

## ORIGINAL RESEARCH

## The Top 100 Most Cited Articles on Hidradenitis Suppurativa

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## ABSTRACT

**Background:** Hidradenitis Suppurativa (HS) is a chronic condition that requires prompt diagnosis and treatment. To date, no bibliometric analysis on HS exists. Analyzing the top 100 citations is important to understand the characteristics of the most influential studies in the HS research landscape, and to guide future research.

**Objective:** To analyze the top 100 most cited articles on HS using bibliometric analysis.

**Methods:** Searches within Scopus and Web of Science using "Hidradenitis Suppurativa" and "Acne Inversa" were conducted on May 14th, 2020. After excluding non-original articles, data for the top 100 articles were analyzed using R-studio and Bibliometrix. Five independent reviewers identified study topic and design.

**Results:** The top 100 most cited articles on HS were published between 1982 and 2017 with an average of 128.3 citations. The top research topic and design were treatment (40 articles) and randomized controlled trials (9), respectively. 2011 had the highest number of publications (9), and the 2012 article by Gregor B. E. Jemec had the highest citations (439). These articles were from 14 different countries with the United States and Denmark as top countries. 27 journals published these articles with the British Journal of Dermatology (BJD) as the top journal. Denmark had the greatest outside country collaborations.

**Conclusions:** The results of our study showed that HS research is steadily growing with greatest support from the BJD. There is a focus on treatments in HS research with the United States and European countries leading the way. However, greater worldwide research of HS is needed.

## INTRODUCTION

Hidradenitis Suppurativa (HS), or acne inversa, is a devastating chronic inflammatory follicular skin disease that usually starts after puberty.<sup>1</sup> HS primarily affects folds of the body, including the axilla, groin, inframammary, and anogenital regions. There is an average of 7.2-year

delay in HS diagnosis leading to delays in effective treatment.<sup>2</sup> Substantial research has explored associations between HS and environmental factors and comorbidities.<sup>1-3</sup> The pathophysiology of HS is not entirely elucidated, but much has been learned recently.<sup>3,4</sup> There are multiple treatment modalities, though none are consistently curative.<sup>5,6</sup> Currently, there are increasing number of clinical trials on HS, and with all

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the research being conducted on HS, evaluating research trends using bibliometric analysis can inform future directions.

Bibliometric analysis is defined as a statistical evaluation of published scientific articles and is a tool used to evaluate research published on a certain topic.<sup>7</sup> This quantitative study can provide useful information about contributions made by various authors, countries, institutions, and journals which can be useful in facilitating future research collaborations. Important quantitative information can be learned to understand the progress and trends of research in the field of medicine.<sup>8</sup> Bibliometric analyses have been performed for rosacea, psoriasis, and melanoma.<sup>9-12</sup> However, HS, a devastating disease for patients, has not been studied to date. In this study, we identified and analyzed the top 100 most cited articles on HS to evaluate the characteristics of the most impactful published HS research articles.

## METHODS

### Data Sources

A search of all databases and journals accessible within Elsevier's Scopus and Thomson Reuter's Web of Science from inception was performed on May 14th, 2020. A second search was performed on June 14th, 2020 to identify total number of publications for additional data and comparison. Document search was performed using the Boolean query "Hidradenitis Suppurativa" and "Acne Inversa" and was made without restrictions. From the search results, meta-analyses, systematic reviews, guidelines, letters, book chapters, notes, editorials, short surveys, conference papers, and news items were excluded. The remaining original publications from the databases were

combined and sorted, and the 100 most cited papers were included. (Figure 1)

### Data Collection

Data extracted from Scopus included first author name and country of origin, corresponding author name and country of origin, journal name, and year of journal publication. Additional data was abstracted by five investigators (SS, DH, SG, MR, JB), which included: study design and study topic. Study design was abstracted and categorized as: "case reports/case-series," "cohort/case control/cross-sectional studies," or "randomized controlled trials (RCTs)." Study topic was categorized based on the article's main conclusion: "clinical features/diagnosis," "epidemiology," "pathogenesis/pathophysiology," or "treatment." All research topics and designs were reviewed independently by five reviewers with consensus reached for all 100 articles. The Bradford Zone comprising three zones (Zones 1, 2 and 3) was obtained as a measure of journal productivity.<sup>13</sup>

