Depression and Anxiety in Adults With Hidradenitis Suppurativa
A Systematic Review and Meta-analysis

Myrela O. Machado, MD; Vicky Stergiopoulos, MD; Michael Maes, MD; Paul A. Kurdyak, MD; Pao-Yen Lin, MD; Liang-Jen Wang, MD; Yu-Chiau Shyu, PhD; Joseph Firth, PhD; Ai Koyanagi, MD; Marco Solmi, MD; Afsaneh Alavi, MD; Vincent Piguet, MD; Andre F. Carvalho, MD

+ **Supplemental content**

IMPORTANCE Previous studies suggest that depression and anxiety are common in patients with hidradenitis suppurativa (HS), more so than other dermatological conditions. Yet, to the authors' knowledge, no previous systematic review or meta-analysis has estimated the prevalence or odds ratio (OR) for those psychiatric comorbidities in this population.

OBJECTIVE To assess the prevalence and odds for depression and anxiety in patients with HS.

DATA SOURCES From July 25 to September 30, 2018, observational studies investigating the prevalence and odds for depression and anxiety in adults with HS were systematically searched without language restriction from the inception of each database to July 25, 2018, in PubMed/MEDLINE, Embase, and PsycINFO databases. Searches used various configurations of the terms *hidradenitis suppurativa*; *acne inversa*; *depressive disorder*; *depression*; *anxiety*; *anxiety disorders*; *phobia, social*; *suicide*; and *suicide, attempted*. In addition, the reference lists of included references were screened manually.

STUDY SELECTION Two investigators independently screened references that measured prevalence rates and odds for depressive and anxiety symptoms in patients with HS. Of 136 unique references, 10 ultimately met inclusion criteria.

DATA EXTRACTION AND SYNTHESIS Relevant data were extracted from eligible references. Authors were contacted to provide further information when necessary. Methodological quality of included studies was assessed through a modified version of the Newcastle-Ottawa Scale. Random-effects models were used to synthesize available evidence.

MAIN OUTCOMES AND MEASURES Prevalence rates and ORs for depression and anxiety in adults with HS were the primary outcome measures. Heterogeneity across studies was assessed with the I^2 statistic. Sources of heterogeneity were explored through subgroup and meta-regression analyses.

RESULTS Ten studies comprising 40 307 participants with HS met inclusion criteria. The overall prevalence of depression was 16.9% (95% CI, 9.9%-27.2%). Heterogeneity was large. In the subgroup of studies that considered a clinical criteria–based diagnosis of depression, the prevalence of depression was 11.9% (95% CI, 4.9%-26.2%), compared with 26.8% (95% CI, 20.4%-34.5%) in studies that used a screening instrument. The methodological quality of included studies moderated those findings. The OR for depression in individuals with HS compared with individuals without HS was 1.84 (95% CI, 1.57-2.15). The prevalence of anxiety was 4.9% (95% CI, 1.7%-13.2%); there were insufficient data to determine an odds ratio for anxiety in persons with HS because 2 studies included a comparison group.

CONCLUSIONS AND RELEVANCE This systematic review and meta-analysis indicates that depression and anxiety are common comorbid conditions in patients with HS. Results suggest that the development of strategies to recognize and treat those psychiatric comorbidities in patients with HS is warranted.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Andre F. Carvalho, MD, Centre for Addiction and Mental Health (CAMH), 33 Russell St, Tower Bldg, T314, Toronto, ON, M5S 2S1, Canada (andre.carvalho@camh.ca).

H idradenitis suppurativa (HS) is a chronic recurrent inflammatory skin disease with a characteristic clinical presentation of painful and suppurating lesions in apocrine-gland bearing intertriginous regions.[1] The prevalence of HS varies between 0.05% to 4.00% depending on the methodology used to estimate the prevalence and the population studied.[2] Hidradenitis suppurativa commonly affects young populations with a female to male ratio of 3:1. It is associated with significant disability,[3-5] impaired quality of life,[5-7] sexual dysfunction,[8] and disturbed body image.[9] Furthermore, patient perspectives of living with HS convey physical, psychological, social, and emotional distress.[4]

Several studies[10-15] have assessed the prevalence of psychiatric comorbidities in patients with HS. Some studies have indicated an increased prevalence of depression[10,16,17] and anxiety[10,11] and an increased risk of suicide in people with HS compared with their healthy peers.[11,15] However, studies have used different methodological designs and have included samples from different settings (eg, clinical vs population-based samples). Therefore, the exact magnitude of the prevalence and odds of depression and anxiety in patients with HS is unclear.

