

Hyperhidrosis: Prevalence, Predisposing Factors, and Psychological Comorbidities

by

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Abstract

Background: Hyperhidrosis (HH) is a disorder in which patient suffers from excessive sweating without any known etiology such as the rise in temperature. Although there have been some epidemiological studies on hyperhidrosis, questions still remain regarding the prevalence of hyperhidrosis and associated demographical, ethnic or geographical factors. Similarly, the association of hyperhidrosis with anxiety and depression has not been systematically investigated. Finally, the relationship between daytime hyperhidrosis and nighttime sweating has not been examined.

Methods: One thousand and ten consecutive subjects attending dermatology outpatient clinics in Shanghai Skin Disease Hospital and 1017 subjects in Skin Care Center of Vancouver General Hospital were investigated for this case-control, cross-sectional study after filling out a questionnaire on their presenting concerns, demographical information and mental stress and sweating symptoms. The subjects were then classified to have primary HH subtypes using the criteria of International Hyperhidrosis Society, late onset hyperhidrosis, or no-HH. Then the prevalence of HH and its correlation with anxiety, depression and NS was examined in both single variants and multivariate logistic regression analyses, stratified according to age at examination, sex, ethnicity, presenting diagnosis, BMI, and specific study cities.

Results: The prevalence of total HH is very similar in Shanghai and Vancouver (about 18%). Primary HH subtypes have the highest prevalence in those younger than 30 years old, decreasing dramatically in later years. Caucasian subjects are more likely to develop axillary hyperhidrosis compared to Chinese subjects. The prevalence of anxiety and depression was 21.3% and 27.2% in hyperhidrosis patients, respectively, and 7.5% and 9.7% in patients without hyperhidrosis. Among

the effects of ethnicity, mental stress symptoms and HH, which are correlated with NS, HH is the most associated factor with NS as more than half of the patients with HH suffer from NS.

Conclusion: Prevalence of total HH is similar in different geographical locations.

However, certain specific HH subtypes can show great variations according to ethnicity, age, body mass index and sex and based on the severity of sweating. Similar to NS, both anxiety and depression were more prevalent in patients with HH, than those without HH.

Preface

1- A version of the prevalence of hyperhidrosis section (chapters 2-4) is published in Plos One Journal.

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2- Additionally, a version of anxiety and depression in patients with hyperhidrosis (chapters 2-4) is accepted for JAAD. [Rayeh Bahar], Yudan Liu, Yuanshen Huang, Arlie Phillips, Tim K. Lee, Mingwan Su, , Sen Yang, Sunil Kalia, Xuejun Zhang, Pingyu Zhou, and Youwen Zhou. Title: Prevalence of Anxiety and Depression in Patients with or without Hyperhidrosis

Dr. Youwen Zhou is my primary supervisor and provided financial support for this study. Dr. Sunil Kalia is my co-supervisor in Vancouver. Drs. Huang and Su helped me with some data analyses and assisted in the preparation of the manuscripts. Dr. Su is my supervisor in the laboratory, was assisting us in troubleshooting at each stage. Ms. Phillips, RN, helped me in collection of questionnaires from the patients and in writing. Dr. Lee provided invaluable suggestions on statistical analysis and the final draft approval. Drs. Sen Yang, Xuejun Zhang and Pingyu Zhou assisted in the design of the entire hyperhidrosis project and, together with Dr. Youwen Zhou, obtained funding for this project. Drs. Yudan Liu, Pingyu Zhou and Youwen Zhou coordinated the Shanghai arm of this multicenter study, and collected the questionnaires in Shanghai, performed data analyses and wrote most parts of the first manuscript (on hyperhidrosis prevalence), with myself performing additional data analyses and helping with the final draft

preparation.

Dr. Youwen Zhou coordinated the entire project in Vancouver and Shanghai, with additional coordination from Professor Pingyu Zhou in Shanghai, Sen Yang and Xuejun Zhang in Hefei China, and Dr. Sunil Kalia in Vancouver.

- The questionnaire was designed by me and my supervisor Dr. Youwen Zhou
- The study design was done by my supervisor, Dr. Youwen Zhou, with input from Dr. Kalia, Dr. Pingyu Zhou and myself.
- The questionnaires from Vancouver patients were distributed to new consult patients by the office staff to the patients as part of the standard care of outpatient dermatology clinics of Drs. Zhou and Kalia. Dr. Zhou and I verified the completeness of the questionnaires. Finally Dr. Zhou confirmed the clinical diagnoses of the skin-disease specific questions, and provided a system for disease classification of both the presenting diagnosis and other disease related coding of the database.
- The Vancouver data entry and the whole data analysis for this thesis was done by me under the guidance of Dr. Youwen Zhou
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A version of night sweating in patients with hyperhidrosis (chapters 2-4), will also be published

soon after conducting some additional studies.

This work has been approved by UBC's Research Ethics Boards (certificate number: H12-02653

Youwen Zhou, PI).

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List of Abbreviations

Abbreviation	Definition
Adj.	adjusted
AH	axillary hyperhidrosis
BMI	body mass index
Chi-Sha	Chinese from Shanghai
Chi-Van	Chinese from Vancouver
C.I.	confidence interval
ECZ	eczematous conditions
GFH	generalized or facial hyperhidrosis
Hair Ds	hair disorders
HH	hyperhidrosis
INF	infections
LOHH	late onset hyperhidrosis
MISC	miscellaneous
NI	negative impact
NS	night sweating
OR	odds ratio
PIG-MISC	miscellaneous pigmentation disorders
PIG-VIT	vitiligo related pigmentation disorders
PPH	palmar or plantar hyperhidrosis
PSO	psoriasis

ROS	rosacea
Sig.	significance
SSEA	South and Southeast Asian
Tumor-BN	benign tumors
Tumor D/IS/M	dysplastic/ in-situ/ metastatic tumors

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Dedication

*With love and appreciation, to my **dearest father**. He is always there for me and I know with his support, I am capable of doing anything. He always sees the best in me and he is my role model in life.*

*To my **beloved mother**. Her affection and support made my path much easier. I know that I never can thank her enough.*

*To my **kindest bother**, who cares a lot about me and by sharing his experiments always tries to pull me up.*

*To my **gorgeous sister**, with whom my life is much more beautiful and her positive energy affects my life.*

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Chapter 1: Introduction

1.1 Normal Physiological Sweating

In humans, sweating is the most important thermoregulatory system to radiate excess heat. Increase in body's core temperature is 9 times more effective in stimulating sweating center, which is located in preoptical hypothalamic region, than increasing skin temperature. [1, 2] Minor daily sweating of the palm and sole is helpful for fine hand movements and the anti-skid function [3]. Sweating of the palms and soles is provoked by some emotional circumstances, which was needed from a long time ago as a preliminary escape response in danger [4]. Human sweat glands are classified under apocrine, eccrine or apoecrine categories [5].

1.1.1 Eccrine Sweat Glands

These glands are distributed on the whole body except the areas with modified skin such as nail bed and external auditory conduit, and open onto the skin surface including hairy and glabrous skin. [6, 7] They are less commonly distributed on the areas where the apocrine glands are scattered and are maximally distributed on soles, forehead, palms and cheeks and axillae.[6, 8] These sweat glands are innervated by post-ganglionic cholinergic sympathetic nerve fibers. [9] Environmental temperature and physical exercise doesn't facilitate sweat secretion from the eccrine glands, which are located on the glabrous skin [10].

1.1.2 Apocrine Sweat Glands

Apocrine sweat glands (scent glands) are larger than eccrine sweat glands and are distributed in particular areas such as axilla, areola, pubic and perianal regions and eyelids, adjacent to the hair

follicles, however they are sometimes seen on the face, abdomen and scalp too. Apocrine glands compared to eccrine glands are located farther to the dermal surface and are odorous. [6, 11].

Apocrine glands can be stimulated by local or systemic administered, epinephrine and norepinephrine and some parasympathetic stimuli such as metacholine [12].

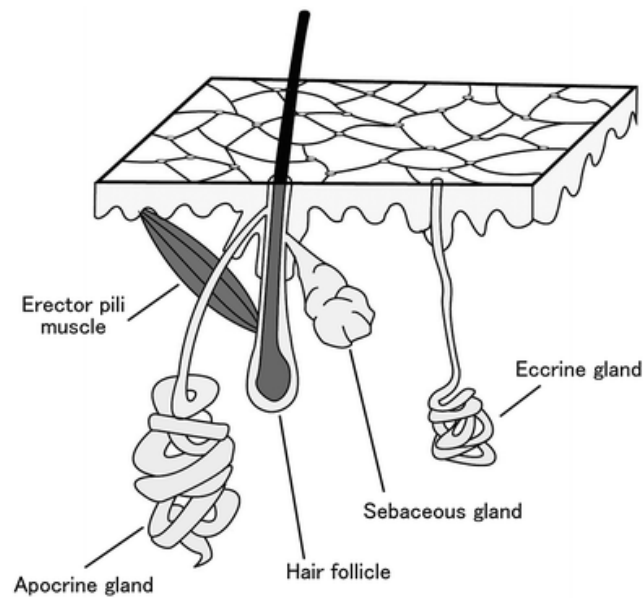


Figure 1-1: Anatomy of Sweat Glands. The eccrine gland is smaller and located closer to the skin surface than the apocrine gland, and sweat pores opens directly onto the skin surface. On the other hand, the apocrine gland opens into the hair pore

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1.1.3 Apoeccrine Sweat Glands

Apoeccrine sweat glands have features of both apocrine and eccrine glands and they are mostly distributed in the axillary region [6, 8, 11]. They are in different sizes but are generally larger than eccrine and smaller than apocrine sweat glands [13]. Apoeccrine glands respond to cholinergic stimuli, as well as epinephrine and isoproterenol infusion [12].

1.2 Hyperhidrosis

Hyperhidrosis (HH) is excessive sweating beyond what is necessary for maintenance of thermal regulation, in which patients sweat without any known etiology, such as rise in temperature or any mental stimuli [14, 15]. The sweating pattern is symmetric and can affect palms, soles, axillae, face and other areas. It has detrimental effects on patient's quality of life, occupational activities and social interactions [16-18]. According to the anatomical site of the sweating, patients suffer from different limitations; patients with palmar sweating do not wish to shake hands; some patients can not wear light colored shirts even in summer; others have problems in relationship with their partner; and finally many of them experience difficulty in occupations such as computer-based jobs [19]. However not many patients seek medical help mainly due to 2 reasons: they think it is an embarrassing condition about which they do not like to talk about and many of them are unaware that this is a treatable condition [20]. Therefore HH has a considerable negative impact on their personal, social and occupational lives. There are two main categories of HH: secondary and primary.

1.2.1 Secondary Hyperhidrosis

Usually secondary HH manifests as generalized or less common, focal excessive sweating. It is usually due to an underlying medical condition or use of medication, [21, 22] therefore, for the treatment, correcting the underlying causes should be considered.

Common secondary causes of **focal HH** include:

- Frey's syndrome
- Neuropathies and spinal injury.

Generalized HH can be secondary to:

- Endocrine defects such as diabetes mellitus, hyperthyroidism, menopause, pregnancy, hyperpituitarism, pheochromocytoma and acromegaly
- Neurologic problems such as spinal cord injury, Parkinson's disease, and cerebrovascular accident
- Malignant diseases like: Hodgkin's disease and myeloproliferative disorders
- Infection
- Cardiovascular problems like: heart failure and shock
- Drugs such as: Fluoxetine, Doxepin and Venlafaxine
- Toxicities: alcohol and substance abuse

1.2.2 Primary Hyperhidrosis

Primary HH, in contrast to secondary HH is idiopathic. Primary HH is also categorized as focal and generalized. Focal primary HH affects axillae, palms, soles or less commonly the face.

Generalized HH affects body and face [20]. However sometimes there is no cutoff point which can exactly distinct the primary and secondary HH from each other.

1.2.2.1 Anatomy

Hyperhidrosis happens as a process of autonomic neuronal dysfunction. The dysfunction tends to happen more in the area of eccrine (sweat-producing) glands, such as on palms, soles, and axillae and less common on scalp and face. [9, 23] Sympathetic and postganglionic nerves, which have acetylcholine as their primary neurotransmitter, innervate the sweat glands. [24] A pseudomotor efferent pathway, which is suggested for HH is as follow:

1) From cerebral cortex to hypothalamus; 2) hypothalamus to medulla; 3) from medulla oblongata fibers crossing to spinal cord lateral horn; 4) lateral horn to sympathetic ganglia and 5) sympathetic ganglia to sweat glands. [9] Therefore lesions in the medulla and pons may lead to sweating such as in Horner's syndrome in which, the patient presents with ipsilateral sweating.

1.2.2.2 Pathophysiology

The pathophysiology is poorly understood. Mainly, eccrine glands which are located near the skin surface, are the responsible sweat glands for focal HH although they do not show histopathological changes, increased numbers or abnormal sizes. [9] However in some types of localized HH, both apocrine and eccrine glands or even only apocrine glands are involved [25]. Birner et al. basing on observed heart rate patterns, suggested parasympathetic dysfunction as a cause of focal HH [26]. However, the prevailing evidence support over-active sympathetic nervous system in patients with primary hyperhidrosis [27].

1.2.2.3 Epidemiology

Walling et al. in a retrospective chart review found that 93% of patients with HH had primary HH and most of them had a typical pattern of distribution involving palms, soles, axillae and crainio-facial areas. The majority had isolated distribution in one area but <1% had atypical distribution of sweating on inguinal folds, legs, buttocks, neck, wrist and mammary folds [14]. Lear et al. suggested that post-pubertal onset is more associated with an axillary distribution [28]. Although not systematically investigated, some suggest that low prevalence of HH in elderly is suggestive of HH regression over time [29] Patients with lower age of onset for HH are likely to have a history of having at least one affected family member. The pattern of inheritance is

autosomal dominant and 35-56% of patients have a positive family history of HH although due to patient's embarrassment the effect of family history may be underestimated [16, 23, 28-30]. Also Strutton et al. in a survey revealed that about 70% of patients with HH do not consult with a physician. [16]

1.2.2.4 Prevalence

Prevalence of primary HH is reported differently in various geographical areas. It varies from 2.8% in United States [16] to 16.3% in Germany [31]. In Japan the reported prevalence rate is 12.8% [32]. It is unknown why there are such a wide variance in HH prevalence in different studies, although non-uniform methods used, racial factors as well as geographical locations may partly explain the differing prevalence reported in different studies.

1.2.2.5 Diagnosis

The most commonly used criteria for the diagnosis of primary, focal, idiopathic HH which is also used by International Hyperhidrosis Society, is described by Hornberger et al. as follow: at least 6 months duration of focal, visible, excessive sweating without any secondary causes with at least 2 of the following features: [22]

- Bilateral and relatively symmetric sweating
- Frequency of at least one episode per week
- Impairment of daily activities
- Age of onset less than 25 years
- Positive family history
- Cessation of sweating during sleep

Diagnosis of focal HH does not need a lab investigation. Although starch-iodine test is not necessary for diagnosis, it allows identifying the area of sweating comparable before and after treatment. For the best results, patients are asked to discontinue antiperspirants 5 days before the test [33]. The orange-brown iodine solution is applied over the skin area that needs to be evaluated and is allowed to dry shortly. Then corn or potato starch is spread over the area. The sweat causes that area to become dark blue and the parts with maximal sweating are easily evaluated and may be recorded with photographs for future assessments [33].