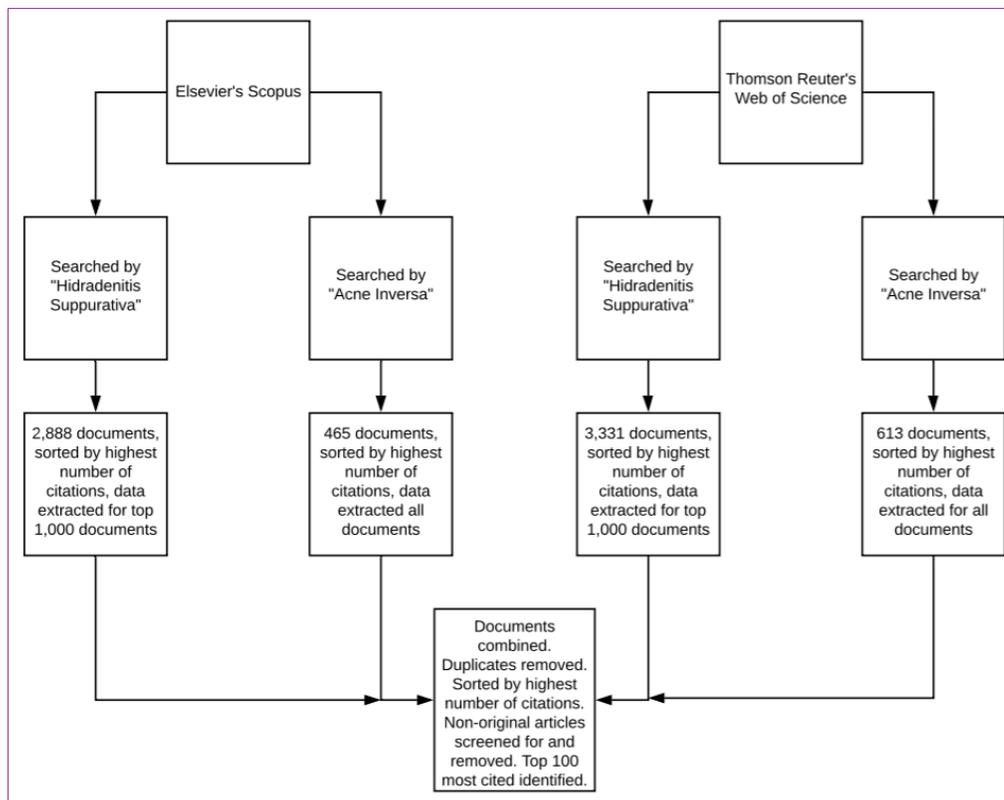
### Data Analysis

Data analysis was performed using R-Studio (R-Studio, Boston, MA) and Bibliometrix (Università degli Studi di Napoli Federico II, Naples, Italy), according to the methods described in Bibliometrix: An R-tool for comprehensive science mapping analysis.<sup>14</sup> Graphs and tables were created, and basic descriptive statistics were calculated using Microsoft Excel (Microsoft Corporation, Redmond, WA).

## RESULTS

### Article Analysis

Figure 1 shows the results of the queries. The top 100 most cited articles were published between 1982 and 2017 and



**Figure 1.** Workflow for 100 citations data extraction

mean age was 15.4 years old from the first day of publication (Table S1). The mean total and annual citations per article were 128.3 and 10.58, respectively. The top research topic was treatment (40%), followed by epidemiology (32%), pathogenesis/pathophysiology (20%), and clinical features/diagnosis (8%). The most frequent article design was cohort/case control/cross-sectional studies (84%), followed by RCTs (9%), case reports/case-series (7%) (Table 1). The top five most cited articles are listed in Table 2. Most of these articles were categorized as epidemiology and cohort/case control/cross-sectional studies, for their topic and design, respectively. Furthermore, most of the top five highly cited articles were published in the Journal of the American Academy of Dermatology. The years with the highest number of top 100 articles were: 1996 (7), 2007 (5), 2009 (7), 2010 (6), 2011 (9), 2012 (6), 2013 (5), 2014 (7), and 2016 (5) (Figure

2). Over a 3-year interval, the most prolific periods for top 100 articles were 2009 to 2011 (22), followed closely by 2012 to 2014 (18).