Hidradenitis suppurativa is damaging to patient psychosocial well-being and daily activities with an added burden of stigma and shame when HS involves intimate body areas.[18,19] It is important to have a proper understanding of the magnitude of the burden of depression and anxiety among individuals with HS to determine whether targeted interventions for these psychiatric disorders in this population are warranted.

In the current systematic review and meta-analysis, we set out to examine the prevalence and odds for depression and anxiety in adults with HS. In addition, we aimed to explore potential sources of heterogeneity across studies.

Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline[20] and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guideline (eAppendix in the Supplement).[21] The literature search, title screening, abstract screening, final decision on eligibility after full-text review, methodological quality appraisal of included studies, and data extraction were independently performed by 2 investigators (M.O.M. and A.F.C.).

Search Strategy

From July 15, 2018, to September 30, 2018, we conducted a systematic search of the PubMed/MEDLINE, Embase, and PsycINFO electronic databases from inception to July 25, 2018. We used various forms and combinations of the search terms *hidradenitis suppurativa*; *acne inversa*; *depressive disorder*; *depression*; *anxiety*; *anxiety disorders*; *phobia, social*; *suicide*; and *suicide, attempted*. The search strings that were used are available in the eAppendix in the Supplement. This search strategy was augmented through hand searching the reference lists of included references.

Key Points

Question What are the prevalence rates of and odds for depression and anxiety in adults with hidradenitis suppurativa?

Findings This systematic review and meta-analysis of 10 studies comprising 40 307 participants with hidradenitis suppurativa found a prevalence of depression of 16.9% and a prevalence of anxiety of 4.9%. The odds ratio for depression among people with hidradenitis suppurativa was 1.84.

Meaning Depression and anxiety are common comorbidities in people with hidradenitis suppurativa; efforts toward recognition, prevention, and management of those psychiatric comorbidities are warranted.

Eligibility Criteria

Inclusion and exclusion criteria were specified before the literature search was initiated. No restrictions were made as to publication date or language. Observational studies of any design were considered for inclusion. We included studies in which participants with HS were diagnosed by a physician. In addition, studies had to provide either the prevalence or the association (when a reference comparison group was available) of depression or anxiety. Specifically, we included studies that provided either *Diagnostic and Statistical Manual of Mental Disorders* fifth edition (DSM-5)[22] or *International Classification of Diseases, Tenth Revision* (ICD-10)[23] diagnoses of a depressive disorder or an anxiety disorder. In addition, we included studies in which a validated screening tool with a cutoff score indicated the possible occurrence of depression or anxiety as well as studies that used validated algorithms to detect the possible presence of those mental health conditions. There were no limitations regarding the comparison group in studies that assessed the odds for depression and anxiety in adults with HS. When more than 1 comparison group was provided, we prioritized a healthy control group. Studies that enrolled pediatric patients (ie, with participants aged <18 years) were excluded.

Data Extraction

We extracted data regarding the prevalence or odds of depression and anxiety from eligible studies. When ORs were not provided, we calculated this metric based on raw data provided by the included studies. In addition, the following variables were also extracted when available: (1) sample size; (2) mean age; (3) sex (% female); (4) measure of severity for HS; (5) method used to assess depression or anxiety (ie, structured diagnostic interview or coded diagnosis given by clinician or screening tool or validated algorithm); (6) study design; and (7) setting (eg, outpatient services or population-based sample). Both crude and adjusted association metrics with 95% CIs were extracted from included studies. When a study did not provide extractable information, the corresponding author was contacted in at least 2 different occasions over a period of 2 weeks to obtain the relevant primary epidemiologic data.