Gravimetry is also an objective test for quantifying the volume of sweating. A filter paper is used on the sweating area and is weighted before and after 5 minutes contact. This method can be done sometimes to find the best therapeutic options. [34-36]

1.2.3 Treatment

HH treatment options are different according to their efficacy, side effects, cost and duration of action.

1.2.3.1 Topical Agents

Antiperspirants such as Drysol, which contain aluminum chloride, are the first-line treatment for mild axillary HH. Aluminum chloride either interacts with the keratin in the sweat ducts or directly acts on the epithelium of excretory eccrine gland. [37] They can cause mechanical obstruction of the eccrine gland duct. As a side effect, aluminum chloride can cause burning sensation, stinging and irritation [38].

1.2.3.2 Systemic Agents

Most commonly used oral agents in the clinic are a) anticholinergic agents (glycopyrrolate, menthatheline bromide, oxybutinin) which competitively inhibit acetylcholine at muscarinic receptors and b) alpha-adrenergic agonists (clonidine). Side effects include, dry mouth, blurred vision dizziness and confusion, urinary incontinency, constipation and tachycardia. This group can be used for all HH subtypes [39]. However, these drugs should not be used in patients with: myasthenia gravis, narrow angle glaucoma, pyloric stenosis and paralytic ileus. Also patients with gastroesophageal reflux, bladder outflow obstruction and cardiac insufficiency should use it with caution [39].

1.2.3.3 Iontophoresis

An electrical current, which is applied to the skin for ion passage, occludes the eccrine glands. However, the exact mechanism is unknown. This method is considered as a second-line treatment for palmar or plantar HH. This method is time consuming, may cause skin irritation or peeling and requires long-term maintenance [38]. However if its use is combined with Botox, significant improvement is observed [40, 41]. The contraindications for the use of iontophoresis are: pregnancy and presence of metallic implants such as artificial orthopedic joints, pacemakers and bone implants [42].

1.2.3.4 Surgical Treatments

Thoracoscopic sympathectomy has a success rate of >80% in primary HH, although compensatory HH is one major limitation of this surgical procedure. Pneumothorax and

hemothorax are other complications [22, 43]. Liposuction and subcutaneous curettage are other surgical options for proper candidates.

In case of sympathectomy, the patient should undergo general anesthesia for this surgery. Then the segment of the sympathetic chain which is responsible for the sweating on hands or axillae are visualized and after the incision of the pleura on that section and then the chain is isolated by the cautery and excised [43].

1.2.3.5 Botulinum Toxin (Botox)

It is produced by *Clostridium botulinum* and inhibits acetylcholine release at neuromuscular junction. There are 4 types of botulinum toxins: onabotulinumtoxinA, incobotulinumtoxinA, abobotulinumtoxin A and rimabotulinumtoxin B. This method has more than 90% efficacy for primary focal HH in soles, palms and axillary areas. [44, 45] This method is quite safe and only <1% report muscle weakness. Contraindications include: pregnancy and lactation, myasthenia gravis and medications, which might interfere with neuromuscular transmission. The cost is also another limitation, as it has to be repeated every 6-12 months [38]. Dosage ranges from 50 to 100 unit per axilla and is injected into the axillae after the starch-iodine test. Topical anesthetics may be used to minimize the pain. Injection into the palms and soles is very painful for many patients and the pain is the main limitation for use of this method. Therefore, regional block is recommended before the injection [38]. In order to limit the toxin effect to the local desired area: injection should be done slowly, needle angle should be well controlled, adjuvant adrenalin can be used, no pressure should be applied after injection and injection in smaller (more concentrated) volumes is suggested. [46-48]

1.2.3.6 Alternative Treatments

Biofeedback training and hypnosis are relaxation techniques used for treating HH although the data regarding their effectiveness is nonexistent. [49, 50]

1.3 Unresolved Questions, hypotheses and Objectives

1.3.1 True Prevalence of Hyperhidrosis and Demographic Characteristics

Due to the importance of primary HH conditions, there have been several epidemiological studies in different countries to find out the prevalence of HH. The most cited study in North America, reported the prevalence of HH 2.8% in 2003, which is, a lot less than other locations around the world [16]. Prevalence of primary HH has been reported 9% in Brazil in 2009 [51], 12.8% in Japan in 2013 [32] and 16.3% in Germany in 2013 [52]. Although the possible reasons for this difference are the variation in sampling methods and using different criteria for describing the patients with HH, the effect of geographical region influence hasn't been studied yet and it is yet unknown if people from same ethnicities have different rate of HH prevalence in different regions. There is no knowledge in the literature regarding the effect of all the demographical parameters such as gender, BMI, age, ethnicity and presenting skin dermatology diagnosis on HH and HH subtypes in a multivariate analysis.

There is neither any study to investigate the correlation between different demographical parameters as well as presenting skin disease according to the severity of HH.

Therefore we hypothesize that the true prevalence of HH is yet unknown and there is a difference in HH prevalence among different ethnicities.

As for objectives of this study we want to:

- Find the true prevalence of HH in different geographical areas (Vancouver, Canada and Shanghai, China)
- Explain the correlation between demographical factors and the presenting skin diagnoses on HH prevalence at different severity levels.

1.3.2 Relationship between Hyperhidrosis and Psychological Comorbidities

Although primary HH is known to have no known etiology, many primary HH patients report mental distress symptoms [16, 53-55]. It is still unresolved if prevalence of anxiety and depression in HH patients is truly different from those without HH.

The role of anxiety and depression has been demonstrated in different studies on many skin disorders such as alopecia, psoriasis, urticarial, eczema and acne [56-61].

With respect to primary HH, there have been previous attempts to quantify the prevalence of anxiety and depression. On one hand, Weber et al. in a study, which only focused on HH population and no HH group, revealed no increase in prevalence of anxiety in HH-subjects studied [62]. On the other hand, other studies showed increased anxiety in primary HH patients. [55, 63, 64] Yet, there was no consistent pattern between severity of sweating and incidence of anxiety in these studies.

Further, two additional groups have studied the relationship between depression and HH. Braganca et al. found that there is a low prevalence of depression in HH patients. [63] In contrast, Gross et al. showed that people who were affected by HH have more depression symptoms. [55]

Finally, common to all previous studies addressing stress in HH patients, there is lack of a

study which assesses the effect of confounding factors simultaneously on anxiety and depression, including, age, BMI, gender and so on in a multivariate analysis.

We hypothesize that both anxiety and depression are more common in patients with HH, independent of the effect of other factors.

Therefore, the objectives of this section of the study are to:

- Calculate the prevalence of anxiety and depression in HH patients and compare it to the population without HH
- Find the prevalence of stress symptoms according to different demographic characteristics in a multivariate logistic regression analysis, where the results are controlled for the other variables too.

1.3.3 Relationship between Night-time Sweating and Daytime Sweating (Hyperhidrosis)

Night sweating (NS) is defined as sweating at nights even when it is not excessively hot in the bedroom during the past month [65].

NS is an important sign for the physicians because of potential association with serious underlying conditions such as tuberculosis, malignancies, infections or autoimmune diseases. In these conditions, the release of inflammatory mediators can temporarily raise the thermo-neutral zone (TNZ) and cause increase in body core temperature. Sweating stops when the levels of mediators and TNZ return to normal [66]. Non-thermoregulatory regulations are also responsible for NS. It can be due to toxins and medications, which activate sympathetic system or sweat glands, abnormality in autonomic nervous system and serum osmolality imbalances such as hypercapnia [67]. Although the overall survival of a patient is not dependent on NS, the presence

of “B symptom complex” is an indicator of poor prognosis in patients with Hodgkin Lymphoma [68].

The prevalence of NS varies in different studies according to population of the study and the sampling method. For example it has been reported to be as high as 28% in patients undergoing polysomnography to as low as 4.4% in a random population sample in Thailand [69, 70].

There is an unclear relationship between NS and primary HH in the literature as many primary HH patients referring to dermatology outpatient clinic report to have NS and instead, NS is believed to be an exclusion criterion for diagnosing primary HH [22]. There are some cross-sectional studies available, which assess the effect of different factors on NS [69, 71], however in none of the studies, the effect of HH and its subtypes were assessed. Therefore, in this study, we wanted to compare the prevalence of NS in patients with and without HH. Also, the effect of other variables including daytime sweating is going to be evaluated in this study.

Thus, we hypothesize that NS is more common in patients with HH.

And the objectives for this part of the study are to:

- Find the prevalence of NS in the population according to different demographic features
- Evaluate the effect of HH and other variables including gender, age, BMI, ethnicity, presenting skin diagnosis and anxiety and depression on NS in a multivariate logistic regression analysis (where the effect of one variable on NS is controlled for other variables).

Chapter 2: Body of Thesis

2.1 Methods and Subjects

2.1.1 Population:

Two sites contributed for this questionnaire-based study (Dermatology Clinic at Vancouver General Hospital, a referral hospital in Canada, from June 2014 to May 2015 and Shanghai Skin Hospital, a referral hospital in China, from June 2014 to March 2015) all in total 2059 patients were recruited and this cross-sectional and case-control study was done on 2017 patients. Forty-two Patients were excluded before the data analysis due to incomplete responses to the questionnaire. In Vancouver, 95% filled the questionnaire in English and 5% in Chinese and in Shanghai all the subjects filled out the questionnaire in Chinese.

2.1.2 Questions Asked on the Questionnaire

The questionnaires were given to the new-coming patients who self-referred or were referred to Dermatology Clinics by other physicians. They were filled out by the patient in about 10 minutes while sitting in the waiting area. Both English (appendix A) and Chinese versions (appendix B) of the questionnaire were available according to patients' desire. The questions included the following: date of consultation, ethnic origin, country of birth, weight, height, gender, age, chief complaint and its duration, family history of the same problem, previously diagnosed medical or skin diseases, chronic comorbidity, drug history, history of allergic reactions, mental stress symptoms such as anxiety and depression, daytime unprovoked sweating, night-time sweating

during sleep and negative impact of excessive sweating on patient's life. The dermatologists then verified the questionnaire for the accuracy of the answers and symptoms.

2.1.2.1 Assessment of Stress Symptoms

We used GAD-7 and PHQ-9 scales for assessment of presence or absence of anxiety and depression, respectively [11, 12]. Each one of the questions on both scales was scored (between 0 to 3), according to the frequency of different symptoms. The cutoff point of 10 was used to define the presence and absence of anxiety and depression. The specificity and sensitivity of both of the scales are >80% [11, 12]. Also patients who were currently taking anxiolytic or anti-depressant medications, even with a score <10, were considered as suffering from anxiety or depression.

- On the **GAD-7** scale, the following questions were asked from the patients that how often they were bothered by each mentioned symptom in a two week period (0: not at all, 1: in less than half of the days, 2: in more than half of the days and 3: nearly every day).
 - 1- Feeling nervous, anxious or on edge
 - 2- Not being able to stop or control worrying
 - 3- Worrying too much about different things
 - 4- Trouble relaxing
 - 5- Being so restless that it is hard to sit still
 - 6- Becoming easily annoyed or irritable
 - 7- Feeling afraid as if something awful might happen
- On the **PHQ-9** scale the patients were asked about the frequency of experiencing the following symptoms;

- 1- Having little interest or pleasure
- 2- Feeling down, depressed, or hopeless
- 3- Having trouble falling or staying asleep; Or opposite sleeping too much
- 4- Feeling tired, or having little energy
- 5- Having poor appetite; Or opposite eating too much
- 6- Feeling bad about yourself, or thinking that you are a failure, or feeling having let yourself or family down
- 7- Trouble concentrating on things, such as reading the newspaper or watching TV
- 8- Moving or speaking so slowly that other people could have noticed? Or the opposite, being so fidgety or restless that you have been moving around a lot more than usual
- 9- Thoughts that you would be better off dead or of hurting yourself in some way.

2.1.2.2 Assessment of Hyperhidrosis

In order to demonstrate the severity of HH, we asked about the frequency of excessive sweating in a 2-week period, as follow; have you experienced excessive sweating on any body area with no specific reason like rise in temperature, exercise or nervousness in the past 2 weeks (Score 3: almost everyday, score 2: more than half of the days, score 1: less than half of the days and score 0: not at all). Our group designed this scoring, according to the frequency of sweating. Presence of HH was confirmed if score 1-3 were selected. Score 0 indicated that the patient is in the category of patients without HH. We also asked the patients about what they think about the severity of the sweating, (score 0-3). The frequency score and self reported HH severity score (1-3) were highly correlated (Spearman's rho: 0.995, p-value <0.001), therefore for the purpose of this study we used the frequency score as an indicator for demonstrating HH severity as its

definition in this study is less subjective than the self-described sweating severity. To differentiate the primary vs. late onset hyperhidrosis we also asked about the onset of excessive sweating.

2.1.2.3 Assessment of Night Sweating

The frequency of night sweating during sleep was also asked in a 2-week period. (Score 3: almost every night, score 2: more than half of the nights, score 1: less than half of the nights and score 0: not at all)

2.1.2.4 Assessment of Negative Impact of Hyperhidrosis

The patients were also asked how much sweating has negatively affected their lives? (Score 3: negatively bothered nearly every day, score 2: more than half of the days, score 1: less than half of the days; 0: not at all)

2.1.3 Data Harmonization

After the self-reported questionnaires were completed, the dermatologists in Vancouver and China verified the questionnaire for accuracy. All the data from China was transferred to our group in Vancouver. The next step was to categorize the patients into different groups.

2.1.3.1 Hyperhidrosis Categories

The patients who reported to have excessive sweating, were categorized into:

- Primary HH group
- Late onset HH (LOHH) group

According to International Hyperhidrosis Society (IHS), we defined primary HH, as patients with excessive sweating onset less than 25 years old, and LOHH, as excessive sweating with an onset over 25 years of age.

In our study we used the term LOHH instead of secondary HH as we only used the age criteria for defining it as many of the patients over 25 y/o did not have signs or symptoms of an underlying condition so for this study we used the term LOHH.

Although secondary HH and LOHH may overlap in many other aspects such as underlying causes, which needs to be further verified.

According to International Hyperhidrosis Society (IHS), the primary HH patients were further divided into 3 subtypes:

- PPH (palmar or plantar HH)
- AH (axillary HH)
- GFH (generalized or facial HH)

2.1.3.2 Age Categories

For the purpose of this study, all available ages were categorized into 3 roughly equal groups:

- <30 y/o
- 30-59 y/o
- => 60 y/o

2.1.3.3 Ethnicity Categories

Regarding the ethnic background, according to patients' self-reports on the questionnaire, we divided the patients into four categories:

- Chinese: further, to Chinese from Shanghai (Chi-Sha) and Chinese from Vancouver (Chi-Van)
- Caucasian
- SSEA (South and Southeast Asian)
- Other ethnic groups

2.1.4 Statistical Analysis

The data was entered into Microsoft Excel. Data analyses were performed with Microsoft Excel 2008 (Microsoft Corporation, Redmond WA, USA), SPSS 22 (IBM, Endicott, NY, USA), and R software version 3.2.0 (R Foundation for Statistical Computing, Vienna, Austria). The “prevalence” is defined as the proportion of the population that has HH, HH subtypes, anxiety, depression or NS in each cohort and it represents the prevalence in this study. Chi-square and logistic regression models were used and p-value <0.05 was considered as significant. Odds ratios in multivariate regression analyses are relative to the reference variable that is defined to be “1”.

For the first part of our study, which is prevalence of HH in different ethnicities, in order to remove the referral bias, patients who referred with HH were excluded and the analysis was done on all the other new-coming patients (81 patients in total were excluded).