### Journal Analysis

The top 100 articles related to HS were published in 27 different journals. The top five journals contributed two-thirds (n=65) of the top 100 articles. The British Journal of Dermatology had the highest number of articles (n=28) while the Journal of the American Academy of Dermatology had the second highest (n= 19). The 27 journals that published the top 100 HS articles were separated into three Bradford zones. Zone 1 includes the British Journal of Dermatology and Journal of the American Academy of Dermatology, representing the top two core journals having the largest publishing productivity among the top 100 citations. Four journals in Bradford Zone 2 were Dermatology, Archives of Dermatology,

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**Table 1.** Top 100 citations main characteristics

Timespan (years)	1982-2017
<b>Number of publications per year</b>	
1982-1984	2
1985-1987	7
1988-1990	5
1991-1993	1
1994-1996	9
1997-1999	5
2000-2002	6
2003-2005	5
2006-2008	11
2009-2011	22
2012-2014	18
2015-2017	9
2018-2020	0
<b>Research Topic</b>	
Clinical features/diagnosis	8
Epidemiology	32
Pathogenesis/pathophysiology	20
Treatment	40
<b>Research Design</b>	
Case reports/case-series	7
Cohort/case control/cross-sectional studies	84
Randomized controlled trials	9
<b>Sources (Journals)</b>	
Mean years from publication	15.4
Mean total citations per publication	128.3
Mean annual citations per publication	10.58
<b>Total References</b>	2030
<b>Total Authors</b>	382
<b>Mean authors per document*</b>	3.82
<b>Mean co-authors per document**</b>	5.18

\*Calculated as total number of unique authors divided by total number of articles

\*\*Calculated as total number of authors divided by total number of articles

JAMA Dermatology, and Journal of the European Academy of Dermatology and Venereology, representing the second highest publishing productivity. The remaining 21 journals were assigned to Zone 3, which included journals with the lowest publishing productivity.

### Countries and Collaborations

A total of 14 countries participated in publishing the retrieved articles. Denmark (2808) had the greatest share of citations

followed by the United States (USA) (2268), the United Kingdom (1417), and France (1414) (Table 3). For the USA, only 15.8% of the articles had co-authors from different countries, and for Denmark, only 11.8%. For the USA, approximately 84% of articles were published by domestic authors presented as percentage of single country publication (SCP). On the other hand, approximately 33% of articles produced by researchers from France (n=9) and Greece (n=3) had co-authors from different countries. For the top 10 active countries, a total of 13 (15.7%) articles were considered multiple country publication (MCP) while 69 (84.3%) of articles were considered SCP (Table 3).

