenitis Suppurativa Patients in the USA. *Skin Appendage Disord*.
751 2023;9(2):94-98.
- 752 13. Garg A. HiSTORIC: Hidradenitis Suppurativa Core Outcomes Set International Collaboration.
753 C3 The CHORD COUSIN Collaboration. <https://www.c3outcomes.org/historic>. Accessed July 7,
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756 <https://www.c3outcomes.org/>. Accessed July 7, 2023.
- 757 15. Thorlacius L, Ingram JR, Villumsen B, et al. A core domain set for hidradenitis suppurativa trial
758 outcomes: an international Delphi process. *Br J Dermatol*. 2018;179(3):642-650.
- 759 16. Garg A, Zema C, Kim K, et al. Development and initial validation of the HS-IGA: a novel
760 hidradenitis suppurativa-specific investigator global assessment for use in interventional trials. *Br*
761 *J Dermatol*. 2022;187(2):203-210.

- 762 17. Garg A, Zema C, Ciaravino V, Rolleri R, Peterson L, Garcia L, Massaro T, Jemec GBE, Kirby
763 JS, Thorlacius L, Ingram JR. Validation of the HS-IGA: a novel hidradenitis suppurativa-specific
764 investigator global assessment for use in interventional trials. *JAMA Dermatol.* 2023;159(6):606-
765 612.
- 766 18. Goldfarb N, Lowes MA, Butt M, King T, Alavi A, Kirby JS. Hidradenitis Suppurativa Area and
767 Severity Index Revised (HASI-R): psychometric property assessment. *Br J Dermatol.*
768 2021;184(5):905-912.
- 769 19. Kirby JS, Thorlacius L, Villumsen B, et al. The Hidradenitis Suppurativa Quality of Life
770 (HiSQOL) score: development and validation of a measure for clinical trials. *Br J Dermatol.*
771 2020;183(2):340-348.
- 772 20. Kursawe Larsen C, Kjaersgaard Andersen R, Kirby JS, Tan J, Saunte DML, Jemec GBE.
773 Convergent Validity of Suffering and Quality of Life as Measured by The Hidradenitis
774 Suppurativa Quality of Life. *J Eur Acad Dermatol Venereol.* 2021;35(7):1577-1581.
- 775 21. Kirby JS, Hereford B, Thorlacius L, et al. Validation of global item for assessing impact on
776 quality of life of patients with hidradenitis suppurativa. *Br J Dermatol.* 2021;184(4):681-687.
- 777 22. Machado MO, Lu JD, Brar R, et al. Hidradenitis suppurativa odour and drainage scale: a novel
778 method for evaluating odour and drainage in patients with hidradenitis suppurativa. *Br J*
779 *Dermatol.* 2021;184(4):772-774.
- 780 23. Jünger S, Payne SA, Brine J, Radbruch L, Brearley SG. Guidance on Conducting and REporting
781 DElphi Studies (CREDES) in palliative care: Recommendations based on a methodological
782 systematic review. *Palliat Med.* 2017;31(8):684-706.
- 783 24. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. SQUIRE 2.0 (Standards for
784 QQuality Improvement Reporting Excellence): revised publication guidelines from a detailed
785 consensus process. *BMJ Qual Saf.* 2016;25(12):986-992.