Because 3 of the used variables in this study including severity of sweating, HH subtypes and reported NI were highly correlated to each other and including all of them in one model may have caused concealing of the effect of one variable by the other 2 variables also the results would not reflect the true influence of variables on the outcome, it was not possible to run one multivariable logistic regression analysis and include all them in one model. We ran 3

multivariable regression analyses each time using one of the 3 mentioned variables with other variables (gender, BMI, age, ethnicity, presenting diagnosis). The effect of other variables (including gender, BMI, age, ethnicity and presenting diagnosis) remained very similar on anxiety and depression for all the 3 models.

Chapter 3: Results

3.1 The Demographics and the Presenting Diagnoses in Outpatient Dermatology Clinics

Due to the differences in referral patterns, there are significant differences between the two study centers in ethnicity, age, gender, body mass index, and primary dermatological diagnoses (table 3-1).

The Shanghai study group consists of only Chinese and has a higher female ratio (62.5%), a younger presenting age (34.5 years) and a lower body mass index (BMI= 21.7) compared with the Vancouver cohort (Caucasian, Chinese and South & Southeast Asian; 55.7% female, 45.1 years of average age, and an average BMI of 23.9, p-values are significant statistically for all parameters). The presenting diagnoses are also very different, with the top five diagnoses for Vancouver being benign tumors (22.3%), eczematous conditions (16.5%), dysplastic/in-situ or invasive malignancies (10.2%), hyperhidrosis (8%) and pigmentations disorders (7.8%); whereas the most common diagnoses in Shanghai center being eczematous disorders (32.4%), skin infections (23%), acne (19.5%), hair disorders (11%), and psoriasis (7.4%).

Table 3-1: The Demographics and the Presenting Diagnoses in Outpatient Dermatology Clinics in Vancouver and Shanghai

Subjects (2017)		Total	Vancouver		Shanghai		P-value
			Number	%	Number	%	
Gender	Male	826	447	43.9%	379	37.5%	0.002
	Female	1190	559	55.0%	631	62.5%	
Ethnicity	Caucasian	355	355	34.9%	0	0.0%	<0.001
	Chinese	1493	483	47.5%	1010	100.0%	
	SSEA	106	106	10.4%	0	0.0%	
	Other	63	63	6.2%	0	0.0%	

Subjects (2017)		Total	Vancouver		Shanghai		P-value
			Number	%	Number	%	
Age (y/o)			45.1	-	34.5	-	<0.001
BMI			23.9	-	21.7	-	<0.001
Presenting Skin Diagnosis	Tumor-BN	238	225	22.1%	13	1.3%	<0.001
	MISC	255	115	11.3%	140	13.9%	0.109
	Acne	243	46	4.5%	197	19.5%	<0.001
	ECZ	492	165	16.2%	327	32.4%	<0.001
	Hair Ds	46	35	3.4%	11	1.1%	<0.001
	HH	81	81	8.0%	0	0.0%	<0.001
	INF	274	42	4.1%	232	23.0%	<0.001
	PIG-MISC	83	78	7.7%	5	0.5%	<0.001
	PIG-VIT	41	35	3.4%	6	0.6%	<0.001
	PSO	109	34	3.3%	75	7.4%	<0.001
	ROS	27	25	2.5%	2	0.0%	<0.001
	Scars	24	23	2.3%	1	0.1%	<0.001
Tumor-D/IS/M	104	103	10.1%	1	0.1%	<0.001	

Abbreviations: BMI: body mass index; ECZ: eczematous conditions; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections SSEA: South and Southeast Asian; Tumor-BN: benign tumors; MISC: miscellaneous; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PSO: psoriasis; ROS: rosacea; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors; y/o: years old. The gender of 1 patient could not be identified as he showed up in male appearance and he reported to be a female therefore the gender data for that patient was not inputted.

3.2 Primary and Late Onset Hyperhidrosis Based on Patient Demographics

The association between HH, including primary HH in total, PPH, AH, GFH and LOHH was calculated for different severities of sweating, with the categories of different variables including gender, ethnicity, age, BMI and presenting skin diagnosis and then compared to the reference group of each variable.

All the patients who presented with HH to our clinic and sought medical help had moderate or severe HH and none of them had mild HH, therefore we divided the HH patients to whether mild or moderate-severe for further analysis.

3.2.1 Hyperhidrosis in Different Genders

3.2.1.1 Primary and Late Onset Hyperhidrosis in Different Genders

In this part of the study, the prevalence of primary HH and LOHH was calculated for different severities. Then females were compared to males, which we used as the reference group, to assess their association with HH and subtypes.

Both single variants and multivariate logistic regression analyses were done for each cohort. In this section and other sections of this study, for each outcome including primary HH and LOHH, multivariate logistic regression analysis was done separately. For making it easier to follow, the results were combined in one table. We focus mainly on the multivariate logistic regression results because they are adjusted for other variables and therefore more reliable. The results of the multivariate logistic regression analyses are shown as adjusted p-value and adjusted OR in the tables.

3.2.1.1.1 Primary HH and LOHH of All Severities in Different Genders

Female gender is less associated with primary HH than male gender (p-value: 0.007, OR: 0.67 [0.5-0.9]) when considering all the severities of sweating. Oppositely women are more likely to have LOHH than men, (p-value: 0.010, OR: 1.77 [1.1-2.7]) when the results are controlled for the other variables including ethnicity, age, BMI and presenting skin disease (table 3-2).

Table 3-2: Primary HH and LOHH of All Severities in Different Genders

All Severities	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Male	14.3%	Reference		Reference	
	Female	11.6%	0.097	0.79 (0.6-1.0)	0.007	0.67 (0.5-0.9)
LOHH	Male	4.8%	Reference		Reference	
	Female	6.4%	0.147	1.37 (0.9-2.1)	0.010	1.77 (1.1-2.7)

The total number of males: 798, total number of females: 1137. The results on the adj. P-value and adj. OR columns are adjusted for ethnicity, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio

3.2.1.1.2 Moderate and Severe Primary HH and LOHH in Different Genders

Compared to male gender, female gender is less likely associated with primary HH of moderate and severe sweating, (p-value: 0.036, OR: 0.68 [0.5-1.0]), when adjusting the results for the effect of other variables including ethnicity, age, BMI and presenting skin disease (table 3-3). However, there is no significant association between gender and moderate or severe LOHH (table 3-3).

Table 3-3: Moderate and Severe Primary HH and LOHH in Different Genders

Moderate and Severe	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Male	8.5%	Reference		Reference	
	Female	6.9%	0.205	0.79 (0.6-1.1)	0.036	0.68 (0.5-0.95)
LOHH	Male	2.8%	Reference		Reference	
	Female	2.7%	1.0	0.99 (0.6-1.8)	0.307	1.37 (0.8-2.5)

The total number of males: 798, total number of females: 1137. The results on the adj. P-value and adj. OR columns are adjusted for ethnicity, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio

3.2.1.1.3 Prevalence of Mild Primary HH and LOHH in Different Genders

While there is no significant association between the gender and mild primary HH, female patients compared to male patients are more likely to have mild LOHH (p-value: 0.014, OR: 2.16 [1.2-4.0]) when controlling for the effect of other variables including age, BMI, ethnicity and presenting skin diagnosis (table 3-4).

Table 3-4: Mild Primary HH and LOHH in Different Genders

Mild	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Male	5.8%	Reference		Reference	
	Female	4.7%	0.378	0.82 (0.5-1.3)	0.123	0.71 (0.5-1.1)
LOHH	Male	2.0%	Reference		Reference	
	Female	3.7%	0.040	0.53 (0.3-1.0)	0.014	2.16 (1.2-4.0)

The total number of males: 798, total number of females: 1137. The results on the adj. P-value and adj. OR columns

are adjusted for ethnicity, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; HH:

hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio

3.2.1.2 Primary Hyperhidrosis Subtypes in Different Genders

The prevalence of primary HH subtypes (PPH, AH and GFH) was calculated for different severities and then the association between gender and HH subtype was assessed. For each outcome including PPH, AH and GFH, multivariate logistic regression analysis was done separately and then for making it easier to follow, the results were combined in one table.

3.2.1.2.1 Primary Hyperhidrosis Subtypes of All Severities in Different Genders

Compared to male group, female group is significantly less correlated with PPH of all severities (p-value: 0.042, OR: 0.65 [0.2-1.0]) and GFH of all severities (p-value: 0.045, OR: 0.62 [0.4-

1.0]) when controlled for other variables including ethnicity, age, BMI and presenting skin diagnosis (table3-5). Male and female patients in AH group with all severities of sweating, revealed no significant difference (table 3-5).

Table 3-5: Primary HH Subtypes of all Severities in Different Genders

All Severities	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Male	6.5%	Reference		Reference	
	Female	4.8%	0.138	0.73 (0.5-1.1)	0.042	0.65 (0.2-0.95)
AH	Male	2.9%	Reference		Reference	
	Female	3.1%	0.906	1.07 (0.6-1.9)	0.929	0.98 (0.6-1.7)
GFH	Male	4.9%	Reference		Reference	
	Female	3.7%	0.242	0.75 (0.5-1.2)	0.045	0.62 (0.4-0.95)

The total number of males: 798, total number of females: 1137. The results on the adj. P-value and adj. OR columns are adjusted for ethnicity, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.2.1.2.2 Moderate and Severe Primary Hyperhidrosis Subtypes in Different Genders

The evaluation of the moderate and severe primary HH subtypes shows that only the PPH is different between females and males (p-value: 0.020, OR: 0.53 [0.3-0.9]) when controlling for ethnicity, age, BMI and presenting skin diagnosis. There is no significant association between moderate and severe AH and GFH and different genders (table 3-6).

Table 3-6: Moderate and Severe Primary HH Subtypes in Different Genders

Moderate and Severe	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Male	4.3%	Reference		Reference	

Moderate and Severe	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	Female	2.6%	0.050	0.59 (0.3-1.0)	0.020	0.53 (0.3-0.9)
AH	Male	1.3%	Reference		Reference	
	Female	2.2%	0.172	1.77 (0.8-4.2)	0.271	1.54 (0.7-3.3)
GFH	Male	3.0%	Reference		Reference	
	Female	2.1%	0.335	0.73 (0.4-1.3)	0.115	0.62 (0.3-1.1)

The total number of males: 798, total number of females: 1137. The results on the adj. P-value and adj. OR columns are adjusted for ethnicity, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.2.1.2.3 Mild Primary Hyperhidrosis Subtypes in Different Genders

The results of the multivariate logistic regression analysis show that there is no significant difference among genders and mild PPH, mild AH or mild GFH, when controlling for other variables (table 3-7).

Table 3-7: Mild Primary HH Subtypes in Different Genders

Mild	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Male	2.3%	Reference		Reference	
	Female	2.3%	1.0	1.02 (0.5-2.0)	0.789	0.92 (0.5-1.7)
AH	Male	1.6%	Reference		Reference	
	Female	0.9%	0.200	0.54 (0.2-1.3)	0.130	0.51 (0.2-2.1)
GFH	Male	1.9%	Reference		Reference	
	Female	1.6%	0.640	0.79 (0.4-1.7)	0.241	0.64 (0.3-1.3)

The total number of males: 798, total number of females: 1137. The results on the adj. P-value and adj. OR columns are adjusted for ethnicity, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.2.2 Hyperhidrosis in Different Ethnicities

3.2.2.1 Primary and Late Onset Hyperhidrosis in Different Ethnicities

The prevalence of different severities of primary HH and LOHH was calculated and then the association between different ethnicities and HH and HH subtypes were assessed compared to the Caucasian ethnicity, which we used as the reference group.

Both single variants and multivariate logistic regression analyses were done for each group and as explained earlier, we are going to focus mainly on the multivariate logistic regression results, which are shown as adjusted p-value and adjusted OR in the tables.

3.2.2.1.1 Primary HH and LOHH of All Severities in Different Ethnic Groups

The results of the multivariate analysis show that primary HH in all severities (severe, moderate and mild) is significantly less associated with Chi-Van ethnicity than the Caucasian ethnicity, after controlling for all the other variables including gender, age, BMI and presenting skin diagnosis (p-value: 0.042 and OR: 0.59 [0.4-1.0]). However, no other ethnic group showed a significant association with primary or late-onset HH when compared to the Caucasian group, according to the multivariate logistic regression analysis (table 3-8)

Table 3-8: Primary HH and LOHH of all Severities in Different Ethnic Groups

All Severities	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Caucasian	12.3%	Reference		Reference	
	SSEA	13.8%	0.831	1.14 (0.5-2.3)	0.527	0.6 (0.4-1.7)
	Other	17.9%	0.360	1.55 (0.6-3.5)	0.938	1.03 (0.5-2.4)
	Chi-Sha	13.9%	0.539	1.15 (0.8-1.8)	0.146	0.69 (0.4-1.1)

All Severities	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	Chi-Van	9.6%	0.291	0.76 (0.5-1.2)	0.042	0.59 (0.4-0.95)
LOHH	Caucasian	9.3%	Reference		Reference	
	SSEA	4.3%	0.177	0.43 (0.1-1.3)	0.115	0.41 (0.1-1.2)
	Other	7.1%	0.791	0.75 (0.2-2.3)	0.605	0.74 (0.2-2.3)
	Chi-Sha	4.6%	0.003	0.47 (0.3-0.8)	0.179	0.64 (0.3-1.2)
	Chi-Van	6.1%	0.122	0.63 (0.4-1.1)	0.255	0.71 (0.4-1.3)

The total number of Caucasians: 301, the total number of patients from Chi-Sha: 1008, the total number of patients from Chi-Van: 478, the total number of patients from SSEA: 94 and the total number of patients from other ethnicities: 56. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio; SSEA: South and Southeast Asian

3.2.2.1.2 Moderate and Severe Primary HH and LOHH in Different Ethnic Groups

Table 3-9 and the results of the multivariate analysis show that the correlation between moderate and severe primary or LOHH and ethnicities is not significantly different between Caucasian ethnicity and other ethnicities, after adjusting the p-value and the odds ratio for all the other variables including gender, age, BMI and presenting skin diagnosis.

Table 3-9: Moderate and Severe Primary HH and LOHH in Different Ethnic Groups

Moderate and Severe	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Caucasian	7.0%	Reference		Reference	
	SSEA	8.5%	0.786	1.24 (0.5-3.0)	0.771	0.87 (0.3-2.2)
	Other	8.9%	0.579	1.31 (0.4-3.8)	0.675	0.79 (0.3-2.3)
	Chi-Sha	7.8%	0.712	1.13 (0.7-2.0)	0.148	0.63 (0.3-1.2)
	Chi-Van	6.9%	1.0	0.99 (0.5-1.8)	0.298	0.72 (0.4-1.3)
LOHH	Caucasian	5.3%	Reference		Reference	
	SSEA	2.1%	0.263	0.39 (0.0-1.7)	0.192	0.36 (0.1-1.7)
	Other	3.6%	0.750	0.66 (0.1-2.9)	0.685	0.72 (0.2-3.5)

Moderate and Severe	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	Chi-Sha	2.3%	0.012	0.42 (0.2-0.9)	0.540	0.76 (0.3-1.8)
	Chi-Van	2.1%	0.025	0.38 (0.2-0.9)	0.109	0.49 (0.2-1.2)

The total number of Caucasians: 301, the total number of patients from Chi-Sha: 1008, the total number of patients from Chi-Van: 478, the total number of patients from SSEA: 94 and the total number of patients from other ethnicities: 56. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio; SSEA: South and Southeast Asian

3.2.2.1.3 Mild Primary HH and LOHH in Different Ethnic Groups

The association between mild primary HH and LOHH and either of the ethnic groups was not significantly different than the Caucasian ethnic group when adjusting the p-value and the OR for all the other variables including, gender, age, BMI and presenting skin diagnosis in a multivariate analysis (table 3-10).