### Authors and Affiliations

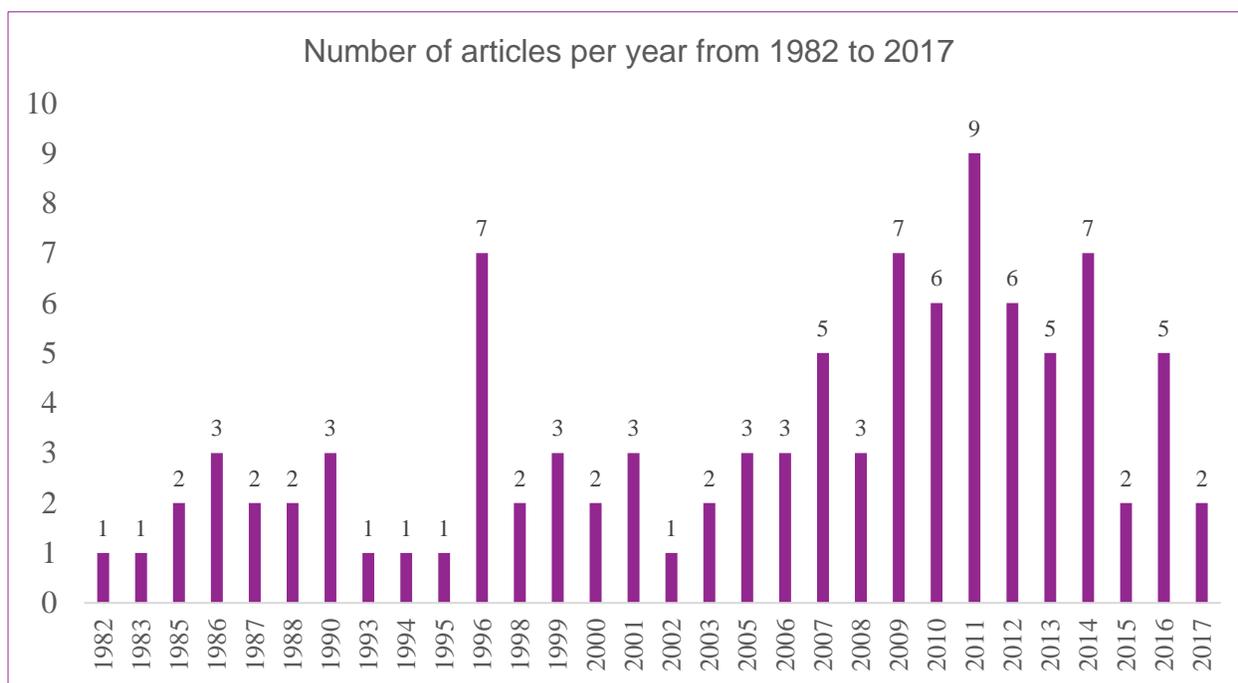
A total of 382 authors contributed to the top 100 most cited articles on HS. Analysis of the authors regardless of their authorship order showed that Gregor B. E. Jemec from the University of Copenhagen in Denmark published the greatest number of the most cited articles (n=21), followed by Jurr Boer (n=10) from Deventer Hospital in the Netherlands, Errol P. Prens (n=9) from Erasmus Medical Center in the Netherlands, and Hessel H. van der Zee (n=8) from Erasmus Medical Center in the Netherlands. Most of the corresponding authors were from the USA (n=19) and Denmark (n=17) (Table 3). The frequency distribution of author productivity in HS is out of 382 authors. 316 authors (82.7%) contributed to just one article. 46 authors (12%) contributed to two articles, and five authors (1.3%) contributed to three articles.

### All Articles on HS per Year

A total of 1629 original articles on HS were published between 1939 and 2020 (82 years). There have been 22.63 articles published per year. 850 articles have been published from 2015 to the capture date, which represents 52.1% of all the published

**Table 2.** Top 5 Most Cited Articles in HS

Rank	Title	Year	Journal Name	Total Citations	Total Citations per Year
1	Hidradenitis suppurativa <sup>16</sup>	2012	New England Journal Of Medicine	439	48.78
2	Prevalence and factors associated with hidradenitis suppurativa: Results from two case-control studies <sup>22</sup>	2008	Journal Of The American Academy Of Dermatology	355	27.31
3	The prevalence of hidradenitis suppurativa and its potential precursor lesions	1996	Journal Of The American Academy Of Dermatology	316	12.64
4	Objective scoring of hidradenitis suppurativa reflecting the role of tobacco smoking and obesity	2009	British Journal Of Dermatology	288	24.00
5	Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: A randomized, double-blind, placebo-controlled crossover trial <sup>20</sup>	2010	Journal Of The American Academy Of Dermatology	252	22.91