- 786 25. Wiebe S, Guyatt G, Weaver B, Matijevic S, Sidwell C. Comparative responsiveness of generic
787 and specific quality-of-life instruments. *J Clin Epidemiol.* 2003;56(1):52-60. doi:10.1016/s0895-
788 4356(02)00537-1
- 789 26. Zouboulis CC, Tzellos T, Kyrgidis A, et al. Development and validation of the International
790 Hidradenitis Suppurativa Severity Score System (IHS4), a novel dynamic scoring system to
791 assess HS severity. *Br J Dermatol.* 2017;177(5):1401-1409.
- 792 27. Kimball AB, Kerdel F, Adams D, et al. Adalimumab for the treatment of moderate to severe
793 Hidradenitis suppurativa: a parallel randomized trial. *Ann Intern Med.* 2012;157(12):846-855.
- 794 28. Kimball AB, Jemec GB, Yang M, et al. Assessing the validity, responsiveness and
795 meaningfulness of the Hidradenitis Suppurativa Clinical Response (HiSCR) as the clinical
796 endpoint for hidradenitis suppurativa treatment. *Br J Dermatol.* 2014;171(6):1434-1442.
- 797 29. Hessam S, Scholl L, Sand M, Schmitz L, Reitenbach S, Bechara FG. A Novel Severity
798 Assessment Scoring System for Hidradenitis Suppurativa. *JAMA Dermatol.* 2018;154(3):330-
799 335.
- 800 30. Grant A, Gonzalez T, Montgomery MO, Cardenas V, Kerdel FA. Infliximab therapy for patients
801 with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled
802 crossover trial. *J Am Acad Dermatol.* 2010;62(2):205-217.
- 803 31. Kimball AB, Sundaram M, Banderas B, Foley C, Shields AL. Development and initial
804 psychometric evaluation of patient-reported outcome questionnaires to evaluate the symptoms
805 and impact of hidradenitis suppurativa. *J Dermatolog Treat.* 2018;29(2):152-164.
- 806 32. Alavi A, Anand N, Yamanaka-Takaichi M, Piguet V, Simmers J, Machado M, Todd A, Kirby J.
807 Evaluating the hidradenitis odor and drainage scale (HODS): A new validated potential
808 instrument to assess odor and drainage in hidradenitis suppurativa-A cross-sectional study. *JAAD*
809 *Int.* 2022;10:75-76.
- 810 33. Horváth B, Janse IC, Sibbald GR. Pain management in patients with hidradenitis suppurativa. *J*
811 *Am Acad Dermatol.* 2015;73(5 Suppl 1):S47-S51.

- 812 34. Włodarek K, Stefaniak A, Matusiak Ł, Szepietowski JC. Could Residents Adequately Assess the
813 Severity of Hidradenitis Suppurativa? Interrater and Intrarater Reliability Assessment of Major
814 Scoring Systems. *Dermatology*. 2020;236(1):8-14.
- 815 35. Gergely LH, Gáspár K, Brodsky V, et al. Validity of EQ-5D-5L, Skindex-16, DLQI and DLQI-
816 R in patients with hidradenitis suppurativa. *J Eur Acad Dermatol Venereol*. 2020;34(11):2584-
817 2592.
- 818 36. Krajewski PK, Matusiak Ł, von Stebut E, et al. Quality-of-Life Impairment among Patients with
819 Hidradenitis Suppurativa: A Cross-Sectional Study of 1795 Patients. *Life (Basel)*. 2021;11(1):34.
- 820 37. Hirvonen M, J, Pasternack R, Lipitsä T, Vihervaara A, Harvima R, Ranta M, Sintonen H, Huilaja
821 L: Patients with Hidradenitis Suppurativa Suffer from Low Health-Related Quality of Life as
822 Measured by the Generic 15D Instrument. *Skin Appendage Disord*. 2022;8:221-227.
- 823 38. Zouboulis CC, Matusiak Ł, Jemec GBE, et al. Inter-rater and intrarater agreement and reliability
824 in clinical staging of hidradenitis suppurativa/acne inversa. *Br J Dermatol*. 2019;181(4):852-854.
- 825 39. Lyons AB, Narla S, Kohli I, et al. Assessment of inter-rater reliability of clinical hidradenitis
826 suppurativa outcome measures using ultrasonography. *Clin Exp Dermatol*. 2022;47(2):319-324.
- 827 40. Prouteau C, Dinulescu M, Oger E, et al. Concordance of severity scores for photographic
828 assessment of hidradenitis suppurativa. *Br J Dermatol*. 2020;182(2):515-516.
- 829 41. Thorlacius L, Garg A, Riis PT, et al. Inter-rater agreement and reliability of outcome
830 measurement instruments and staging systems used in hidradenitis suppurativa. *Br J Dermatol*.
831 2019;181(3):483-491.
- 832 42. Kimball AB, Ganguli A, Fleischer A. Reliability of the hidradenitis suppurativa clinical response
833 in the assessment of patients with hidradenitis suppurativa. *J Eur Acad Dermatol Venereol*.
834 2018;32(12):2254-2256.
- 835 43. Chiarotto A, Boers M, Deyo RA, et al. Core outcome measurement instruments for clinical trials
836 in nonspecific low back pain. *Pain*. 2018;159(3):481-495.