Table 3-10: Mild Primary HH and LOHH in Different Ethnic Groups

Mild	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Caucasian	5.3%	Reference		Reference	
	SSEA	5.3%	1.0	1.00 (0.3-3.0)	0.590	0.72 (0.2-2.4)
	Other	8.9%	0.348	1.74 (0.5-5.3)	0.517	1.45 (0.5-4.4)
	Chi-Sha	6.1%	0.736	1.15 (0.6-2.2)	0.708	0.87 (0.4-1.8)
	Chi-Van	2.7%	0.095	0.50 (0.2-1.1)	0.061	0.47 (0.2-1.0)
LOHH	Caucasian	4.0%	Reference		Reference	
	SSEA	2.1%	0.534	0.52 (0.1-2.4)	0.408	0.52 (0.1-2.5)
	Other	3.6%	1.0	0.89 (0.1-4.2)	0.783	0.80 (0.2-3.9)
	Chi-Sha	2.3%	0.160	0.56 (0.3-1.3)	0.256	0.60 (0.2-1.5)
	Chi-Van	4.0%	1.0	1.00 (0.5-2.3)	0.932	0.97 (0.4-2.2)

The total number of Caucasians: 301, the total number of patients from Chi-Sha: 1008, the total number of patients from Chi-Van: 478, the total number of patients from SSEA: 94 and the total number of patients from other

ethnicities: 56. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio; SSEA: South and Southeast Asian

3.2.2.2 Primary Hyperhidrosis Subtypes in Different Ethnicities

The prevalence of PPH, AH and GFH was calculated for all severities (including severe, moderate and mild), moderate and severe, and mild severities in different ethnicities. Then the association between primary HH subtypes and ethnicity was assessed (referred to Caucasian ethnicity).

3.2.2.2.1 Primary Hyperhidrosis Subtypes of All Severities in Different Ethnic Groups

Assessing the association between PPH and GFH of all severities of sweating and different ethnicities indicate that there is no significant difference among different ethnicities and Caucasian ethnicity. However, as shown in table 3-11, axillary HH seem to be significantly less associated with Chi-Sha ethnicity (p-value: <0.001 and OR: 0.18 [0.1-0.4]) and Chi-Van (p-value: 0.001 and OR: 0.25 [0.1-0.6]) than the Caucasians, when controlling for all the other variables including gender, age, BMI and Presenting Skin Diagnoses, in a multivariate logistic regression analysis.

Table 3-11: Primary HH Subtypes of All Severities in Different Ethnic Groups

All Severities	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Caucasian	4.3%	Reference		Reference	
	SSEA	8.5%	0.120	2.06 (0.7-5.6)	0.522	1.41 (0.5-4.0)
	Other	3.6%	1.0	0.82 (0.1-3.8)	0.476	0.56 (0.1-2.8)

All Severities	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	Chi-Sha	5.8%	0.412	1.35 (0.7-2.7)	0.991	1.01 (0.5-2.2)
	Chi-Van	5.4%	0.479	1.35 (0.7-2.9)	0.889	1.06 (0.5-2.3)
AH	Caucasian	6.0%	Reference		Reference	
	SSEA	3.2%	0.430	0.52 (0.1-1.8)	0.119	0.35 (0.1-1.3)
	Other	7.1%	0.762	1.21 (0.3-3.9)	0.692	0.79 (0.2-2.6)
	Chi-Sha	2.3%	0.002	0.37 (0.2-0.7)	<0.001	0.18 (0.1-0.4)
	Chi-Van	2.1%	0.008	0.34 (0.1-0.8)	0.001	0.25 (0.1-0.6)
GFH	Caucasian	2.0%	Reference		Reference	
	SSEA	2.1%	1.0	1.07 (0.1-6.1)	0.974	1.03 (0.2-5.5)
	Other	7.1%	0.055	3.76 (0.8-17.0)	0.124	2.92 (0.7-11.4)
	Chi-Sha	5.9%	0.011	3.05 (1.3-8.8)	0.138	2.10 (0.8-5.6)
	Chi-Van	2.1%	1.0	1.05 (0.3-3.6)	0.871	0.92 (0.3-2.6)

The total number of Caucasians: 301, the total number of patients from Chi-Sha: 1008, the total number of patients from Chi-Van: 478, the total number of patients from SSEA: 94 and the total number of patients from other ethnicities: 56. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis; SSEA: South and Southeast Asian

3.2.2.2.2 Moderate and Severe Primary Hyperhidrosis Subtypes in Different Ethnic Groups

No significant association was observed between PPH and GFH of moderate and severe sweating and different ethnic groups when compared to Caucasians. However, patients with Chinese ethnicity, both Chi-Sha (p-value: <0.001 and OR: 0.11 [0.04-0.3]) and Chi-Van (p-value: 0.003 and OR: 0.21 [0.1-0.6]), showed lower association with AH when compared to Caucasians and controlled for gender, age, BMI and presenting skin diagnosis (table 3-12).

Table 3-12: Moderate and Severe Primary HH Subtypes in Different Ethnic Groups

Moderate and Severe	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Caucasian	2.0%	Reference		Reference	
	SSEA	6.4%	0.069	3.34 (0.9-12.8)	0.219	2.23 (0.6-8.0)
	Other	1.8%	1.0	0.89 (0.0-7.6)	0.600	0.55 (0.1-5.1)
	Chi-Sha	3.1%	0.426	1.56 (0.6-4.6)	0.982	1.01 (0.4-2.9)
	Chi-Van	4.0%	0.187	2.03 (0.8-6.3)	0.451	1.49 (0.5-4.2)
AH	Caucasian	4.3%	Reference		Reference	
	SSEA	2.1%	0.537	0.48 (0.1-2.2)	0.172	0.33 (0.1-1.6)
	Other	3.6%	1.0	0.82 (0.1-3.8)	0.305	0.44 (0.1-2.1)
	Chi-Sha	1.1%	<0.001	0.24 (0.1-0.6)	<0.001	0.11 (0.0-0.3)
	Chi-Van	1.5%	0.026	0.33 (0.1-0.9)	0.003	0.21 (0.1-0.6)
GFH	Caucasian	0.7%	Reference		Reference	
	SSEA	0.0%	0.559	1.61 (0.0-31.2)	0.705	1.61 (0.1-19.3)
	Other	3.6%	0.118	5.50 (0.4-77.2)	0.130	4.88 (0.6-37.9)
	Chi-Sha	3.7%	0.006	5.69 (1.5-49.0)	0.072	4.23 (0.9-20.4)
	Chi-Van	1.5%	0.495	2.22 (0.4-22.0)	0.370	2.09 (0.4-10.5)

The total number of Caucasians: 301, the total number of patients from Chi-Sha: 1008, the total number of patients from Chi-Van: 478, the total number of patients from SSEA: 94 and the total number of patients from other ethnicities: 56. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis; SSEA: South and Southeast Asian

3.2.2.2.3 Mild Primary Hyperhidrosis Subtypes in Different Ethnic Groups

As demonstrated in table 3-13, no significant association was observed between mild PPH, AH and GFH and different ethnicities when compared to Caucasian ethnicity after controlling for all the other variables including, gender, age, BMI and presenting skin diagnosis in a multivariate logistic regression analysis.

Table 3-13: Mild Primary HH Subtypes in Different Ethnic Groups

Mild	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Caucasian	2.3%	Reference		Reference	
	SSEA	2.1%	1.0	0.91 (0.1-4.9)	0.531	0.49 (0.1-4.5)
	Other	1.8%	1.0	0.76 (0.0-6.1)	0.689	0.64 (0.1-5.8)
	Chi-Sha	2.7%	0.896	1.16 (0.5-3.2)	0.769	1.19 (0.4-3.8)
	Chi-Van	1.5%	0.546	0.62 (0.2-2.1)	0.458	0.65 (0.2-2.0)
AH	Caucasian	1.7%	Reference		Reference	
	SSEA	1.1%	1.0	0.64 (0.0-5.8)	0.530	0.48 (0.0-4.8)
	Other	3.6%	0.302	2.19 (0.2-13.8)	0.339	2.43 (0.4-15.0)
	Chi-Sha	1.2%	0.562	0.71 (0.2-2.6)	0.265	0.47 (0.1-1.8)
	Chi-Van	0.6%	0.272	0.37 (0.1-1.9)	0.202	0.37 (0.1-1.7)
GFH	Caucasian	1.3%	Reference		Reference	
	SSEA	2.1%	1.0	0.80 (0.0-8.2)	0.785	0.73 (0.1-7.0)
	Other	3.6%	0.239	2.74 (0.2-19.7)	0.523	1.79 (0.3-10.7)
	Chi-Sha	2.2%	0.482	1.66 (0.6-6.7)	0.957	1.04 (0.3-3.7)
	Chi-Van	0.6%	0.439	0.47 (0.1-2.8)	0.209	0.37 (0.1-1.7)

The total number of Caucasians: 301, the total number of patients from Chi-Sha: 1008, the total number of patients from Chi-Van: 478, the total number of patients from SSEA: 94 and the total number of patients from other ethnicities: 56. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis; SSEA: South and Southeast Asian

3.2.3 Hyperhidrosis in Different Age Groups

3.2.3.1 Primary and Late Onset Hyperhidrosis in Different Age Groups

The prevalence of different severities of primary HH and LOHH was calculated for different age groups and then primary HH and LOHH correlation with different age groups was calculated and

compared the >60y/o age group, which we used as the reference group, in this part of the study. The tables in each part illustrate the analyses for both single variants and multivariate logistic regression analyses and we are going to focus mainly on the multivariate logistic regression results.

3.2.3.1.1 Primary HH and LOHH of All Severities in Different Age Groups

After controlling for all the other variables including gender, ethnicity, BMI and presenting skin diagnosis, as presented on table 3-14, primary HH (all severities) is significantly more correlated with age groups <30 (p-value: <0.001 and OR: 17.17 [7.5-38.5]) and 30-59 (p-value: <0.001 and OR: 5.22 [2.4-11.6]) than =>60 y/o age group.

LOHH of all severities of sweating is significantly less correlated with <30 y/o age group than >60 y/o age group (p-value <0.001, OR: 0.11 [0.0-0.3]), after adjusting the results for other mentioned variables, however, there is no significant difference between LOHH and 30-59 y/o age group than =>60 y/o age groups (table 3-14).

Table 3-14: Primary HH and LOHH of All Severities in Different Age Groups

All Severities	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	=>60	2.1%	Reference		Reference	
	<30	22.8%	<0.001	13.59 (6.3-34.8)	<0.001	17.17 (7.7-38.5)
	30-59	9.0%	<0.001	4.56 (2.1-11.8)	<0.001	5.22 (2.4-11.6)
LOHH	=>60	8.2%	Reference		Reference	
	<30	0.9%	<0.001	0.10 (0.0-0.3)	<0.001	0.11 (0.0-0.3)
	30-59	8.5%	0.968	1.04 (0.7-1.7)	0.947	0.98 (0.6-1.6)

The total number of patients in =>60 y/o age group: 330, the total number of patients in age group <30 y/o age group: 685, the total number of patients in 30-59 y/o age group: 922. The results on the adj. P-value and adj. OR

columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio; y/o: year old

3.2.3.1.2 Moderate and Severe Primary HH and LOHH in Different Age Groups

Table 3-15 and the results of the multivariate analysis indicate that moderate and severe primary HH is significantly more associated with age groups <30 y/o and 30-59 y/o than =>60 y/o.

LOHH of moderate and severe sweating is not differently associated with 30-59 y/o than the =>60 y/o age groups, but is significantly less associated with <30 y/o age group after adjusting the p-value and the odds ratio for all the other variables including gender, ethnicity, BMI and presenting skin diagnosis (table 3-15).

Table 3-15: Moderate and Severe Primary HH and LOHH in Different Age Groups

Moderate and Severe	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	=>60	1.2%	Reference		Reference	
	<30	13.7%	<0.001	12.94 (4.8-49.0)	<0.001	15.55 (5.5-44.4)
	30-59	5.2%	<0.001	4.47 (1.6-17.2)	0.003	4.92 (1.7-14.0)
LOHH	=>60	4.8%	Reference		Reference	
	<30	0.1%	<0.001	0.03 (0.0-0.1)	0.002	0.04 (0.0-0.3)
	30-59	3.9%	0.564	0.80 (0.4-1.6)	0.398	0.76 (0.4-1.4)

The total number of patients in =>60 y/o age group: 330, the total number of patients in age group <30 y/o age group: 685, the total number of patients in 30-59 y/o age group: 922. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio; y/o: year old

3.2.3.1.3 Mild Primary HH and LOHH in Different Age Groups

Mild primary HH is significantly more associated with <30 y/o and 30-59 y/o age groups than

=>60 y/o age group (table 3-16).

Compared to =>60 y/o age group, <30 y/o age group and LOHH are significantly less associated when adjusting the p-value and the OR for all the other variables including, gender, ethnicity, BMI and presenting skin diagnosis in a multivariate analysis. There is no meaningful association between mild LOHH and 30-59 y/o age group (table 3-4).

Table 3-16: Mild Primary HH and LOHH in different age groups

Mild	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	=>60	0.9%	Reference		Reference	
	<30	9.1%	<0.001	10.8 (3.5-54.4)	<0.001	13.61 (4.0-46.2)
	30-59	3.8%	0.008	4.30 (1.3-22.0)	0.010	4.96 (1.5-16.7)
LOHH	=>60	3.3%	Reference		Reference	
	<30	0.7%	0.004	0.21 (0.1-0.7)	0.009	0.22 (0.1-0.7)
	30-59	4.6%	0.431	1.38 (0.7-3.0)	0.466	1.30 (0.6-2.7)

The total number of patients in =>60 y/o age group: 330, the total number of patients in age group <30 y/o age group: 685, the total number of patients in 30-59 y/o age group: 922. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio; y/o: year old

3.2.3.2 Primary Hyperhidrosis Subtypes in Different Age Groups

In different severities (severe, moderate and severe, and mild), the prevalence of PPH, AH and GFH was calculated for different age groups. Then the association between different age groups compared to >60 y/o age group and the HH subtypes were assessed.

3.2.3.2.1 Primary Hyperhidrosis Subtypes of All Severities in Different Age Groups

Assessing the association between primary HH subtypes of all severities of sweating and different age groups demonstrates that PPH is significantly more associated with <30 y/o age group than >60 y/o age group but there is no meaningful difference between 30-59 y/o and =>60 y/o age groups (table 3-17).

Because the sample size in the age group >60 y/o was 0, the true difference between other groups and the reference group could not be assessed (table 3-17).

Also GFH of all severities is significantly more correlated with <30 and 30-50 y/o age groups than >60 y/o age group, when controlling for all the other variables including gender, ethnicity, BMI and presenting skin diagnosis, in a multivariate logistic regression analysis (table 3-17).

