Treatment Patterns and Depression and Anxiety among Patients Newly Identified with Hyperhidrosis in a Real-World Database Representing US Commercial Health Plan Members

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Introduction

- Hyperhidrosis is a condition characterized by excessive sweating and, frequently, concomitant social and emotional stress.[1] Hyperhidrosis affects an estimated one to five percent of individuals in the United States (US).[1,2]
- Primary hyperhidrosis is idiopathic and often multi-focal, and results from over-activity of the sympathetic nerves; the most common affected area is the axillae, but other affected areas include the palms, soles, and craniofacial regions.[2] Another type of hyperhidrosis is secondary hyperhidrosis, which is attributable to underlying medical conditions or medications.
- Hyperhidrosis is associated with concomitant social and emotional stress due to limitations on health-related quality of life.[4] The limited real-world observational data available in this population suggests that additional research is warranted.

Objective

This study examined the patient characteristics, treatment patterns, and factors associated with concomitant depression and anxiety in patients newly treated with hyperhidrosis.

Methods

Patient Selection

- Commercial health plan members with ≥2 hyperhidrosis diagnosis codes and/or antiperspirant prescription claims were identified from January 2010 through November 2017 from the Optum Research Database, a de-identified research database that contains commercial and Medicare Advantage claims, containing both medical and pharmacy information from 1993 to current and covering over 60 million lives.
  - The index date was the first observed claim indicating hyperhidrosis.
- Patients had continuous enrollment with medical and pharmacy coverage for 12 months before (the *baseline* or *pre-index period*) and ≥12 months after the index date (the *post-index*, or *follow-up period*).
- Patients had no claims for related medical procedures (botulinum toxin A, microwave thermolysis, suction curettage, iontophoresis, or endoscopic thoracic sympathectomy) during the baseline period for codes indicating procedures specific to the treatment of hyperhidrosis, and no claims for these related medical procedures or pharmacy claims for oral systemic therapies within 7 days of the index date for codes indicating procedures or medications not specific to the treatment of hyperhidrosis.
  - Oral systemic therapy included medications to control sweating such as anticholinergics, and specific calcium channel blockers and beta blockers.
- A control cohort (CC) was identified of patients comparable to the hyperhidrosis cohort, but without evidence of hyperhidrosis. These patients were matched 1:1 on index year, age group, gender, and health plan region to a superset of patients with ≥1 indication of hyperhidrosis.
  - The index date for the CC patients was selected as a random date of health care resource utilization (HCRU) during the identification period, such as an office visit, inpatient admission, or a prescription claim.
  - A uniform twelve-month follow-up period was used for the comparative analyses of the hyperhidrosis and control cohorts.
  - CC patients were followed for twelve months starting on the index date. They required continuous enrollment in their twelve-month pre- and post-index periods, as well as valid data in the fields of gender, age, and geographic region.

Outcomes

- Depression and/or anxiety were identified by ≥1 relevant diagnosis code or pharmacy claim.
  - Depression was defined as ≥1 medical claim with a diagnosis code for depression in any position and/or ≥1 pharmacy claim for a medication indicated specifically as an antidepressant. A second indicator variable identified patients with new depression; i.e., depression that was not identified during the pre-index period.
  - Anxiety was defined as ≥1 medical claim with a diagnosis code for anxiety in any position and/or ≥1 pharmacy claim for a medication indicated specifically as an anxiolytic. A second indicator variable identified patients with new anxiety; i.e., anxiety that was not identified during the pre-index period.
  - Depression and/or anxiety was defined as above in the first year of follow-up and the total follow-up period while also including patients without a diagnosis code for depression or anxiety but with ≥1 pharmacy claim for a medication indicated for the treatment of both depression and anxiety. A second indicator variable identified patients with new depression or anxiety; i.e., depression or anxiety that was not identified during the pre-index period.
- Proportion of days covered (PDC) was defined as adherence for 1) prescription-strength antiperspirants and 2) oral systemic therapies. PDC was calculated for the first twelve months of the follow-up period.
  - The PDC represents the proportion of time over the course of a subject's treatment that the patient was theoretically in possession of medication.
  - PDC was calculated by dividing the number of days on which medication was available based on filled prescriptions by the number of days between the earliest prescription claim in the observation period through the end of the observation period (i.e., twelve months of follow-up).

Analysis

- All variables were analyzed descriptively.
- A multivariable logistic regression model examined the presence of depression/anxiety on patient cohort while controlling for patient characteristics including gender, age, and geographic region, any post-index hyperhidrosis treatment, and five common comorbidities (respiratory infections, other lower respiratory infections, other upper respiratory infections, other gastrointestinal disorders, and other skin conditions) identified by the AHRQ[3] in this sample.