- 837 44. Lowes MA, Goldberg SR, Alavi A, Naik HB. Combining medical and surgical management
838 strategies for hidradenitis suppurativa: Need for a treat to target approach. *Dermatology Reviews*.
839 2022;3(3):123.
- 840 45. van Straalen KR, Ingram JR, Augustin M, Zouboulis CC. New treatments and new assessment
841 instruments for Hidradenitis suppurativa. *Exp Dermatol*. 2022 Sep;31 Suppl 1(Suppl 1):33-39.
- 842 46. Krajewski PK, Matusiak Ł, Szepietowska M, Rymaszewska JE, Jemec GBE, Kirby JS,
843 Szepietowski JC. Hidradenitis Suppurativa Quality of Life (HiSQOL): creation and validation of
844 the Polish language version. *Postepy Dermatol Alergol*. 2021 Dec;38(6):967-972.
- 845 47. Ingram JR, Ciaravino V, Roller R, et al. Content Validity, Acceptability and Usability of the
846 Electronic Hidradenitis Suppurativa Symptom Daily Diary and the Electronic Hidradenitis
847 Suppurativa Symptom Questionnaire [abstract]. International Society for Pharmacoeconomics
848 and Outcomes Research. ISPOR Europe 2022, November 6-9, 2022
- 849 48. Santos LL, Zhu Z, Brown K, Kirby JS. Initial validation of the Hidradenitis Suppurativa
850 Quality of Life tool in a clinical trial setting. *Br J Dermatol*. 2023;188(5):672-673.
- 851 49. Atar D, Birkeland KI, Uhlig T. 'Treat to target': moving targets from hypertension,
852 hyperlipidaemia and diabetes to rheumatoid arthritis. *Ann Rheum Dis*. 2010;69(4):629-630.
- 853 50. Nathan DM, Genuth S, Lachin J, et al.. The effect of intensive treatment of diabetes on the
854 development and progression of long-term complications in insulin-dependent diabetes mellitus.
855 *N Engl J Med* 1993;329:977–86.
- 856 51. Hansson L, Zanchetti A, Carruthers SG, et al.. Effects of intensive blood-pressure lowering and
857 low-dose aspirin in patients with hypertension: principal results of the hypertension optimal
858 treatment (HOT) randomised trial. HOT Study Group. *Lancet*. 1998;351:1755–62.
- 859 52. Dures E, Shepperd S, Mukherjee S, et al. Treat-to-target in PSA: methods and necessity. *RMD*
860 *Open*. 2020;6(1):e001083.

861 53. Smolen JS, Breedveld FC, Burmester GR, et al. Treating rheumatoid arthritis to target: 2014
862 update of the recommendations of an international task force. *Ann Rheum Dis.* 2016;75(1):3-15.