Methodological Quality Appraisal

The Newcastle-Ottawa Scale (NOS) was used to rate the methodological quality of included studies. Because the NOS was

primarily designed to assess the methodological quality of case-control or cohort studies, we used an adapted version to rate the methodological quality of cross-sectional studies.[24,25] Higher scores in the NOS indicate better methodological quality.[25]

Statistical Analysis

The prevalence rates or unadjusted ORs and 95% CIs obtained or calculated from included studies were synthesized by random-effects models when at least 3 independent datasets were available for each prevalence or association measure. Heterogeneity across studies was measured with the I^2 statistic; values greater than 50% are indicative of greater heterogeneity.[26] When at least 10 studies were available, we estimated the likelihood of publication bias using the Egger asymmetry test.[27,28] We used the following assumptions to assess the existence of small-study effect, an indication of publication bias: (1) the effect size of the largest study is more conservative than the effect size of the meta-analysis and (2) $P < .10$ in the Egger test.[29] The trim-and-fill procedure was used to estimate the effect size when publication bias was noted.[30]

We explored potential sources of heterogeneity across studies using either subgroup (when at least 3 independent datasets were available per subgroup) or unrestricted maximum likelihood random-effects meta-regression analyses. The method used to assess depression and anxiety and the study setting were considered in subgroup analyses. Meta-regression analyses were conducted only when there were data from more than 5 independent datasets. For meta-regression analyses, we considered the following variables: (1) mean age; (2) percentage of female participants; (3) severity of HS as determined by physician; and (4) methodological quality (ie, NOS score). In addition, sensitivity analyses in which 1 study was excluded from analysis at a time were conducted for studies that assessed the odds for depression in adults with HS.

The statistical significance level for effect size estimates was set at a 2-tailed α of .05. All statistical analyses were conducted in Comprehensive Meta-Analysis Software version 3 (Biostat).

Results

Study Selection

Our literature search and study selection process are depicted in **Figure 1**. The initial search of databases retrieved 137 references. After 1 duplicate record was removed, 136 references were screened on the basis of title, abstract, or both to determine potential eligibility. Ten unique references met inclusion criteria.[10-12,14,16,17,31-34] No additional references were identified from the bibliographies of included articles.

Hidradenitis Suppurativa and Depression

Ten studies assessed the prevalence of depression in patients with HS (**Table 1** and **Figure 2**A). The median (interquartile range [IQR]) modified NOS score of those studies was 4.5 (3.0-7.0). The overall prevalence of depression was 16.9% (95% CI, 9.9%-27.2%). There was no evidence of publication bias (Egger test, $P = .22$; eFigure 1 in the Supplement). Heterogeneity was great (I^2 =

Figure 1. Flowchart of Study Selection
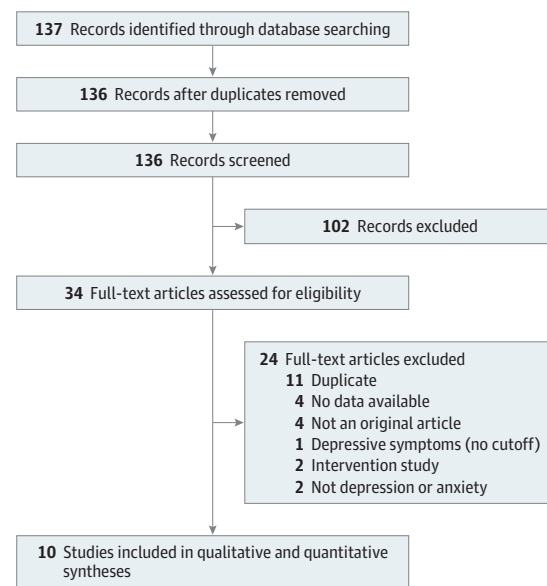
99.4%). In subgroup analysis, the prevalence was 11.9% (95% CI, 4.9%-26.2%; κ = 4; I^2 = 99.7%) in studies that considered a clinical criteria–based diagnosis of depression; whereas in studies that used a screening instrument, the prevalence of probable depression as determined by the instrument was 26.8% (95% CI, 20.4%-34.5%; κ = 5; I^2 = 73.8%). The prevalence of depression was 25.9% (95% CI, 22.7%-29.4%; κ = 7; I^2 = 61.9%) among outpatients with HS. The methodological quality of included studies did not appear to moderate the prevalence of depression in HS (coefficient of variation = 0.06; z = 0.34; κ = 10; $P = .73$). In addition, the percentage of female patients (coefficient of variation = 0.00; z = 0.16; κ = 8; $P = .87$) and mean age (coefficient of variation = −0.20; z = −1.89; κ = 8; $P = .06$) did not moderate the prevalence of depression in HS. The pooled OR for depression was 1.84 (95% CI, 1.57-2.15; κ = 5) in studies that included a comparison group (**Table 2** and Figure 2B). In sensitivity analyses where 1 study was excluded from analysis at a time, the OR for depression in HS remained significant (eFigure 2 in the Supplement).