Table 3-17: Primary HH Subtypes of All Severities in Different Age Groups

All Severities	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	=>60	1.8%	Reference		Reference	
	<30	10.7%	<0.001	6.43 (2.8-18.3)	<0.001	9.14 (3.7-22.7)
	30-59	3.0%	0.331	1.69 (0.7-5.0)	0.125	2.07 (0.8-5.2)
AH	=>60	0.0%	Reference		Reference	
	<30	4.8%	<0.001	b	0.993	b
	30-59	2.7%	<0.001	b	0.993	b
GFH	=>60	0.3%	Reference		Reference	
	<30	7.3%	<0.001	25.87 (4.4-1041)	0.003	20.42 (2.7-153.3)
	30-59	3.3%	<0.001	11.05 (1.8-452)	0.028	9.52 (1.3-70.8)

The total number of patients in =>60 y/o age group: 330, the total number of patients in age group <30 y/o age group: 685, the total number of patients in 30-59 y/o age group: 922. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis; y/o: year old. b: no p-value or OR can be calculated

3.2.3.2.2 Moderate and Severe Primary Hyperhidrosis Subtypes in Different Age Groups

The difference in the association between AH or GFH of moderate and severe HH and different age groups could not be calculated due to the absence of any patients in >60 y/o age group (table 3-18).

However, <30 y/o age group is significantly more correlated with moderate and severe PPH than the =>60 y/o age group when controlled for gender, ethnicity, BMI and presenting skin diagnosis variables. No significant difference was observed between 30-59 y/o and =>60 y/o age groups in PPH (table 3-18).

Table 3-18: Prevalence of Moderate and Severe Primary Subtypes in Different Age Groups

Moderate and Severe	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	=>60	1.2%	Reference		Reference	
	<30	6.4%	<0.001	5.59 (2.0-21.6)	<0.001	7.60 (2.5-23.0)
	30-59	1.6%	0.794	1.35 (0.4-5.6)	0.420	1.61 (0.5-5.1)
AH	=>60	0.0%	Reference		Reference	
	<30	2.6%	0.001	b	0.993	b
	30-59	1.8%	0.010	b	0.994	b
GFH	=>60	0.0%	Reference		Reference	
	<30	4.7%	<0.001	b	0.993	b
	30-59	1.7%	<0.001	b	0.994	b

The total number of patients in =>60 y/o age group: 330, the total number of patients in age group <30 y/o age group: 685, the total number of patients in 30-59 y/o age group: 922. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis; y/o: year old. b: no p-value or OR can be calculated

3.2.3.2.3 Mild Primary Hyperhidrosis Subtypes in Different Age Groups

Patients <30 y/o showed an increased association with mild PPH compared to the reference group, after controlling for all the other variables including, gender, ethnicity, BMI and presenting skin diagnosis in a multivariate logistic regression analysis (table 3-19).

The difference between <30 and 30-59 y/o age groups and =>60 y/o age group could not be calculated for AH, because 0.0% of the population was categorized into mild AH group (table 3-19).

As demonstrated in table 3-19, there is no significant difference in the association between mild GFH and different age groups (table 3-19).

Table 3-19: Mild Primary HH Subtypes in Different Age Groups

Mild	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	=>60	0.6%	Reference		Reference	
	<30	4.2%	<0.001	7.24 (1.8-63.1)	0.003	10.02 (2.1-46.9)
	30-59	1.4%	0.378	2.34 (0.5-21.5)	0.189	2.82 (0.6-13.2)
AH	=>60	0.0%	Reference		Reference	
	<30	2.2%	0.004	b	0.993	b
	30-59	0.9%	0.119	b	0.994	b
GFH	=>60	0.3%	Reference		Reference	
	<30	2.6%	0.011	8.36 (1.3-350.5)	0.086	6.22 (0.8-50.0)
	30-59	1.5%	0.135	5.07 (0.8-215.0)	0.158	4.37 (0.6-33.9)

The total number of patients in =>60 y/o age group: 330, the total number of patients in age group <30 y/o age group: 685, the total number of patients in 30-59 y/o age group: 922. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis; y/o: year old. b: no p-value or OR can be calculated

3.2.4 Hyperhidrosis in Obese and Non-Obese Patients

3.2.4.1 Primary and Late Onset Hyperhidrosis in Obese and Non-Obese Patients

The prevalence of different severities of primary HH and LOHH was calculated for overweight (BMI>24.9) [72] and non-obese (BMI<= 24.9) patients.

The tables in each section will demonstrate the analyses of both single variants and multivariate logistic regression analyses and we are going to focus mainly on the logistic regression results.

3.2.4.1.1 Primary HH and LOHH of All Severities in Different BMIs

The association between primary HH of all severities and BMI>24.9 is not significantly different than in BMI <=24.9, after controlling for all the other variables including gender, age ethnicity and presenting skin diagnosis (Table 3-20).

However, LOHH of all severities of sweating is more correlated with BMI>24.9 than the BMI <=24.9 (p-value: 0.003, OR: 1.97 [1.3-3.1]), after adjusting the results for other mentioned variables (table 3-20).

Table 3-20: Primary HH and LOHH of All Severities in Different BMIs

All Severities	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	<= 24.9	12.9%	Reference		Reference	
	>24.9	12.2%	0.755	0.94 (0.7-1.3)	0.302	1.22 (0.8-1.8)
LOHH	<= 24.9	4.4%	Reference		Reference	
	>24.9	10.2%	<0.001	2.64 (1.6-3.7)	0.003	1.97 (1.3-3.1)

The total number of patients with BMI<= 24.9: 1476, the total number of patients with BMI> 24.9: 452. Some patients did not answer to the questions regarding BMI. The results on the adj. P-value and adj. OR columns are

adjusted for gender, ethnicity, age and presenting skin diagnosis. Abbreviations: Adj.: adjusted; BMI: body mass index; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio

3.2.4.1.2 Moderate and Severe Primary HH and LOHH in Different BMIs

There is no significant association between moderate and severe primary HH and different BMIs, however, as shown in table 3-21, LOHH of moderate and severe sweating is significantly more correlated with BMI>24.9 than BMI<=24.9 (p-value: 0.003, OR: 2.57 [1.4-4.8]).

Table 3-21: Moderate and Severe Primary HH and LOHH in Different BMIs

Moderate and Severe	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	<= 24.9	7.8%	Reference		Reference	
	>24.9	6.9%	0.579	1.15 (0.8-1.8)	0.672	1.11 (0.7-1.8)
LOHH	<= 24.9	1.8%	Reference		Reference	
	>24.9	6.0%	<0.001	3.54 (2.0-6.4)	0.003	2.57 (1.4-4.8)

The total number of patients with BMI<= 24.9: 1476, the total number of patients with BMI> 24.9: 452. Some patients did not answer to the questions regarding BMI. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and presenting skin diagnosis. Abbreviations: Adj.: adjusted; BMI: body mass index; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio

3.2.4.1.3 Mild Primary HH and LOHH in Different BMIs

Mild primary HH or LOHH is not significantly associated with BMI after controlling for all the other variables including gender, ethnicity, age and presenting skin diagnosis in a multivariate logistic regression analysis (table 3-22).

Table 3-22: Mild Primary HH and LOHH in Different BMIs

Mild	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	<= 24.9	5.1%	Reference		Reference	
	>24.9	5.3%	0.944	1.05 (0.6-1.7)	0.293	1.33 (0.8-2.3)
LOHH	<= 24.9	2.6%	Reference		Reference	
	>24.9	4.2%	0.123	1.62 (0.9-2.9)	0.266	1.43 (0.8-2.7)

The total number of patients with BMI<= 24.9: 1476, the total number of patients with BMI> 24.9: 452. Some patients did not answer to the questions regarding BMI. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and presenting skin diagnosis. Abbreviations: Adj.: adjusted; BMI: body mass index; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio

3.2.4.2 Primary Hyperhidrosis Subtypes in Different BMIs

The prevalence of PPH, AH and GFH was calculated for different severities of sweating in obese patients and then their association with BMI>24.9 was compared to BMI<=24.9 group (the reference group).

3.2.4.2.1 Primary Hyperhidrosis Subtypes of All Severities in Different Age Groups

The association between primary HH subtypes (PPH, AH and GFH) of all severities and BMI>24.9 is not significantly different than BMI <=24.9 after adjusting the results for all the other variables including gender, ethnicity, age and presenting skin diagnosis in a multivariate logistic regression analysis (table 3-23).

Table 3-23: Primary HH Subtypes of All Severities in Different BMIs

All Severities	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	<= 24.9	5.7%	Reference		Reference	

All Severities	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	>24.9	4.9%	0.579	0.85 (0.3-1.4)	0.653	1.13 (0.7-1.9)
AH	<= 24.9	2.9%	Reference		Reference	
	>24.9	3.3%	0.776	1.14 (0.6-2.1)	0.985	0.99 (0.5-2.0)
GFH	<= 24.9	4.3%	Reference		Reference	
	>24.9	4.0%	0.896	0.93 (0.5-1.6)	0.211	1.47 (0.8-2.7)

The total number of patients with BMI<= 24.9: 1476, the total number of patients with BMI> 24.9: 452. Some patients did not answer to the questions regarding BMI. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; BMI: body mass index; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.2.4.2.2 Moderate and Severe Primary Hyperhidrosis Subtypes in Different BMIs

The association between moderate and severe primary HH subtypes and BMI is not meaningfully different between obese and non-obese patients when adjusting the p-value and the OR after involving other variables including gender, ethnicity, age and presenting skin diagnosis (table 3-24).

Table 3-24: Moderate and Severe Primary Subtypes in Different BMIs

Moderate and Severe	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	<= 24.9	3.4%	Reference		Reference	
	>24.9	2.9%	0.701	0.84 (0.4-1.6)	0.810	1.09 (0.5-2.2)
AH	<= 24.9	1.9%	Reference		Reference	
	>24.9	1.5%	0.776	0.81 (0.3-1.9)	0.308	0.62 (0.2-1.6)
GFH	<= 24.9	2.5%	Reference		Reference	
	>24.9	2.4%	1.0	0.94 (0.4-1.9)	0.158	1.72 (0.8-3.6)

The total number of patients with BMI<= 24.9: 1476, the total number of patients with BMI> 24.9: 452. Some patients did not answer to the questions regarding BMI. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary

hyperhidrosis; BMI: body mass index; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.2.4.2.3 Mild Primary Hyperhidrosis Subtypes in Different BMIs

There is no significant difference between obese and non-obese patients in association with mild primary HH subtypes (PPH, AH and GFH) after controlling for other variables including gender, ethnicity, age and presenting skin diagnosis (table 3-25).

Table 3-25: Mild Primary HH Subtypes in Different BMIs

Mild	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	<= 24.9	2.3%	Reference		Reference	
	>24.9	2.0%	0.833	0.86 (0.4-1.9)	0.641	1.22 (0.5-2.8)
AH	<= 24.9	1.0%	Reference		Reference	
	>24.9	1.8%	0.297	1.75 (0.6-4.4)	0.191	1.94 (0.7-5.2)
GFH	<= 24.9	1.8%	Reference		Reference	
	>24.9	1.5%	0.999	0.91 (0.3-2.2)	0.781	1.14 (0.4-2.9)

The total number of patients with BMI<= 24.9: 1476, the total number of patients with BMI> 24.9: 452. Some patients did not answer to the questions regarding BMI. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and presenting skin diagnosis. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; BMI: body mass index; GFH: generalized or facial hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.2.5 Hyperhidrosis in Different Presenting Skin Diagnoses

3.2.5.1 Primary and Late Onset Hyperhidrosis in Different Presenting Skin Diagnoses

In different skin diagnoses, the prevalence of different severities of primary HH and LOHH was

calculated and their association was evaluated after comparing to the reference group, which is the benign tumor.

The results of both single variants and multivariate logistic regression analyses will be demonstrated and we are going to focus on the multivariate logistic regression results.

3.2.5.2 Primary HH and LOHH of All Severities in Different Presenting Skin Diagnoses

Primary HH or LOHH of all severities are not significantly correlated with different presenting skin diagnose, after controlling for all the other variables including gender, ethnicity, age and BMI (Table 3-26).

Table 3-26: Primary HH and LOHH of All Severities in Different Presenting Skin Diagnoses

All Severities	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Tumor-BN	11.3%	Reference		Reference	
	Acne	18.1%	0.049	1.73 (1.0-3.0)	0.656	0.87 (0.5-1.6)
	ECZ	13.0%	0.604	1.17 (0.7-2.0)	0.598	0.86 (0.5-1.5)
	Hair Ds	10.9%	1.0	0.95 (0.3-2.7)	0.391	0.63 (0.2-1.8)
	INF	14.3%	0.392	1.30 (0.8-2.3)	0.704	0.89 (0.5-1.7)
	PIG-MISC	7.1%	0.378	0.60 (0.2-1.6)	0.491	0.71 (0.3-1.9)
	PIG-VIT	22.0%	0.106	2.19 (0.8-5.4)	0.190	1.87 (0.7-4.7)
	PSO	11.0%	1.0	0.97 (0.4-2.1)	0.703	0.86 (0.4-1.9)
	ROS	14.8%	0.535	1.36 (0.3-4.4)	0.347	1.76 (0.5-5.7)
	Scars	16.7%	0.503	1.56 (0.4-5.2)	0.979	1.02 (0.3-3.4)
	MISC	10.2%	0.779	0.88 (0.5-1.6)	0.295	0.72 (0.4-1.3)
	Tumor-D/IS/M	5.8%	0.159	0.48 (0.2-1.2)	0.364	0.64 (0.2-1.7)
LOHH	Tumor-BN	6.7%	Reference		Reference	
	Acne	2.1%	0.023	0.29 (0.1-0.9)	0.874	0.91 (0.3-2.8)
	ECZ	3.9%	0.131	0.56 (0.3-1.2)	0.915	0.96 (0.5-2.0)
	Hair Ds	8.7%	0.544	1.32 (0.3-4.4)	0.342	1.80 (0.5-6.0)
	INF	5.9%	0.827	0.86 (0.4-1.9)	0.268	1.59 (0.7-3.6)

All Severities	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	PIG-MISC	4.8%	0.706	0.69 (0.2-2.2)	0.677	0.78 (0.2-2.5)
	PIG-VIT	12.2%	0.209	1.92 (0.5-5.9)	0.163	2.21 (0.7-6.7)
	PSO	9.2%	0.558	1.40 (0.6-3.4)	0.186	1.83 (0.7-4.5)
	ROS	14.8%	0.132	2.40 (0.5-8.3)	0.239	2.05 (0.6-6.8)
	Scars	4.2%	1.0	0.60 (0.0-4.3)	0.955	0.94 (0.1-7.8)
	MISC	8.6%	0.543	1.30 (0.6-2.7)	0.110	1.80 (0.9-3.7)
	Tumor-D/IS/M	4.8%	0.664	0.70 (0.2-2.1)	0.232	0.52 (0.2-1.5)

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 256 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI. Abbreviations: Adj.: adjusted; ECZ: eczematous conditions; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; LOHH: late onset hyperhidrosis; MISC: miscellaneous; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors

3.2.5.3 Moderate and Severe Primary HH and LOHH in Different Presenting Skin

Diagnoses

Moderate and severe primary HH and LOHH are not significantly associated with presenting skin diagnoses any different than the benign tumors (the reference group), after controlling for all the other variables including gender, ethnicity, age and BMI (Table 3-27).