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866 **Figure I Title:** Methods Overview

867 **Figure I Legend:** Abbreviations and Acronyms – HS: Hidradenitis Suppurativa, ClinROM: Clinician-
868 reported outcome measure, PROM: Patient-reported outcome measure, HS-IGA: Hidradenitis suppurativa
869 Investigator Global Assessment, HiSQOL: Hidradenitis Suppurativa Quality of Life

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871 **Figure II Title:** e-Delphi Results, Clinician Reported Outcome Measures

872 **Figure II Legend:** Abbreviations and Acronyms – HS-IGA: Hidradenitis suppurativa Investigator Global
873 Assessment, IHS-4: International Hidradenitis Suppurativa Severity Score System, HS-PGA: Hidradenitis
874 Suppurativa Physician Global Assessment, HiSCR: Hidradenitis Suppurativa Clinical Response

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876 **Figure III Title:** e-Delphi Results, Patient Reported Outcome Measures

877 **Figure III Legend:** Abbreviations and Acronyms – HiSQOL: Hidradenitis Suppurativa Quality of Life,
878 HSIA: Hidradenitis Suppurativa Impact Assessment, HSSA: Hidradenitis Suppurativa Symptom
879 Assessment

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881 **Table I Title:** Characteristics of Experts in Hidradenitis Suppurativa

882 **Table I Legend:** Abbreviations and Acronyms: Q1/Q3: Quartile 1 (25th percentile)/ Quartile 3 (75th
883 percentile)

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885 **Table II Title:** Characteristics of Hidradenitis Suppurativa Patient Research Participants

886 **Table II Legend:** Abbreviations and Acronyms: Q1/Q3: Quartile 1 (25th percentile)/ Quartile 3 (75th
887 percentile)

888 a - Missing for some participants

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891 **Table I. Characteristics of Experts in Hidradenitis Suppurativa**

	Item-reduction survey	e-Delphi Round I	e-Delphi Round II
Total # of participants	42	38	39
Response Rate	42/55 (76.4%)	38/42 (90.5%)	39/42 (92.9%)
Geographic Region			
USA	17 (40.5)	15 (39.5)	15 (38.4)
Europe	16 (38.1)	15 (39.5)	16 (41)
Canada	3 (7.1)	3 (7.9)	3 (7.7)
SE Asia	3 (7.1)	2 (5.3)	2 (5.1)
Australia	2 (4.8)	2 (5.3)	2 (5.1)
South America	1 (2.4)	1 (2.6)	1 (2.6)
Primary Specialty			
Dermatology	39 (92.9)	36 (94.7)	37 (94.9)
Surgery	1 (2.4)	1 (2.6)	1 (2.6)
Other (Internal Medicine)	2 (4.8)	1 (2.6)	1 (2.6)
Years in Practice (post-training completion)			
Median (Q1, Q3)	18.5 (10, 28.75)	19 (9.25, 25.75)	18 (10.25, 29.5)
Practice Setting			
Academic/ University	34 (81)	29 (76.3)	32 (82.1)
Community-based	7 (16.7)	8 (21.1)	7 (17.9)
Research	1 (2.4)	1 (2.6)	0 (0)

892 Abbreviations and Acronyms: Q1/Q3: Quartile 1 (25th percentile)/ Quartile 3 (75th percentile)

893 **Table II. Characteristics of Hidradenitis Suppurativa Patient Research Participants**

	Item reduction survey	e-Delphi Round I	e-Delphi Round II
Total # of participants	17	17	14
Response Rate	17/24 (70.8%)	17/17 (100%)	14/17 (82.4%)
Geographic Region			
USA	6 (35.3)	6 (35.3)	5 (35.7)
Europe	9 (52.9)	9 (52.9)	6 (42.9)
Canada	2 (17.6)	2 (11.8)	2 (14.3)
Age Category			
18-29	0 (0)	0 (0)	0 (0)
30-39	4 (23.5)	4 (23.5)	3 (21.4)
40-49	9 (52.9)	9 (52.9)	8 (57.1)
50-59	2 (11.8)	2 (11.8)	2 (14.3)
60+	2 (11.8)	2 (11.8)	1 (7.1)
Female Sex	15 (88.2)	13 (76.5) ^a	12 (85.7)
Race			
White	17 (100)	17 (100)	14 (100)
Years since HS symptom onset			
Median (Q1, Q3)	28 (24, 34)	27 (23, 33)	27.5 (22.5, 33.5)
Years since HS diagnosis			
Median (Q1, Q3)	16 (10, 23)	17 (11, 23)	14.5 (10.25, 22.25)
HS Disease Severity			
Mild	3 (17.6)	3 (17.6)	4 (28.6)
Moderate	9 (52.9)	9 (52.9)	9 (57.1)
Severe	5 (29.4)	5 (29.4)	2 (14.3)