Hidradenitis Suppurativa and Anxiety

Four studies measured the prevalence of anxiety in patients with HS (Table 1 and **Figure 3**). The median (IQR) modified NOS score of included studies was 6.6 (5.5-7.7). The prevalence of anxiety was 4.9% (95% CI, 1.7%-13.2%). Heterogeneity across studies was high (I^2 = 99.1%). Of the 4 studies, 2 included a comparison group (Table 2). The unadjusted ORs for those studies were 1.6 and 2.3, whereas the ORs of both studies were 1.7 after multivariable adjustment for potential confounding variables.

Discussion

To our knowledge, this is the first systematic review and meta-analysis to assess the prevalence and relative odds for depression and anxiety in adults with HS. Our results indicate that

Table 1. Characteristics of Studies Measuring the Prevalence of Depression and Anxiety in People With HS

Source	Country	Study Design	Mean Age, y	Female, %	Sample Size, No.	Setting	Severity Assessment	Severe HS (%)	Diagnosis HS	Diagnosis MDD	Prevalence, % (95% CI)	P Value	NOS Score
Depression													
Ingram et al,[16] 2018	United Kingdom	Cross-sectional study	43.2	74.3	24 027	Outpatient	NA	NA	Physician diagnosis	*ICD-10*	25.5 (25.00-26.10)	<.001	5
Thorlacius et al,[11] 2018	Denmark	Prospective cohort study	45.8	73.6	7732	Population-based study	Hurley staging system	NA	*ICD-10*	*ICD-10*	1.6 (1.4-1.9)	<.001	7
Huilaja et al,[14] 2017	Finland	Retro-spective study	39.6	58.7	4381	Inpatient/outpatient	NA	NA	Physician diagnosis	*ICD-10*	15.1 (14.1-16.2)	<.001	8
Shavit et al,[10] 2015	Israel	Cross-sectional study	39.6	61.6	3207	Inpatient/outpatient	NA	NA	Physician diagnosis	Clinical diagnosis	5.9 (5.1-6.8)	<.001	7
Vangipuram et al,[31] 2016	United States	Retro-spective study	NA	81.3	283	Outpatient	Hurley staging system	18.7	Physician diagnosis	*ICD-10*	24.4 (19.7-29.7)	<.001	3
Rayner et al,[33] 2015	United Kingdom	Cross-sectional study	NA	NA	213	Outpatient	NA	NA	Physician diagnosis	PHQ-9 ≥10	23.0 (17.8-29.1)	<.001	5
Onderdijk et al,[12] 2013	The Netherlands	Cross-sectional study	43.0	77.0	211	Outpatient	Hurley staging system	13.5	Physician diagnosis	MDI ≥20	20.9 (15.9-26.9)	<.001	5
Kirby et al,[34] 2017	United States/Denmark	Cross-sectional study	40.9	84.4	154	Outpatient	NA	NA	Physician diagnosis	HADS ≥11	35.7 (28.5-43.6)	<.001	3
Matusiak et al,[32] 2010	Poland	Cross-sectional study	39.9	51.8	54	Outpatient	Hurley stage system	22.2	Physician diagnosis	BDI-SF ≥10	20.4 (11.7-33.2)	.11	3
Kurek et al,[17] 2013	Germany	Cross-sectional study	34.3	54.5	45	Outpatient	Sartorius score	NA	Physician diagnosis	HADS ≥8	37.8 (24.9-52.6)	<.001	4
Anxiety													
Thorlacius et al,[11] 2018	Denmark	Prospective cohort study	45.8	73.6	7732	Population-based study	Hurley staging system	NA	*ICD-10*	*ICD-10*	0.8 (0.6-1.1)	<.001	7
Huilaja et al,[14] 2017	Finland	Retro-spective study	39.6	58.7	4381	Population-based study	NA	NA	Physician diagnosis	*ICD-10*	6.9 (6.2-7.7)	<.001	8
Shavit et al,[10] 2015	Israel	Cross-sectional study	39.6	61.6	3207	Inpatient/outpatient	NA	NA	Physician diagnosis	Clinical diagnosis	3.9 (3.3-4.6)	<.001	7
Rayner et al,[33] 2015	United Kingdom	Cross-sectional study	NA	NA	213	Outpatient	NA	NA	Physician diagnosis	PHQ-9 ≥10	22.5 (17.4-28.6)	<.001	5