**Figure 2.** Number of Top 100 HS Articles per Year

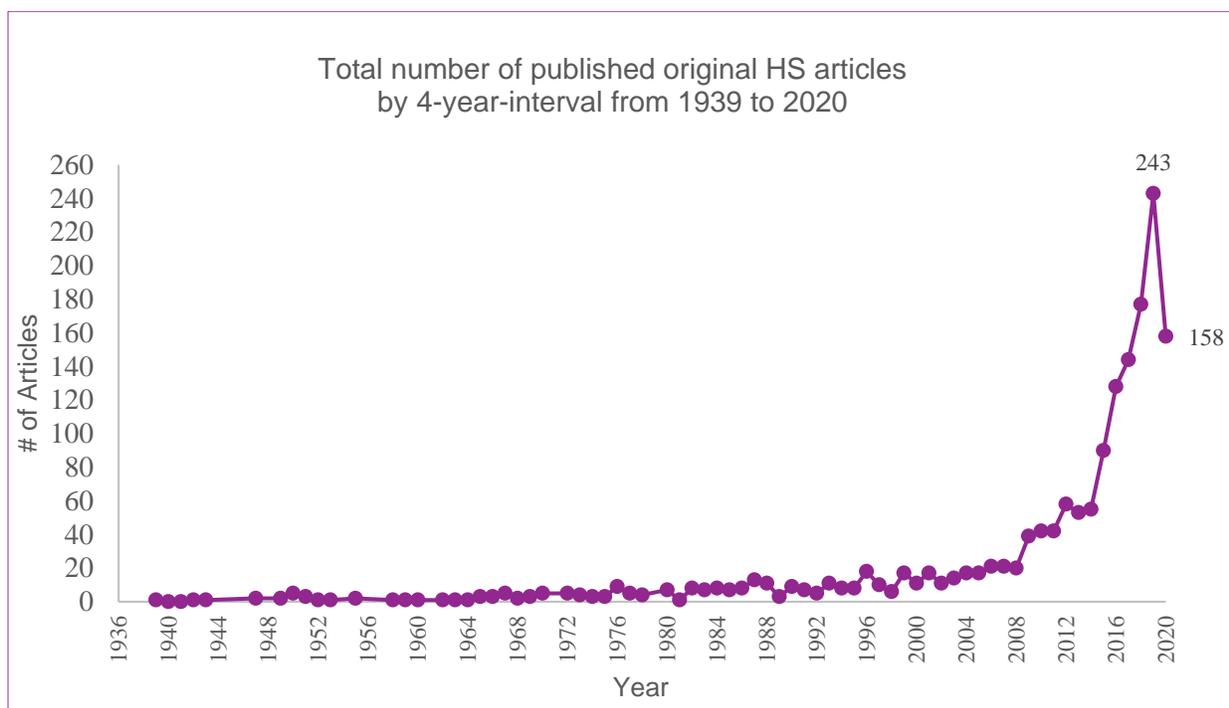
HS articles over the past 82 years. The largest percentage increase in articles was from 2014 to 2015 where there was a jump from 55 to 90 published articles. The greatest number of articles was published in 2019 (243 articles), and 158 articles have been published so far in 2020 (Figure 3).

## DISCUSSION

The top 100 citations were published between 1982 and 2017 (36 years); reflecting a more recent trend of influential HS research. The majority of the top 100 publications (60%) were published in the

**Table 3.** Bibliometric features of top articles by country

Country	Total Citations	Average Article Citations	Corresponding Authors	SCP	MCP	MCP Ratio
Denmark	2808	165	17	15	2	0.118
USA	2268	119	19	16	3	0.158
United Kingdom	1417	142	10	8	2	0.2
France	1414	157	9	6	3	0.333
Netherlands	1173	117	10	8	2	0.2
Germany	890	127	7	7	0	0
Sweden	403	101	4	4	0	0
Greece	294	98	3	2	1	0
Poland	261	130	2	2	0	0
Switzerland	167	167	1	1	0	0
Spain	141	141	1	1	0	0
Ireland	128	128	1	1	0	0
India	82	82	1	1	0	0
Canada	78	78	1	1	0	0



**Figure 3.** Number of Published HS Articles by 4-year intervals from 1939 to 2020 (current)

most recent 12-year period between 2006 and 2017 and similarly, there was a notable increase starting in 2013 of an increase in all HS publications. Szepietowski et al. found a similar increase in overall articles published on HS in PubMed after 2013, which is consistent with our data.<sup>2</sup> This increase in all and top 100 publications coincides with the

founding of the HS Foundation in 2005. This may have contributed to the increase in publications through grants and a network of collaborators.<sup>2,15</sup>

Of the 100 most cited articles, only 20 articles were classified as “pathogenesis/pathophysiology.”