Results

Sample Selection

- A total of 44,484 patients with hyperhidrosis were identified (**Figure 1**).
- 58.5% were female, with mean (±SD) age 36.5±16.5 years. A total of 83.5% were ≥18 years old (**Figure 2**).
- For the CC cohort (n=137,451) 56.0% were female, with a mean (±SD) age 40.2±16.9 years (with 87.8% ≥18 years old).

Figure 1. Sample Selection

≥ 1 of the following: A prescription claim for an extra- or prescription-strength antiperspirant or an ICD-9 or ICD-10 diagnosis code for hyperhidrosis in any position
(n=309,709)

↓

Continuous enrollment in the health plan with medical and pharmacy benefits for 12 months before the index date and ≥ 12 months beginning with the index date
(n=143,876)

↓

At least one additional record or claim to confirm diagnosis of hyperhidrosis during the post-index period, and valid data for gender, age, and geographic region
(n=47,570)

↓

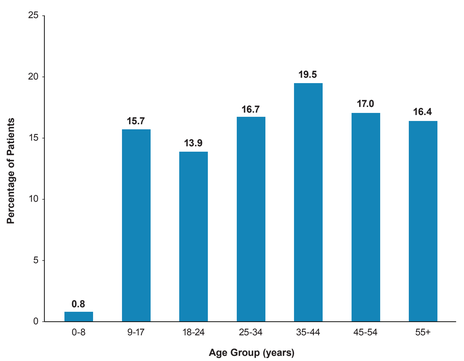
No medical claims for botulinum toxin A, microwave thermolysis, suction curettage, iontophoresis, or endoscopic thoracic sympathectomy during the pre-index period for codes indicating procedures specific to the treatment of hyperhidrosis, or within 7 days before or after the index date for codes indicating procedures not specific to the treatment of hyperhidrosis
(n=46,960)

↓

Final Sample
No pharmacy claims for systemic therapies within 7 days before or after the index date
(n=44,484)

Abbreviations: ICD: International Classification of Disease

Figure 2. Age Distribution



Patient Characteristics

- The most commonly occurring comorbid conditions (**Table 1**) for the hyperhidrosis cohort as identified by the AHRQ were respiratory infections (39.0%) and other skin disorders (30.9%).

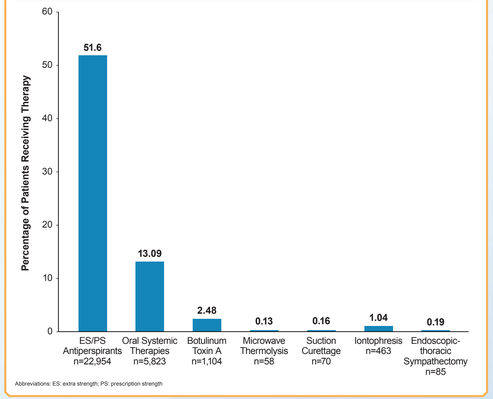
Table 1. Patient Comorbidities

AHRQ comorbidities		Control Cohort (N=137,451)	Hyperhidrosis Cohort (N=44,484)	*P*-value
Respiratory infections	n	42,227	17,330	<0.001
	%	30.72	38.96	
Other connective tissue disease	n	33,509	12,745	<0.001
	%	24.38	28.65	
Disorders of lipid metabolism	n	29,148	8,929	<0.001
	%	21.21	20.07	
Other skin disorders	n	28,187	13,734	<0.001
	%	20.51	30.87	
Hypertension	n	27,769	8,220	<0.001
	%	20.20	18.48	
Diseases of the heart	n	20,395	7,870	<0.001
	%	14.84	17.69	
Other lower respiratory disease	n	20,785	8,840	<0.001
	%	15.12	19.87	
Other upper respiratory disease	n	19,394	8,029	<0.001
	%	14.11	18.05	
Other nervous system disorders	n	14,801	6,211	<0.001
	%	10.77	13.96	
Other gastrointestinal disorders	n	13,438	6,310	<0.001
	%	9.78	14.18	

Treatment Patterns

- A small majority of patients (51.6%) had received treatment with prescription antiperspirants.
- Twelve-month adherence as measured by PDC was low for prescription antiperspirants (mean±SD 13±9%) (**Table 2**).
- Only 13.1% were treated with oral systemic therapies; mean±SD time to treatment was 16.9±19.1 months and mean±SD PDC was 30±28%.
- Post-index medical procedures and surgical options were uncommon (**Figure 3**).