Abbreviations: BDI-SF, Beck Depression Inventory Short Form; HADS, Hospital Anxiety and Depression Scale; HS, hidradenitis suppurativa; *ICD-10, International Classification of Diseases, Tenth Revision*; MDD, major depressive disorder; MDI, Major Depression Inventory; NA, not available; NOS, Newcastle-Ottawa Scale; OR, odds ratio; PHQ-9, Patient Health Questionnaire 9.

both comorbidities are common among adults with HS, although fewer studies assessed anxiety in this population, and hence evidence remains preliminary. In addition, the prevalence of depression was higher among patients with HS compared with the respective comparison groups of included studies. Two studies compared the prevalence of anxiety in patients with HS to healthy controls,[10,11] and thus a meta-analysis could not be conducted.
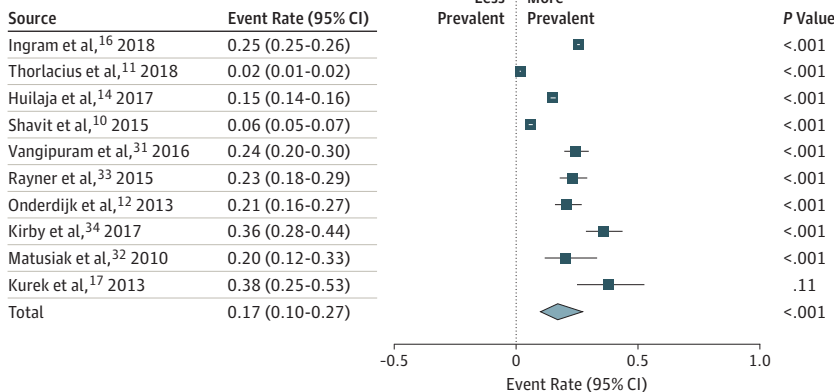
Our results highlight that efforts toward the recognition and management of depression among patients with HS are warranted. Furthermore, the consequences of depression and anxiety on HS-related outcomes have recently received more attention. For example, those psychological distress symptoms may be independently associated with health-related quality of life in patients with HS.[6,34] In addition, impaired body image in patients with HS was associated with symptoms of

both depression and anxiety in a previous study, suggesting that the association between depression and the manifestations of HS may not be independent.[9] Therefore, clinical correlates of depression and anxiety among people with HS as well as the interaction of those psychiatric comorbidities with HS merit further investigation. Our exploratory meta-regression analysis did not provide evidence that sex and age moderate the prevalence of depression among adults with HS. However, this is a topic that merits further investigation.
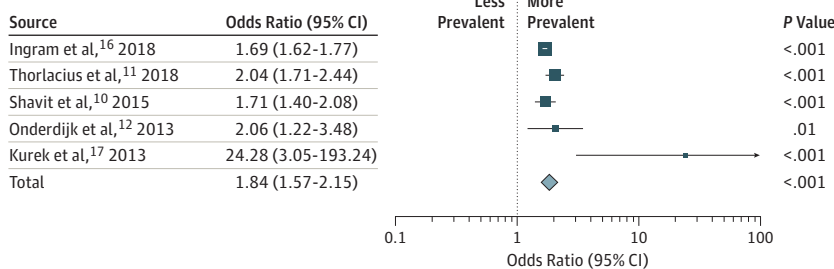
Although our findings indicate that depression and anxiety may be common among people with HS, whether there is a causal relationship in those associations remains to be proved. For example, obesity and related metabolic disturbances are common in both HS[35] and depression,[36] and may thus at least partly explain the associations herein reported. On the other hand, common pathophysiological mechanisms may under-

Figure 2. Prevalence of Depression in Patients With Hidradenitis Suppurativa (HS)

A Prevalence of depression

Source	Event Rate (95% CI)		P Value
Ingram et al,[16] 2018	0.25 (0.25-0.26)		<.001
Thorlacius et al,[11] 2018	0.02 (0.01-0.02)		<.001
Huilaja et al,[14] 2017	0.15 (0.14-0.16)		<.001
Shavit et al,[10] 2015	0.06 (0.05-0.07)		<.001
Vangipuram et al,[31] 2016	0.24 (0.20-0.30)		<.001
Rayner et al,[33] 2015	0.23 (0.18-0.29)		<.001
Onderdijk et al,[12] 2013	0.21 (0.16-0.27)		<.001
Kirby et al,[34] 2017	0.36 (0.28-0.44)		<.001
Matusiak et al,[32] 2010	0.20 (0.12-0.33)		<.001
Kurek et al,[17] 2013	0.38 (0.25-0.53)		.11
Total	0.17 (0.10-0.27)		<.001