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Furthermore, Jemec mentioned in his 2012 HS article that the pathogenesis of HS remains unclear; HS is a disease characterized by sebaceous gland atrophy, lymphocytic infiltration, pilosebaceous unit hyperkeratosis and formation of granulomas with hair follicle destruction.<sup>16</sup> A more recent article by Goldberg et al. in 2020 confirms the complexity and lack of clarity of HS pathogenesis with the addition of TNF-alpha and IL-17 as key cytokines involved.<sup>17</sup> Even with multiple suggestive theories for the pathogenesis of HS, without true understanding of the disease pathophysiology, research in development of diagnostic tests and treatment options may be stagnated.<sup>18,19</sup>

After analyzing the 100 top cited articles by research topic, 40 out of 100 papers were related to treatments. Within treatments, there were 9 RCTs. The increased number of research articles regarding treatment may be associated with introduction of new pharmacotherapy options for HS. Many of the articles are focused on the new surge of biologics, such as TNF-alpha inhibitors, which have been studied in dermatological conditions with rheumatology overlap. Grant et al. had the highest cited article under treatment showing the efficacy and tolerability of infliximab as a treatment option for HS, which is a breakthrough in HS management.<sup>20</sup> This study provided an important landmark trial of infliximab as a treatment, which is still currently used as a medical therapy option today. Kimball et al. in 2012, the second highest cited article under treatment, conducted a phase 2 trial with 154 patients and showed promising benefits of adalimumab in moderate-to-severe HS. This led to two phase 3 trials completed in early 2014 called PIONEER I and II with bigger cohorts. The article was published in 2016 and is the second highest annually cited article.<sup>21</sup>

Interestingly, epidemiology was a second highest study topic. The number one article was *Prevalence and factors associated with hidradenitis suppurativa: Results from two case-control studies* by Revuz et al. This retrospective case control study showed HS had a strong association with smoking and obesity, two important risk factors that are clinically relevant to HS management today.<sup>22</sup> On the other extreme, clinical features and diagnosis had the lowest articles. This may be due to the “obliteration by incorporation” phenomenon. This occurs over time because the findings may become common knowledge and as a result do not get appropriately cited. Many important articles not cited within the top 100 may have been incorporated into HS common knowledge.<sup>12,23</sup>

Furthermore, 86 different corresponding authors from 14 countries were represented, illustrating the worldwide prevalence of HS and the collaborations around the world. Gregor B. E. Jemec from the University of Copenhagen in Denmark remains the most influential figure in the HS research landscape. Overall, the USA and Europe are leaders in HS research. The USA and Europe may be leaders in HS research because there is a higher burden of HS. HS prevalence ranges between 0.03% and 4% worldwide, but a meta-analysis by Phan et al. in 2020 shows that prevalence of HS is highest in Europe at 0.8% while the USA is at 0.2%.<sup>24-26</sup>

## Limitations

The top 100 citations highlight HS research over the last 40 years, but it is important to note that many important articles exist outside of the top 100. These articles may represent growth trends in research, but this analysis may bias toward older articles that have had more time to accumulate citations.<sup>12,27</sup> Furthermore, although both

SCOPUS and WOS were searched, their indices do not contain every article ever published. It is likewise difficult to determine whether there were articles missed due to search limitations. The total publications data from 1939-2020 capture articles outside of the top 100, but fail to recognize the influence of the studies, which the top 100 citations show.

## CONCLUSION

To our knowledge, this is the first worldwide bibliometric study on HS. Our study found that HS research has experienced notable growth in the last five years. Gregor B. E. Jemec from the University of Copenhagen in Denmark is most influential because he not only started the HS Foundation in 2005, but also is the most prolific author in HS research. Moreover, the British Journal of Dermatology houses the greatest number of these top 100 articles. The clinical trials with adalimumab remain highly cited each year. The prominent focus of HS research are biological treatments and studies on the reduction of quality of life as demonstrated by the top cited articles. Given the financial, psychological and emotional burden of HS, inter-country collaboration among the top active researchers found in this study is encouraged. The quality and measurement of scientific progress is not solely based on pure number of citations. It is about the research itself in the top 100 citations that made its lasting impact on the HS research community and the patients suffering from HS.

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The rest of authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria;

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