Table 3-27: Moderate and Severe Primary HH and LOHH in Different Presenting Skin Diagnoses

Moderate and Severe	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Tumor-BN	5.9%				
	Acne	11.1%	0.059	2.00 (0.9-4.2)	0.673	1.18 (0.5-2.6)
	ECZ	7.9%	0.398	1.38 (0.7-2.8)	0.727	1.13 (0.6-2.3)
	Hair Ds	6.5%	0.744	1.12 (0.2-4.2)	0.707	0.77 (0.2-3.0)
	INF	7.3%	0.635	1.26 (0.6-2.8)	0.995	1.00 (0.4-2.2)
	PIG-MISC	6.0%	1.0	1.01 (0.3-3.1)	0.772	1.18 (0.4-3.5)
	PIG-VIT	9.8%	0.315	1.73 (0.4-5.9)	0.369	1.75 (0.5-5.9)
	PSO	6.4%	1.0	1.10 (0.4-3.0)	0.845	1.10 (0.4-3.0)
	ROS	11.1%	0.395	1.99 (0.3-7.9)	0.152	2.67 (0.7-10.3)
	Scars	16.7%	0.069	3.18 (0.7-11.5)	0.229	2.15 (0.6-7.5)
	MISC	6.6%	0.872	1.14 (0.5-2.6)	0.975	1.01 (0.5-2.2)
	Tumor-D/IS/M	2.9%	0.291	0.48 (0.1-1.8)	0.567	0.68 (0.2-2.6)
LOHH	Tumor-BN	2.9%	Reference		Reference	
	Acne	0.4%	0.036	0.14 (0.0-1.1)	0.541	0.50 (0.1-4.6)
	ECZ	1.4%	0.247	0.48 (0.1-1.6)	0.653	0.77 (0.2-2.4)
	Hair Ds	6.5%	0.209	2.29 (0.4-4.0)	0.103	3.39 (0.8-14.7)
	INF	3.7%	0.836	1.25 (0.4-4.0)	0.189	2.15 (0.7-6.7)
	PIG-MISC	2.4%	1.0	0.81 (0.1-4.4)	0.853	1.17 (0.2-6.0)
	PIG-VIT	7.3%	0.169	2.59 (0.4-12.0)	0.161	2.83 (0.7-12.1)
	PSO	5.5%	0.240	1.92 (0.5-6.9)	0.254	2.05 (0.6-7.0)
	ROS	7.4%	0.230	2.63 (0.3-14.8)	0.311	2.35 (0.5-12.2)
	Scars	0.0%	1.0	b	0.998	b
	MISC	3.5%	0.916	1.20 (0.4-3.9)	0.396	1.60 (0.5-4.7)
	Tumor-D/IS/M	2.9%	1.0	0.98 (0.2-4.4)	0.434	0.57 (0.1-2.4)

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 256 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI. Abbreviations:

Adj.: adjusted; ECZ: eczematous conditions; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; LOHH: late onset hyperhidrosis; MISC: miscellaneous; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors. b: no p-value or OR can be calculated

3.2.5.4 Mild Primary HH and LOHH in Different Presenting Skin Diagnoses

Presenting skin diagnosis is not significantly correlated with mild primary HH or LOHH any different than the reference group, after controlling for all the other variables including gender, ethnicity, age and BMI (Table 3-28).

Table 3-28: Mild Primary HH and LOHH in Different Presenting Skin Diagnoses

Mild	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Primary HH	Tumor-BN	5.5%	Reference		Reference	
	Acne	7.0%	0.612	1.30 (0.6-3.0)	0.230	0.58 (0.2-1.4)
	ECZ	5.1%	0.969	0.93 (0.5-2.0)	0.214	0.6 (0.3-1.3)
	Hair Ds	4.3%	1.0	0.79 (0.1-3.7)	0.419	0.52 (0.1-2.5)
	INF	7.0%	0.607	1.29 (0.6-2.9)	0.504	0.74 (0.3-1.8)
	PIG-MISC	1.2%	0.125	0.21 (0.0-1.4)	0.200	0.26 (0.0-2.1)
	PIG-VIT	12.2%	0.157	2.39 (0.6-7.7)	0.437	1.63 (0.5-5.6)
	PSO	4.6%	1.0	0.83 (0.2-2.6)	0.413	0.62 (0.2-1.9)
	ROS	3.7%	1.0	0.67 (0.02-4.8)	0.816	0.78 (0.1-6.4)
	Scars	0.0%	0.616	b	0.998	b
	MISC	3.5%	0.407	0.63 (0.2-1.6)	0.106	0.46 (0.2-1.2)
	Tumor-D/IS/M	2.9%	0.409	0.51 (0.1-1.9)	0.506	0.63 (0.2-2.4)
LOHH	Tumor-BN	3.8%	Reference		Reference	
	Acne	1.6%	0.170	0.43 (0.1-1.6)	0.843	1.14 (0.3-4.3)
	ECZ	2.4%	0.435	0.64 (0.2-1.7)	0.833	1.11 (0.4-2.9)
	Hair Ds	2.2%	1.0	0.57 (0.01-4.3)	0.732	0.69 (0.1-5.8)
	INF	2.2%	0.427	0.57 (0.2-1.8)	0.900	1.08 (0.3-3.5)
	PIG-MISC	2.4%	0.734	0.62 (0.1-3.1)	0.475	0.56 (0.1-2.7)

Mild	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	PIG-VIT	4.9%	0.668	1.30 (0.1-6.6)	0.616	1.51 (0.3-7.5)
	PSO	3.7%	1.0	0.97 (0.2-3.6)	0.566	1.45 (0.4-5.1)
	ROS	7.4%	0.311	2.03 (0.2-10.6)	0.542	1.65 (0.3-8.2)
	Scars	4.2%	1.0	1.11 (0.0-8.6)	0.707	1.51 (0.2-12.9)
	MISC	5.1%	0.631	1.36 (0.5-3.7)	0.192	1.85 (0.7-4.6)
	Tumor-D/IS/M	1.9%	0.515	0.50 (0.1-2.5)	0.382	0.49 (0.1-2.4)

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 256 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI. Abbreviations: Adj.: adjusted; ECZ: eczematous conditions; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; LOHH: late onset hyperhidrosis; MISC: miscellaneous; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors. b: no p-value or OR can be calculated

3.2.5.5 Primary Hyperhidrosis Subtypes in Different Presenting Skin Diagnoses

The prevalence of primary HH subtypes was calculated for different skin diseases with different severities of sweating and their association with each other was then evaluated.

3.2.5.5.1 Primary Hyperhidrosis Subtypes of All Severities in Different Skin Diagnoses

According to the results of our study, PPH of all severities is significantly more correlated with vitiligo than patients with benign tumor (p-value: 0.020, OR: 3.82 [1.2-11.8]) after controlling the results for other variables including gender, ethnicity, age and BMI (table 3-29). There is no

other significant correlation between PPH (all severities together) and other skin disorders when compared to benign tumors.

In AH and GFH of all severities together, there are no significant differences between different skin diseases and the reference group after adjusting the p-value and the OR for other variables including gender, ethnicity, age and BMI (table 3-29).

Due to absence of patients in some groups, the result could not be calculated (table 3-29).

Table 3-29: Primary HH Subtypes of All Severities in Different Presenting Skin Diagnoses

All Severities	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Tumor-BN	4.6%	Reference		Reference	
	Acne	4.9%	1.0	1.07 (0.4-2.7)	0.163	0.51 (0.2-1.3)
	ECZ	6.5%	0.398	1.43 (0.7-3.2)	0.927	0.96 (0.4-2.1)
	Hair Ds	2.2%	0.698	0.46 (0.0-3.3)	0.221	0.27 (0.0-2.2)
	INF	7.0%	0.510	1.54 (0.7-3.7)	0.997	0.99 (0.4-2.4)
	PIG-MISC	6.0%	0.573	1.30 (0.3-4.2)	0.503	1.48 (0.5-4.6)
	PIG-VIT	17.1%	0.008	4.22 (1.3-12.9)	0.020	3.82 (1.2-11.8)
	PSO	1.8%	0.360	0.39 (0.0-1.8)	0.177	0.34 (0.1-1.6)
	ROS	0.0%	0.610	b	0.998	b
	Scars	12.5%	0.125	2.93 (0.5-12.4)	0.375	1.89 (0.5-7.7)
	MISC	4.3%	1.0	0.93 (0.4-2.4)	0.458	0.71 (0.3-1.8)
	Tumor-D/IS/M	3.8%	1.0	0.83 (0.2-2.9)	0.714	1.26 (0.4-4.4)
AH	Tumor-BN	3.4%	Reference		Reference	
	Acne	3.7%	1.0	1.11 (0.4-3.4)	0.852	1.11 (0.4-3.4)
	ECZ	3.3%	1.0	0.97 (0.4-2.7)	0.502	1.40 (0.5-3.7)
	Hair Ds	6.5%	0.394	2.00 (0.3-8.8)	0.408	1.83 (0.4-7.7)
	INF	2.2%	0.595	0.65 (0.2-2.2)	0.960	0.97 (0.3-3.2)
	PIG-MISC	1.2%	0.455	0.35 (0.0-2.7)	0.492	0.47 (0.1-4.0)
	PIG-VIT	2.4%	1.0	0.72 (0.0-5.6)	0.722	0.68 (0.1-5.8)
	PSO	4.6%	0.556	1.38 (0.4-4.9)	0.257	2.02 (0.6-6.8)
	ROS	7.4%	0.271	2.29 (0.2-12.4)	0.249	2.66 (0.5-14.0)
	Scars	4.2%	0.585	1.25 (0.0-10.0)	0.982	0.98 (0.1-8.6)

All Severities	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	MISC	1.6%	0.247	0.46 (0.1-1.7)	0.410	0.59 (0.2-2.1)
	Tumor-D/IS/M	1.9%	0.729	0.56 (0.1-2.9)	0.608	0.66 (0.1-3.3)
GFH	Tumor-BN	3.4%	Reference		Reference	
	Acne	9.5%	0.011	3.00 (1.3-7.9)	0.890	1.07 (0.4-2.9)
	ECZ	3.3%	1.0	0.97 (0.4-2.7)	0.139	0.47 (0.2-1.3)
	Hair Ds	2.2%	1.0	0.64 (0.0-5.0)	0.403	0.40 (0.0-3.4)
	INF	5.1%	0.445	1.55 (0.6-4.4)	0.395	0.64 (0.2-1.8)
	PIG-MISC	0.0%	0.117	b	0.997	b
	PIG-VIT	2.4%	1.0	0.72 (0.0-5.6)	0.598	0.56 (0.1-4.8)
	PSO	4.6%	0.556	1.38 (0.4-4.9)	0.682	0.77 (0.2-2.7)
	ROS	7.4%	0.271	2.29 (0.2-12.4)	0.248	2.65 (0.5-13.9)
	Scars	0.0%	1.0	b	0.998	b
	MISC	4.3%	0.760	1.29 (0.5-3.8)	0.583	0.75 (0.3-2.1)
	Tumor-D/IS/M	0.0%	0.112	b	0.996	b

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 256 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; ECZ: eczematous conditions; GFH: generalized or facial hyperhidrosis; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; MISC: miscellaneous; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PPH: palmar and plantar hyperhidrosis; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors; b: no p-value or OR can be calculated

3.2.5.5.2 Moderate and Severe Primary Hyperhidrosis Subtypes in Different Presenting Skin Diagnoses

After controlling for all the other variables including gender, ethnicity, age and BMI, PPH of

moderate and severe sweating is significantly more associated with vitiligo and scars than the benign tumors. However, there are no significant difference between other skin diseases and benign tumors (table 3-30).

There is no significant association between moderate and severe AH and GFH and other skin diseases when compared to benign tumors (table 3-30).

Multivariate logistic regression analysis could not be done for the groups in which no patient was present (table 3-30).

Table 3-30: Moderate and Severe Primary HH Subtypes in Different Presenting Skin Diagnoses

Moderate and Severe	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Tumor-BN	1.7%	Reference		Reference	
	Acne	2.9%	0.544	1.73 (0.4-8.2)	0.967	1.03 (0.3-4.0)
	ECZ	4.5%	0.058	2.74 (0.9-11.1)	0.208	2.11 (0.7-6.7)
	Hair Ds	2.2%	0.590	1.30 (0.0-13.5)	0.816	0.76 (0.1-7.5)
	INF	2.9%	0.396	1.76 (0.5-8.1)	0.638	1.38 (0.4-5.2)
	PIG-MISC	4.8%	0.213	2.91 (0.5-16.0)	0.115	3.25 (0.7-14.1)
	PIG-VIT	7.3%	0.068	4.58 (0.7-28.3)	0.050	4.88 (1.0-24.3)
	PSO	0.9%	1.0	0.54 (0.01-5.6)	0.617	0.56 (0.1-5.3)
	ROS	0.0%	1.0	b	0.998	b
	Scars	12.5%	0.019	8.22 (1.1-52.2)	0.043	5.35 (1.1-27.1)
	MISC	3.1%	0.386	1.88 (0.5-8.7)	0.455	1.62 (0.5-5.7)
	Tumor-D/IS/M	1.9%	1.0	1.15 (0.1-8.1)	0.460	1.98 (0.3-12.2)
AH	Tumor-BN	2.1%	Reference		Reference	
	Acne	2.5%	1.0	1.18 (0.3-5.0)	0.529	1.56 (0.4-6.2)
	ECZ	1.6%	0.766	0.77 (0.2-3.0)	0.592	1.41 (0.4-4.9)
	Hair Ds	4.3%	0.317	2.11 (0.2-13.4)	0.410	2.09 (0.4-12.1)
	INF	0.7%	0.259	0.34 (0.0-2.1)	0.742	0.74 (0.1-4.4)
	PIG-MISC	1.2%	1.0	0.56 (0.0-5.1)	0.722	0.67 (0.1-6.1)
	PIG-VIT	2.4%	1.0	1.16 (0.0-10.8)	0.891	1.17 (0.1-10.9)
	PSO	2.8%	0.710	1.32 (0.2-6.9)	0.272	2.35 (0.5-10.8)

Moderate and Severe	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	ROS	7.4%	0.153	3.70 (0.3-24.1)	0.133	3.86 (0.7-22.5)
	Scars	4.2%	0.441	2.02 (0.0-19.2)	0.571	1.92 (0.2-18.3)
	MISC	1.2%	0.491	0.55 (0.1-2.9)	0.794	0.82 (0.2-3.6)
	Tumor-D/IS/M	1.0%	0.672	0.45 (0.0-4.1)	0.544	0.1 (0.1-4.6)
GFH	Tumor-BN	2.1%	Reference		Reference	
	Acne	5.8%	0.068	2.84 (0.9-10.3)	0.762	0.83 (0.2-2.9)
	ECZ	1.8%	0.780	0.87 (0.3-3.3)	0.111	0.36 (0.1-1.3)
	Hair Ds	0.0%	1.0	1.04 (0.0-9.6)	0.645	0.59 (0.1-5.6)
	INF	3.7%	0.435	1.77 (0.5-6.7)	0.462	0.62 (0.2-2.2)
	PIG-MISC	0.0%	0.332	b	0.997	b
	PIG-VIT	0.0%	1.0	b	0.998	b
	PSO	2.8%	0.710	1.32 (0.2-6.9)	0.628	0.68 (0.1-3.3)
	ROS	3.7%	0.479	1.79 (0.0-16.9)	0.488	2.22 (0.2-21.2)
	Scars	0.0%	1.0	b	0.998	b
	MISC	2.3%	1.0	1.12 (0.3-4.7)	0.398	0.57 (0.2-2.1)
	Tumor-D/IS/M	0.0%	0.328	b	0.996	b

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 256 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; ECZ: eczematous conditions; GFH: generalized or facial hyperhidrosis; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; MISC: miscellaneous; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PPH: palmar and plantar hyperhidrosis; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors; b: no p-value or OR can be calculated

3.2.5.5.3 Mild Primary Hyperhidrosis Subtypes in Different Presenting Skin Diagnoses

Compared to benign tumors, acne is significantly less associated with mild PPH (p-value: 0.042,

OR: 0.24 [0.1-0.9]) after controlling the results for other variables including gender, ethnicity, age and BMI (table 3-31).