Event Rate (95% CI)

B Depression with HS vs healthy controls

Source	Odds Ratio (95% CI)		P Value
Ingram et al,[16] 2018	1.69 (1.62-1.77)		<.001
Thorlacius et al,[11] 2018	2.04 (1.71-2.44)		<.001
Shavit et al,[10] 2015	1.71 (1.40-2.08)		<.001
Onderdijk et al,[12] 2013	2.06 (1.22-3.48)		.01
Kurek et al,[17] 2013	24.28 (3.05-193.24)		<.001
Total	1.84 (1.57-2.15)		<.001

Odds Ratio (95% CI)

A, Prevalence of depression.
B, Association of depression with HS vs healthy control participants. Associations are reported as odds ratios. Sizes of squares are proportional to sample sizes. Squares indicate individual studies; diamonds, pooled effect sizes.

Table 2. Odds for the Occurrence of Depression and Anxiety in Studies That Included a Healthy Control Comparison Group

Source	Country	Sample Size HS	Sample Size Control Group	Setting	Diagnosis	OR (95% CI) Not Adjusted	OR (95% CI) Adjusted	NOS Score
Depression								
Ingram et al,[16] 2018	United Kingdom	24 027	93 869[a]	Outpatient	ICD-10	1.69 (1.62-1.77)	NA	5
Thorlacius et al,[11] 2018	Denmark	7732	4 354 137[b]	Population based study	ICD-10	2.04 (1.71-2.43)	1.13 (0.87-1.47)[c]	7
Shavit et al,[10] 2015	Israel	3207	6412[d]	Inpatient and outpatient	ICD-10	1.71 (1.40-2.08)	1.7 (1.4-2.1)[e]	7
Onderdijk et al,[12] 2013	The Netherlands	211	230[f]	Outpatient	MDI ≥20	2.06 (1.22-3.48)	NA	5
Kurek et al,[17] 2013	Germany	45	41[g]	Outpatient	HADS ≥8	24.28 (3.05-193.24)	NA	4
Anxiety								
Thorlacius et al,[11] 2018	Denmark	7732	4 354 137[b]	Population based study	ICD-10	2.61 (2.04-3.34)	1.73 (1.23-2.41)[c]	7
Shavit et al,[10] 2015	Israel	3207	6412[g]	Population-based study	ICD-10	1.6 (1.3-2.1)	1.7 (1.3-2.1)[e]	7

Abbreviations: HADS, Hospital Anxiety and Depression Scale; HS, hidradenitis suppurativa; ICD-10, International Classification of Diseases, Tenth Revision; MDI, Major Depression Inventory; NA, not available; NOS, Newcastle-Ottawa Scale; OR, odds ratio.

[a] Primary care attendees without HS.

[b] General population controls.

[c] Adjusted for age, sex, socioeconomic status, smoking, alcohol abuse,

and health care consumption.

[d] Patients without HS.

[e] Adjusted for age and sex.

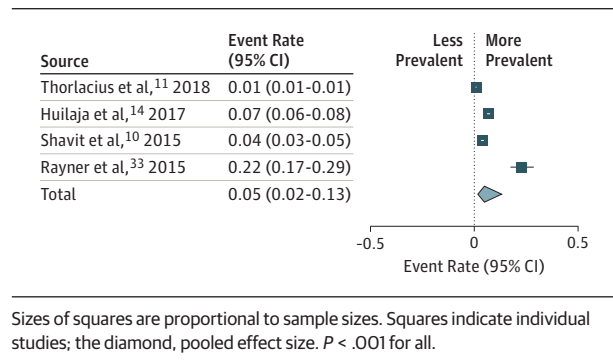[f] Patients with other diseases matched for age and sex to the HS sample.

[g] Healthy controls selected from the general population matched to the HS sample for age, sex, and body mass index.

pin these associations. For instance, peripheral immune activation may contribute to the development of depression in a meaningful subset of patients.[37,38] Accordingly, it has been recently hypothesized that peripheral inflammation may con-

tribute to the frequent occurrence of depressive symptoms in patients with inflammatory skin diseases including HS.[18] Future prospective studies are thus needed to determine whether there is a causal relationship between these disorders.