894 Abbreviations and Acronyms: Q1/Q3: Quartile 1 (25th percentile)/ Quartile 3 (75th percentile)

895 a- Missing for some participants

Figure 1. Methods Overview

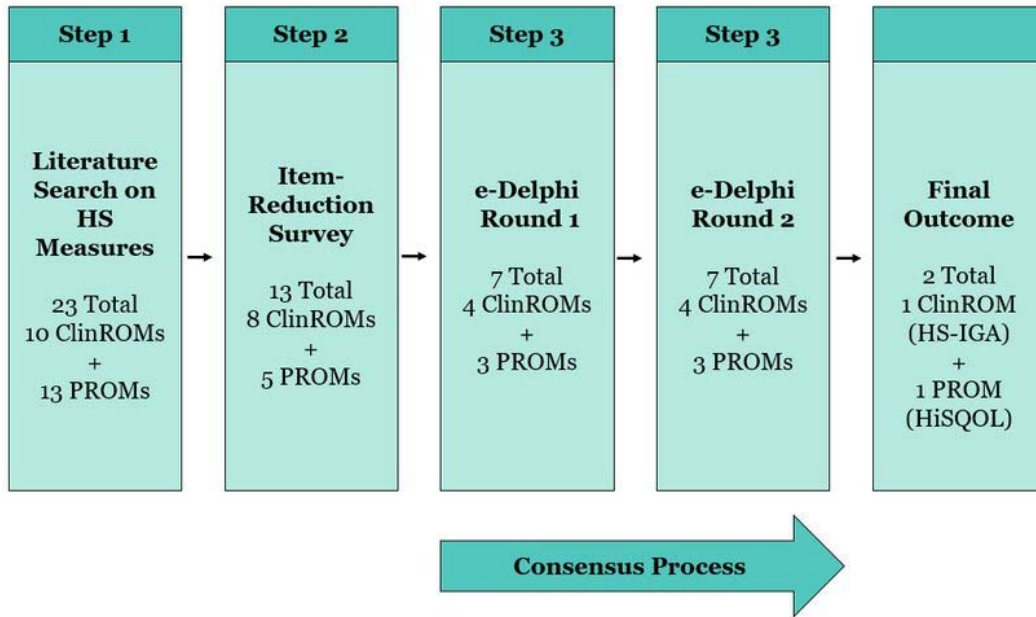


Figure 1 Legend: Abbreviations and Acronyms – HS: Hidradenitis Suppurativa, ClinROM: Clinician-reported outcome measure, PROM: Patient-reported outcome measure, HS-IGA: Hidradenitis suppurativa Investigator Global Assessment, HiSQOL: Hidradenitis Suppurativa Quality of Life