There is no other significant difference between other skin diseases and benign tumor in PPH or other primary HH subtypes (table 3-31).

Because of the absence of any patients in some groups, the result could not be calculated for those skin diagnoses (table 3-31).

Table 3-31: Mild Primary HH Subtypes in Different Presenting Skin Diagnoses

Mild	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
PPH	Tumor-BN	2.9%	Reference		Reference	
	Acne	2.1%	0.742	0.69 (0.2-2.6)	0.042	0.24 (0.1-0.9)
	ECZ	2.0%	0.616	0.69 (0.2-2.2)	0.088	0.36 (0.1-1.2)
	Hair Ds	0.0%	0.603	b	0.997	b
	INF	4.0%	0.671	1.38 (0.5-4.3)	0.484	0.64 (0.2-2.2)
	PIG-MISC	1.2%	0.686	0.40 (0.0-3.2)	0.514	0.49 (0.1-4.2)
	PIG-VIT	9.8%	0.061	3.54 (0.7-14.8)	0.194	2.66 (0.6-11.6)
	PSO	0.9%	0.444	0.31 (0.1-2.4)	0.157	0.21 (0.0-1.8)
	ROS	0.0%	1.0	b	0.998	b
	Scars	0.0%	1.0	b	0.998	b
	MISC	1.2%	0.208	0.39 (0.1-1.7)	0.060	0.24 (0.1-1.1)
	Tumor-D/IS/M	1.9%	0.728	0.65 (0.1-3.5)	0.837	0.84 (0.2-4.5)
AH	Tumor-BN	1.3%	Reference		Reference	
	Acne	1.2%	1.0	0.98 (0.1-7.4)	0.623	0.63 (0.1-3.9)
	ECZ	1.6%	1.0	1.29 (0.3-7.6)	0.777	1.25 (0.3-5.7)
	Hair Ds	2.2%	0.509	1.74 (0.0-22.2)	0.731	1.52 (0.1-16.6)
	INF	1.5%	1.0	1.16 (0.2-8.0)	0.972	1.03 (0.2-5.8)
	PIG-MISC	0.0%	0.570	b	0.997	b
	PIG-VIT	0.0%	1.0	b	0.998	b
	PSO	1.8%	0.651	1.46 (0.1-13.0)	0.690	1.47 (0.2-9.8)
	ROS	0.0%	1.0	b	0.998	b
	Scars	0.0%	1.0	b	0.998	b

Mild	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	MISC	0.4%	0.356	0.31 (0.01-3.9)	0.324	0.31 (0.03-3.2)
	Tumor-D/IS/M	1.0%	1.0	0.76 (0.01-9.6)	0.963	1.06 (0.1-11.0)
GFH	Tumor-BN	1.3%	Reference		Reference	
	Acne	3.7%	0.141	3.01 (0.7-17.5)	0.576	1.57 (0.3-7.5)
	ECZ	1.4%	1.0	1.14 (0.3-6.8)	0.711	0.75 (0.2-3.5)
	Hair Ds	2.2%	1.0	b	0.998	b
	INF	1.5%	1.0	1.16 (0.2-8.0)	0.611	0.64 (0.1-3.5)
	PIG-MISC	0.0%	0.570	b	0.997	b
	PIG-VIT	2.4%	0.472	1.95 (0.04-25.0)	0.718	1.54 (0.1-16.2)
	PSO	1.8%	0.651	1.46 (0.1-13.0)	0.977	0.97 (0.1-6.6)
	ROS	3.7%	0.351	2.99 (0.1-38.9)	0.344	3.09 (0.3-31.9)
	Scars	0.0%	1.0	b	0.998	b
	MISC	2.0%	0.726	1.56 (0.3-10.2)	0.869	1.14 (0.2-5.4)
	Tumor-D/IS/M	0.0%	0.556	b	0.997	b

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 256 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; ECZ: eczematous conditions; GFH: generalized or facial hyperhidrosis; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; MISC: miscellaneous; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PPH: palmar and plantar hyperhidrosis; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors; b: no p-value or OR can be calculated

3.3 Anxiety and Depression according to Patients' Demographics and in Patients with and without Hyperhidrosis and Night Sweating

In this section of the study, all the 2017 patients were involved, including the patients who

presented with excessive sweating. Total prevalence of anxiety and depression was 10.8 % and 13.4% respectively, in our study population.

3.3.1 Anxiety and Depression Based on Patient Demographics

The prevalence of the demographics and the presenting diagnoses of the patients are summarized in section 3.1. Table 3-32 summarizes the total number of each subgroup of each variable including gender, ethnicity, age, BMI, presenting skin diagnosis, HH subtypes, HH severity score, HH negative impact score and NS severity score.

The results of the single variants analysis and the multivariate logistic regression analysis are both displayed in table but we will focus on the more reliable results, which is the results from the multivariate logistic regression analysis. For each outcome including anxiety and depression, multivariate logistic regression analysis was done separately and then for making it easier to follow, the results were combined in one table. Caucasian ethnicity, benign tumor skin disease, BMI<= 24.9, male gender and age =>60 y/o, non HH, severity and NI score of 0 and no NS are used as reference groups for each variable.

Table 3-32: Total Number of Patients and the Prevalence of Anxiety and Depression according to Patients' Demographics, Hyperhidrosis Subtypes and Severities, Sweating Negative Impact Scores and Different Severities of Night Sweating

Subjects		Number	Anxiety %	Depression %
Total		2017	10.8%	13.4%
Gender	Male	826	10.5%	12.7%
	Female	1190	10.9%	13.9%
Ethnicity	Caucasian	355	22.0%	23.9%
	Chi-Sha	1010	6.0%	7.8%
	Chi-Van	483	9.3%	14.1%
	SSEA	106	16.0%	19.8%

Subjects		Number	Anxiety %	Depression %
	Other	63	25.4%	27.0%
Age (year)	>60	332	11.0%	13.0%
	<30	712	11.0%	13.6%
	30-59	973	10.3%	13.3%
BMI	<=24.9	1528	9.2%	12.2%
	>24.9	480	15.8%	17.3%
Presenting Skin Diagnosis	Tumor-BN	238	11.3%	13.9%
	MISC	336	14.0%	16.1%
	Acne	243	8.6%	12.3%
	ECZ	492	6.9%	9.3%
	Hair Ds	46	13.0%	23.9%
	INF	274	9.1%	11.7%
	PIG-MISC	83	10.8%	14.5%
	PIG-VIT	41	19.5%	19.5%
	PSO	109	13.8%	14.7%
	ROS	27	25.9%	18.5%
	Scars	24	8.3%	12.5%
	Tumor-D/IS/M	104	15.4%	19.2%
Hyperhidrosis Subtypes	no HH	1580	7.3%	9.6%
	HH (total)	437	27.2%	23.1%
	PPH	130	22.3%	22.9%
	AH	96	22.9%	27.2%
	GFH	91	28.6%	33.7%
	LOHH	120	20%	27.3%
HH Severity Score	Mild	247	18.6%	23.1%
	Moderate	92	26.1%	27.2%
	Severe	98	31.6%	36.7%
Negative Impact	HH with No NI	214	15.9%	17.8%
	HH with Mild NI	118	28%	32.2%
	HH with Mod. NI	47	25.5%	34%
	HH with Severe NI	58	37.9%	46.6%
NS Severity Score	no NS	1540	7.5%	9.7%
	NS (total)	477	21.4%	25.2%
	Mild	340	18.5%	21.2%
	Moderate	92	23.9%	32.6%
	Severe	45	37.8%	40%

Abbreviations: AH: axillary hyperhidrosis; BMI: body mass index; Chi-Van: Chinese from Vancouver; Chi-Sha: Chinese from Shanghai; ECZ: eczematous conditions; GFH: generalized or facial hyperhidrosis; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; LOHH: late onset hyperhidrosis; MISC: miscellaneous; Mod: moderate; NI: negative impact; NS: night sweating; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT:

vitiligo related pigmentation disorders; PPH: palmar or plantar hyperhidrosis; PSO: psoriasis; ROS: rosacea; SSEA: South and Southeast Asian; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors

3.3.1.1 Prevalence of Anxiety and Depression in Different Genders

As shown in table 3-33, no difference was seen in the association with anxiety or depression among different genders, when adjusting the results for all the variables including ethnicity, age, BMI, presenting skin diagnosis, HH and NS.

Table 3-33: The Association between Gender and Anxiety/Depression

Outcome	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	Male	10.5%	Reference		Reference	
	Female	10.9%	0.837	1.04 (0.8-1.4)	0.301	1.18 (0.9-1.6)
Depression	Male	12.7%	Reference		Reference	
	Female	13.9%	0.496	1.11 (0.8-1.5)	0.215	1.20 (0.9-1.6)

The total number of males: 826, total number of females: 1190. The results on the adj. P-value and adj. OR columns are adjusted for ethnicity, age, BMI and presenting skin diagnosis, HH and NS. Abbreviations: Adj.: adjusted; OR: odds ratio

3.3.1.2 Anxiety and Depression in Different Ethnicities

Chinese ethnicities both from Shanghai (p-value <0.001, OR: 0.22 [0.1-0.4]) and Vancouver (p-value <0.001, OR: 0.45 [0.3-0.7]) are significantly less associated with anxiety than Caucasian ethnicity after controlling the results for other variables including gender, age, BMI, presenting skin diagnosis, HH and NS (table 3-34).

Also Chinese ethnicity from Shanghai (p-value <0.001, OR: 0.23 [0.1-0.4]) and Chinese ethnicity from Vancouver (p-value <0.001, OR: 0.63 [0.4-1]) are significantly less associated with

depression than Caucasian ethnicity after adjusting the results for other mentioned variables (table 3-34).

In association with anxiety and depression, there is no difference in remaining ethnicities and the Caucasian ethnicity after controlling the results for all the other variables (table 3-34).

Table 3-34: The Association between Ethnicity and Anxiety/Depression

Outcome	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	Caucasian	22.0%	Reference		Reference	
	SSEA	16.0%	0.235	0.68 (0.4-1.2)	0.308	0.72 (0.4-1.4)
	Other	25.4%	0.663	1.21 (0.6-2.3)	0.649	1.17 (0.6-2.3)
	Chi-Sha	6.0%	<0.001	0.23 (0.2-0.3)	<0.001	0.22 (0.1-0.4)
	Chi-Van	9.3%	<0.001	0.37 (0.24-0.6)	<0.001	0.45 (0.3-0.7)
Depression	Caucasian	23.9%	Reference		Reference	
	SSEA	19.8%	0.450	0.79 (0.4-1.4)	0.541	0.83 (0.5-1.5)
	Other	27.0%	0.720	1.17 (0.6-2.2)	0.845	1.07 (0.6-2.1)
	Chi-Sha	7.8%	<0.001	0.27 (0.2-0.4)	<0.001	0.23 (0.1-0.4)
	Chi-Van	14.1%	<0.001	0.52 (0.4-0.8)	<0.001	0.63 (0.4-0.95)

The total number of Caucasians: 355, the total number of patients from Chi-Sha: 1010, the total number of patients from Chi-Van: 483, the total number of patients from SSEA: 106 and the total number of patients from other ethnicities: 63. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis, HH and NS. Abbreviations: Adj.: adjusted; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; OR: odds ratio; SSEA: South and Southeast Asian

3.3.1.3 Anxiety and Depression in Different BMIs

No significant difference was seen between obese and non-obese individuals in association with anxiety and depression after controlling the effect of other variables including gender, ethnicity, age, presenting skin diagnosis, HH and NS (table 3-35).

Table 3-35: The Association Between BMI and Anxiety/Depression

Outcome	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	≤ 24.9	9.2%	Reference		Reference	
	>24.9	15.8%	<0.001	1.86 (1.4-2.5)	0.351	1.18 (0.7-1.8)
Depression	≤ 24.9	12.2%	Reference		Reference	
	>24.9	17.3%	0.005	1.51 (1.1-2.0)	0.984	1.00 (0.7-1.4)

The total number of patients with BMI ≤ 24.9: 1476, the total number of patients in with BMI > 24.9: 452. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and presenting skin diagnosis, HH and NS. Abbreviations: Adj.: adjusted; BMI: body mass index; OR: odds ratio

3.3.1.4 Anxiety and Depression in Different Age Groups

Among different age groups, no variation was seen in association with anxiety or depression after adjusting the results for the effect of other variables including gender, ethnicity, BMI, presenting skin diagnosis, HH and NS (table 3-36).

Table 3-36: The Association between Age and Anxiety/Depression

Outcome	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	⇒60	11.1%	Reference		Reference	
	<30	10.3%	0.745	0.91 (0.6-1.4)	0.857	0.95 (0.6-1.6)
	30-59	11.0%	1.0	0.99 (0.7-1.5)	0.971	1.01 (0.6-1.6)
Depression	⇒60	13.0%	Reference		Reference	
	<30	13.3%	0.945	1.03 (0.7-1.6)	0.716	1.09 (0.7-1.8)
	30-59	13.6%	0.849	1.05 (0.7-1.6)	0.652	1.10 (0.7-1.7)

The total number of patients in ⇒60 y/o age group: 332, the total number of patients in age group <30 y/o age group: 712, the total number of patients in 30-59 y/o age group: 973. The results on the adj. P-value and adj. OR

columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis, HH and NS. Abbreviations: Adj.: adjusted; OR: odds ratio; y/o: years old

3.3.1.5 Anxiety and Depression in Different Presenting Skin Diagnoses

Based on the multivariate logistic regression analysis and after controlling for all the other variables, compared to benign tumors, patients with psoriasis seem to have higher association with both anxiety (p-value: 0.019 and OR: 1.51 [1.2-5.0]) and depression (p-value: 0.038 and OR: 2.09 [1.0-3.5]) and patients with skin infections have higher association with depression (p-value: 0.034 and OR: 1.91 [1.1-3.5]). Other skin diseases, (except HH which will be discussed in section 3.3.2) show no increased association with anxiety or depression compared to benign tumors (table 3-37).