Figure 3. Prevalence of Anxiety in Patients With Hidradenitis Suppurativa

Sizes of squares are proportional to sample sizes. Squares indicate individual studies; the diamond, pooled effect size. *P* < .001 for all.

son groups have varied across studies. In addition, the largest population-based study conducted to date found that notwithstanding the odds for depression were higher in adults with HS, those differences disappeared after adjustment for potential confounding variables.[11] It should also be noted that only 2 of the included studies[10,11] provided adjusted association metrics for depression in adults with HS; hence, further large-scale studies considering potential confounding variables are warranted to confirm our findings. Finally, heterogeneity across studies was great. Owing to the relatively few studies available, we could only explore potential sources of heterogeneity in studies that assessed the prevalence of depression in people with HS.

Limitations

Some limitations of the current systematic review and meta-analysis merit discussion. First, to our knowledge, no study has assessed the presence of depression or anxiety among people with HS through validated structured diagnostic interviews, which are the criterion standard for the assessment of those disorders. Our subgroup analysis suggests that the prevalence of depression was greater in studies that used screening instruments (ie, 26.8%) compared with those that considered a clinical criteria–based diagnosis of depression (ie, 11.9%). Thus, the prevalence of depression and anxiety could have been overestimated to a certain extent, owing to differences in the methods used to assess those mental health conditions across studies. Second, the methodological quality of included studies varied. Third, although we observed greater odds for depression among adults with HS, compari-

Conclusions

This systematic review and meta-analysis indicates that depression and anxiety are common in patients with HS, although the evidence base for anxiety was more limited than that for depression. In addition, although our results suggest that the odds of depression could be greater in adults with HS, substantial limitations in the available literature diminish the certainty of those findings. Therefore, research efforts should be directed to further elucidate potential moderators as well as those associations that may indicate a causal relationship. In addition, efforts should be directed to recognizing and treating those psychiatric comorbidities in patients with HS to improve health outcomes. Finally, strategies for the management of depression and anxiety in adults with HS are relevant research directions opened by the current work.

Author Affiliations: Division of Dermatology, Women's College Hospital, Toronto, Ontario, Canada (Machado, Alavi, Piguet, Carvalho); Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada (Stergiopoulos, Kurdyak, Carvalho); Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada (Stergiopoulos, Kurdyak, Carvalho); IMPACT Strategic Research Centre, School of Medicine, Barwon Health, Deakin University, Geelong, Victoria, Australia (Maes); Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (Maes); Institute for Clinical Evaluative Sciences (ICES), Toronto, Ontario, Canada (Kurdyak); Department of Psychiatry, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan (Lin); Institute for Translational Research in Biomedical Sciences, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan (Lin); Department of Child and Adolescent Psychiatry, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan (Wang); Community Medicine Research Center, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan (Shyu); Institute of Molecular Biology, Academia Sinica, Taipei, Taiwan (Shyu); Department of

Nursing, College of Human Ecology, Chang Gung University of Science and Technology, Kaohsiung, Taiwan (Shyu); Department of Nutrition and Health Sciences, College of Human Ecology, Chang Gung University of Science and Technology, Kaohsiung, Taiwan (Shyu); Research Center for Food and Cosmetic Safety, College of Human Ecology, Chang Gung University of Science and Technology, Kaohsiung, Taiwan (Shyu); Research Center for Chinese Herbal Medicine, College of Human Ecology, Chang Gung University of Science and Technology, Kaohsiung, Taiwan (Shyu); NICM Health Research Institute, School of Science and Health, University of Western Sydney, Sydney, Australia (Firth); Division of Psychology and Mental Health, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom (Firth); Centre for Youth Mental Health, University of Melbourne, Melbourne, Australia (Firth); Research and Development Unit, Parc Sanitari Sant Joan de Déu, Universitat de Barcelona, Fundació Sant Joan de Déu, Barcelona, Spain (Koyanagi); Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Salud Mental, CIBERSAM, Madrid, Spain (Koyanagi); Department of Neurosciences, University of Padova, Padova, Italy and Padova Neuroscience Center, University of Padua, Padua, Italy (Solmi); Department of Medicine (Dermatology), University of Toronto, Toronto, Ontario, Canada (Alavi, Piguet); Division of Infection and Immunity, Cardiff

University School of Medicine, Cardiff, United Kingdom (Piguet).

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