Figure 2. e-Delphi Results, Clinician Reported Outcome Measures

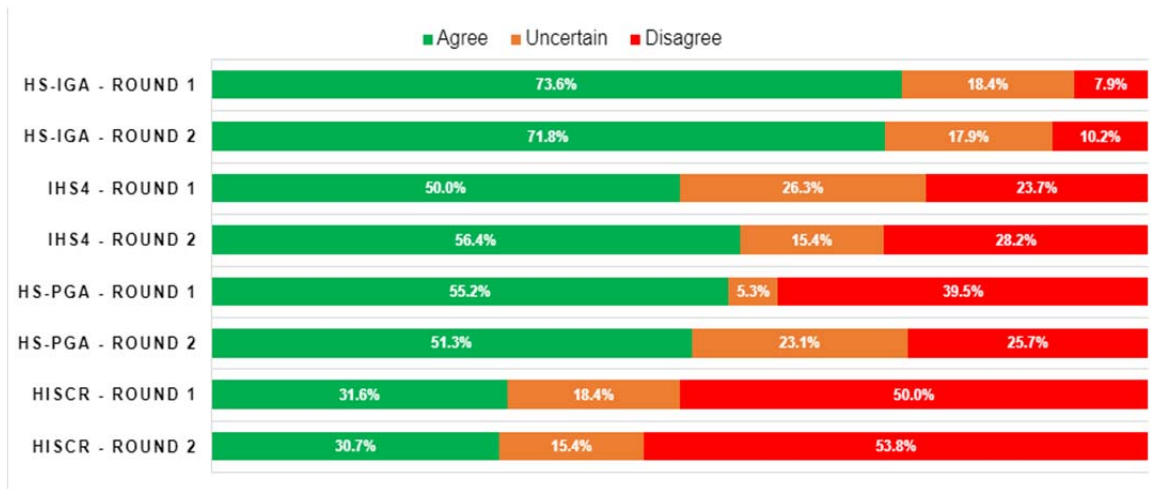


Figure 2 Legend: Abbreviations and Acronyms – HS-IGA: Hidradenitis suppurativa Investigator Global Assessment, IHS-4: International Hidradenitis Suppurativa Severity Score System, HS-PGA: Hidradenitis Suppurativa Physician Global Assessment, HiSCR: Hidradenitis Suppurativa Clinical Response

Figure 3. e-Delphi Results, Patient Reported Outcome Measures

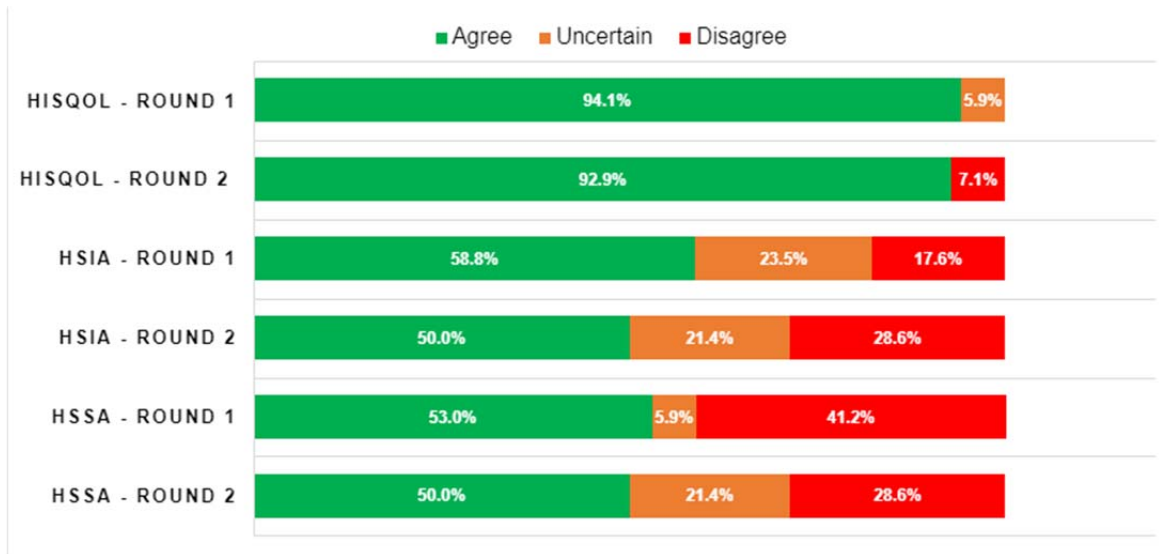


Figure 3 Legend: Abbreviations and Acronyms – HiSQOL: Hidradenitis Suppurativa Quality of Life, HSIA: Hidradenitis Suppurativa Impact Assessment, HSSA: Hidradenitis Suppurativa Symptom Assessment