Figure 3. Treatments in the Hyperhidrosis Cohort



Abbreviations: ES: extra strength; PS: prescription strength

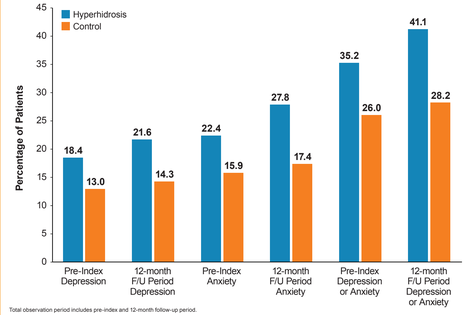
Table 2. Utilization of Pharmacy Treatment for Hyperhidrosis

	Prescription-strength antiperspirants	Oral systemic therapies
Percentage of patients receiving treatment	51.6%	13.1%
Time to first treatment (mean±SD months)	1.4±6.3	16.9±19.1
Twelve-month PDC (mean±SD)	13±9%	30±28%

Emotional Health Characteristics

- Compared with the CC, a higher percentage of patients with hyperhidrosis had any depression/anxiety reported during the uniform twelve-month post-index period (41.1% vs. 28.2%), *P*<0.001). This corresponded to a higher odds of depression/anxiety in patients with hyperhidrosis (odds ratio=1.76, 95% confidence interval 1.72-1.80, *P*<0.001) while controlling for other factors.
- Patients with hyperhidrosis also had a higher percentage of newly diagnosed depression/anxiety during the 12-month post-index period with no evidence of depression/anxiety prior to the index date (18.2% vs. 10.6%, *P*<0.001).
- During the full pre-index and post-index periods, 55.6% of patients with hyperhidrosis had any depression/anxiety reported, including 36.9% with newly diagnosed depression/anxiety.

Figure 4. Patients with Depression and/or Anxiety During Pre-Index and 12-month Follow-Up Period



Total observation period includes pre-index and 12-month follow-up period.

Limitations

- All claims databases have certain inherent limitations affecting generalizability. Presence of a diagnosis code on a medical encounter or outside claim may have not been conclusive or positive presence of disease, as the diagnosis code may have been incorrectly coded or included as rule-out criteria rather than actual disease. However, this risk was mitigated by the requirement that patients had at least two claims for the condition of interest.
- Procedure codes for botulinum toxin A, microwave thermolysis, suction curettage, iontophoresis, and endoscopic thoracic sympathectomy, and pharmacy codes for oral systemic therapies, were generally not specific to the treatment of hyperhidrosis. The study attempted to mitigate this limitation by requiring that patients not have any non-specific codes for these procedures or pharmacy codes for oral systemic therapies within seven days before or after the index date. However, in the follow-up period all instances of these procedures and medications were counted since it was not possible to distinguish usage for the treatment of hyperhidrosis.
- Results and conclusions are limited to the patient population, which consists of patients enrolled in managed care plans, and may not be generalizable to other commercially insured populations in the US.

CONCLUSIONS

- In this real-world database analysis, hyperhidrosis was associated with an increased likelihood of depression and/or anxiety.
- Despite the comorbidity profile and quality-of-life impact, relatively low percentages of patients received topical or oral systemic prescription or surgical treatments, suggesting that tolerability, efficacy, and awareness may be limiting factors as well as patients not being treated in a timely manner.

REFERENCES

1. Smith CC, Parsier D. Primary focal hyperhidrosis. Up-to-date 2018; https://www.uptodate.com/contents/primary-focal-hyperhidrosis?search=hyperhidrosis&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. 2. Doolittle J, Walker P, Mills T, Thurston J. Hyperhidrosis: an update on prevalence and severity in the United States. Arch Dermatol Res 2016; 308(10):743-749. 3. Clinical Classification Software (CCS) for ICD-9-CM/ICD-10-CM. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp; www.hcup-us.ahrq.gov/toolssoftware/ccs10/ccs10.jsp 4. Bahar R, Zhou P, Liu Y, Huang Y, Phillips A, Lee TK, Su M, Yang S, Kalla S, Zhang X, Zhou Y. The prevalence of anxiety and depression in patients with or without hyperhidrosis (HH). J Am Acad Dermatol. 2016 Dec;75(6):1126-1133.

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DISCLOSURES

MH, JPB: Employees of Optum Life Sciences. **KKG:** Employee of Dermira, Inc. **SZK:** Consultant for Dermira, Inc.

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