Table 3-37: The Association between Presenting Skin Diagnosis and Anxiety/Depression

Outcome	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	Tumor-BN	11.3%	Reference		Reference	
	MISC	14.0%	0.421	1.27 (0.8-2.2)	0.574	1.17 (0.7-2.0)
	Acne	8.6%	0.403	0.74 (0.4-1.4)	0.277	1.48 (0.7-3.0)
	ECZ	6.9%	0.059	0.58 (0.3-1.0)	0.75	1.1 (0.6-2.0)
	Hair Ds	13.0%	0.938	1.17 (0.4-3.2)	0.605	1.31 (0.5-3.6)
	INF	9.1%	0.495	0.78 (0.4-1.5)	0.084	1.79 (0.9-3.5)
	PIG-MISC	10.8%	1.0	0.95 (0.4-2.2)	0.842	1.09 (0.5-2.6)
	PIG-VIT	19.5%	0.229	1.89 (0.7-4.8)	0.332	1.58 (0.6-4.0)
	PSO	13.8%	0.643	1.25 (0.6-2.6)	0.019	2.42 (1.2-5.0)
	ROS	25.9%	0.060	2.72 (0.9-7.5)	0.076	2.52 (0.9-7.0)
	Scars	8.3%	1.0	0.71 (0.1-3.2)	0.711	0.75 (0.2-3.5)
Tumor-D/IS/M	15.4%	0.390	1.42 (0.7-2.9)	0.646	1.18 (0.6-2.4)	
Depression	Tumor-BN	13.9%	Reference		Reference	
	MISC	16.1%	0.543	1.19 (0.7-2.0)	0.604	1.14 (0.7-1.9)

Outcome	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	Acne	12.3%	0.720	0.88 (0.5-1.5)	0.080	1.74 (0.9-3.2)
	ECZ	9.3%	0.087	0.64 (0.4-1.1)	0.482	1.21 (0.7-2.0)
	Hair Ds	23.9%	0.133	1.95 (0.8-4.4)	0.058	2.23 (1.0-5.1)
	INF	11.7%	0.543	0.82 (0.5-1.4)	0.034	1.91 (1.1-3.5)
	PIG-MISC	14.5%	1.0	1.05 (0.5-2.2)	0.766	1.12 (0.5-2.4)
	PIG-VIT	19.5%	0.481	1.5 (0.6-3.7)	0.554	1.32 (0.5-3.3)
	PSO	14.7%	0.971	1.07 (0.5-2.1)	0.038	2.09 (1.05-3.5)
	ROS	18.5%	0.561	1.41 (0.4-4.2)	0.809	1.15 (0.4-3.5)
	Scars	12.5%	1.0	0.89 (0.2-3.2)	0.864	0.89 (0.2-3.3)
	Tumor-D/IS/M	19.2%	0.272	1.48 (0.8-2.8)	0.270	1.45 (0.7-2.8)

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 336 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, HH and NS. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; ECZ: eczematous conditions; GFH: generalized or facial hyperhidrosis; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; MISC: miscellaneous; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PPH: palmar and plantar hyperhidrosis; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors

3.3.2 Anxiety and Depression in Patient with or without Hyperhidrosis

The prevalence of anxiety (23.1%) and depression (27.2%) and their association is higher in HH patients compared to patients without HH after controlling the results for all the other variables including gender, ethnicity, age, BMI, presenting skin disease and NS (table 3-38).

Table 3-38: The Association between Presence of Hyperhidrosis and Anxiety/Depression

Outcome	Hyperhidrosis	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	No HH	7.3%	Reference		Reference	
	HH	27.2%	<0.001	3.88 (2.9-5.2)	<0.001	3.25 (2.4-4.5)
Depression	No HH	9.6%	Reference		Reference	
	HH	23.1%	<0.001	3.51 (2.7-4.6)	<0.001	3.23 (2.4-4.3)

The total number of patients with HH: 437 and the total number of the patients without HH: 1580. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and NS.

Abbreviations: Adj.: adjusted; HH: hyperhidrosis; OR: odds ratio

3.3.2.1 Anxiety and Depression in Hyperhidrosis Subtypes

The correlation with anxiety and depression is significantly higher in all HH subtypes, and highest in GFH after controlling the results for all the other variables including gender, ethnicity, age, BMI, presenting skin disease and NS (table 3-39).

Table 3-39: The Association between Hyperhidrosis Subtypes and Anxiety/Depression

Outcome	HH Subtypes	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	No HH	7.3%	Reference		Reference	
	PPH	22.3%	<0.001	3.65 (2.2-5.9)	<0.001	3.76 (2.3-6.2)
	AH	22.9%	<0.001	3.78 (2.2-6.4)	<0.001	2.38 (1.3-4.2)
	GFH	28.6%	<0.001	5.09 (3.0-8.5)	<0.001	5.60 (3.2-9.7)
	LOHH	20.0%	<0.001	3.18 (1.9-5.3)	<0.001	2.39 (1.4-4.0)
Depression	No HH	9.6%	Reference		Reference	
	PPH	23.8%	<0.001	2.89 (1.8-4.6)	<0.001	3.00 (1.9-4.8)
	AH	27.1%	<0.001	3.58 (2.1-5.9)	<0.001	2.40 (1.4-4.1)
	GFH	34.1%	<0.001	4.97 (3.0-8.1)	<0.001	5.70 (3.4-9.5)
	LOHH	25.8%	<0.001	3.65 (2.3-5.8)	<0.001	2.83 (1.8-4.5)

The total number of patients with PPH: 130, the total number of patients with AH: 96, the total number of patients

with GFH: 91, the total number of patients with LOHH: 120 and the total number of the patients without HH: 1580. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and NS. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.3.2.2 Anxiety and Depression in Different Hyperhidrosis Severities

Figure 3-1 shows, as HH severity increases from mild to severe, the prevalence of anxiety and depression rises.

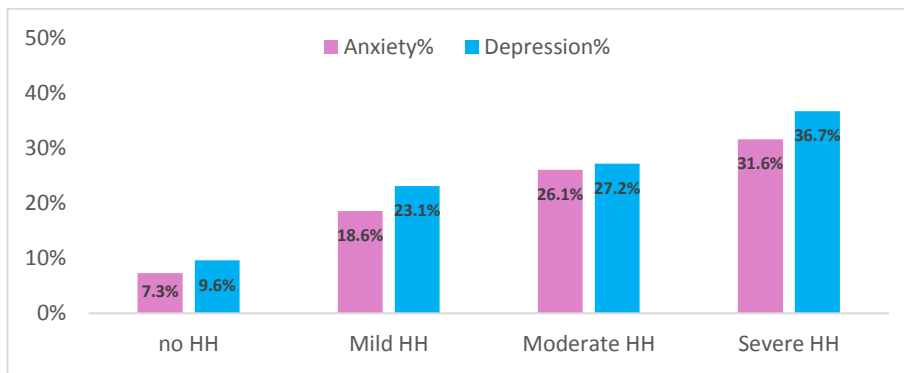


Figure 3-1: Prevalence of Anxiety and Depression in Different Severities of Hyperhidrosis

All HH severities (mild, moderate and severe) are significantly more associated with anxiety and depression than non-HH group after adjusting the p-value and the OR for other variables including gender, ethnicity, age, BMI, presenting skin disease and NS (table 3-40).

Table 3-40: The Association between Hyperhidrosis Severity and Anxiety/Depression

Outcome	HH Severity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	No HH	7.3%	Reference		Reference	
	Mild	18.6%	<0.001	2.91 (2.0-4.3)	<0.001	2.49 (1.5-4.0)

Outcome	HH Severity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	Moderate	26.1%	<0.001	4.49 (2.6-7.6)	<0.001	4.42 (2.9-6.8)
	Severe	31.6%	<0.001	5.88 (3.6-9.6)	<0.001	2.88 (1.7-4.9)
Depression	No HH	9.6%	Reference		Reference	
	Mild	23.5%	<0.001	2.89 (2.0-4.1)	<0.001	2.40 (1.5-3.7)
	Moderate	27.2%	<0.001	3.59 (2.1-6.0)	<0.001	4.23 (2.8-6.3)
	Severe	36.7%	<0.001	5.59 (3.5-8.9)	<0.001	3.28 (2.0-5.3)

The total number of patients with mild HH: 247, the total number of patients with moderate HH: 92, the total number of patients with severe HH: 98 and the total number of the patients without HH: 1580. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and NS. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; OR: odds ratio

3.3.2.3 Anxiety and Depression in Different Negative Impacts from Hyperhidrosis

As shown in figure 3-2, there is an increasing trend in the prevalence of anxiety and depression as the impact of sweating gets worse.

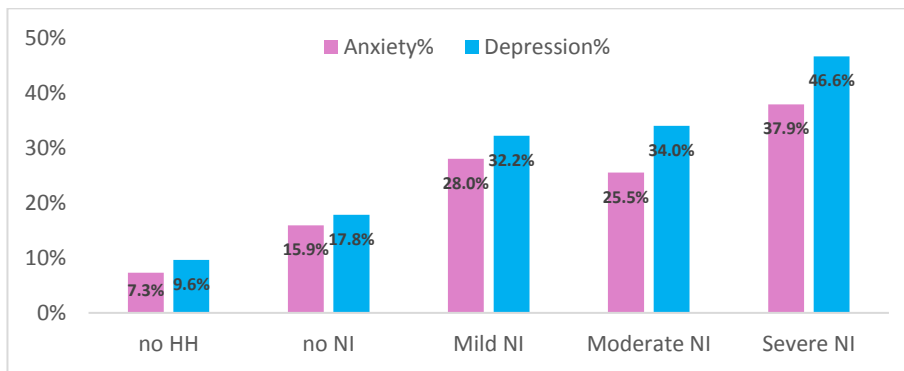


Figure 3-2: The Prevalence of Anxiety and Depression in HH Patients with Different NI Severities

The association between NI and both anxiety and depression is also assessed after including all the other variables. The results are displayed in table 3-41.

Table 3-41: The Association between Hyperhidrosis Negative Impact and Anxiety/Depression

Outcome	Hyperhidrosis Negative Impact	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	No HH	7.3%	Reference		Reference	
	HH with No NI	15.9%	<0.001	2.38 (1.5-3.6)	<0.001	2.32 (1.5-3.6)
	HH with Mild NI	28.0%	<0.001	4.89 (3.0-7.8)	<0.001	4.47 (2.8-7.2)
	HH with Moderate NI	25.5%	<0.001	4.32 (2.0-8.8)	<0.001	3.80 (1.8-8.0)
	HH with Severe NI	37.9%	<0.001	7.69 (4.2-14.0)	<0.001	5.31 (2.7-10.5)
Depression	No HH	9.6%	Reference		Reference	
	HH with No NI	17.8%	<0.001	2.04 (1.4-3.0)	0.001	2.04 (1.4-3.1)
	HH with Mild NI	32.2%	<0.001	4.49 (2.9-7.0)	<0.001	4.60 (2.9-7.2)
	HH with Moderate NI	34.0%	<0.001	4.88 (2.4-9.4)	<0.001	5.01 (2.5-9.9)
	HH with Severe NI	46.6%	<0.001	8.22 (4.6-14.7)	<0.001	6.79 (3.5-13.0)

The total number of HH patients with no NI: 214, the total number of HH patients with mild NI: 118, the total number of patients with moderate NI: 47, the total number of HH patients with severe NI: 58 and the total number of the patients without HH: 1580. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and NS. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; NI: negative impact; OR: odds ratio

3.3.3 Anxiety and Depression in Patients with and without Night Sweating

NS compared to no NS group is more associated with both anxiety (p-value <0.001, OR: 1.92 [1.4-2.7]) and depression (p-value <0.001, OR: 1.80 [1.3-2.5]) after controlling the results for other variables including gender, age, ethnicity, BMI, presenting skin diagnosis and HH (table 3-42).

Table 3-42: The Association between Presence of Night Sweating and Anxiety/Depression

Outcome	Night Sweating	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	No NS	7.5%	Reference		Reference	

Outcome	Night Sweating	Prevalence	P-value	OR	Adj. P-value	Adj. OR
	NS	21.4%	<0.001	3.37 (2.5-4.6)	<0.001	1.92 (1.4-2.7)
Depression	No NS	9.7%	Reference		Reference	
	NS	25.2%	<0.001	3.11 (2.4-4.1)	<0.001	1.80 (1.3-2.5)

The total number of patients with NS: 477 and the total number of the patients without NS: 1540. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and HH. Abbreviations: Adj.: adjusted; NS: night sweating; OR: odds ratio

3.3.3.1 Anxiety and Depression in Different Severities of Night Sweating

Figure 3-3 shows that there is an increasing trend in the prevalence of both anxiety and depression, as NS gets more severe.

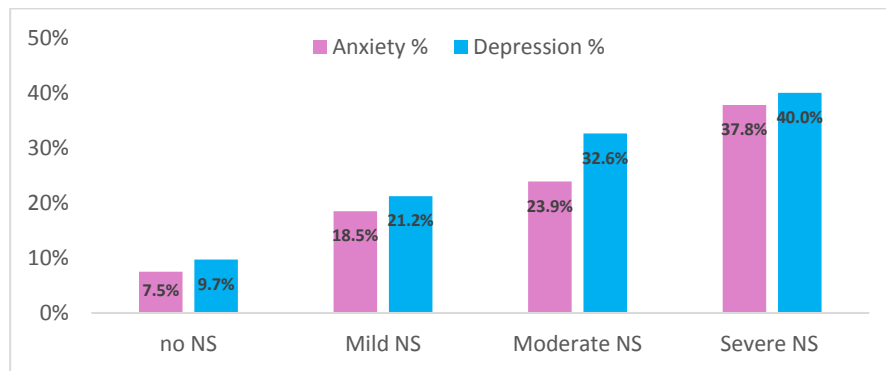


Figure 3-3: Prevalence of Anxiety and Depression in Different Severities of Night Sweating

There is a higher correlation with anxiety and depression in all severities of NS compared to no NS group, after controlling the results for other variables including gender, age, ethnicity, BMI, presenting skin diagnosis an HH (table 3-43).

Table 3-43: The Association between Night Sweating Severity and Anxiety/Depression

Outcome	Night Sweating	Prevalence	P-value	OR	Adj. P-value	Adj. OR
Anxiety	No NS	7.5%	Reference		Reference	
	Mild NS	18.5%	<0.001	2.82 (2.0-4.0)	0.002	1.80 (1.2-2.6)
	Moderate NS	23.9%	<0.001	3.89 (2.2-6.6)	0.045	1.82 (1.3-3.0)
	Severe NS	37.8%	<0.001	7.50 (3.7-14.7)	0.001	3.13 (1.5-6.3)
Depression	No NS	9.7%	Reference		Reference	
	Mild NS	21.2%	<0.001	2.49 (1.8-3.4)	0.007	1.61 (1.1-2.3)
	Moderate NS	32.6%	<0.001	4.48 (2.7-7.3)	0.003	2.22 (1.3-3.8)
	Severe NS	40.0%	<0.001	6.27 (3.1-11.9)	0.006	2.61 (1.3-5.2)

The total number of patients with mild NS: 340, the total number of patients with moderate NS: 92, the total number of patients with severe NS: 45 and the total number of the patients without NS: 1540. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and HH.

Abbreviations: Adj.: adjusted; NS: night sweating; OR: odds ratio

3.4 Night Sweating according to Patient Demographics and in Patients with and without Hyperhidrosis, Anxiety and Depression

In this section of the study, all the 2017 patients were involved, including the patients who presented with excessive sweating (HH). We will investigate how presence of HH, anxiety, depression and other demographic factors can affect the prevalence of NS. Total prevalence of NS in our population was 23.9%.

3.4.1 Night Sweating Based on Patient Demographics

The prevalence of the demographic factors and the presenting skin diagnoses, the prevalence of different HH subtypes and severities, the prevalence of stress symptoms as well as the prevalence of patients with different negative impact scores are summarized in table 3-44.

Table 3-44: Total Number of the Patients and the Prevalence of Night Sweating according to Patients'

Demographics

Subjects		Total	Night Sweating %
Total		2017	23.9%
Gender	Male	826	24.7%
	Female	1190	22.9%
Ethnicity	Caucasian	355	38.6%
	Chi-Sha	1010	20.7%
	Chi-Van	483	18.7%
	SSEA	106	27.4%
	Other	63	34.9%
Age (year)	=>60	332	17.8%
	<30	712	26.1%
	30-59	973	23.8%
BMI	<=24.9	1528	21.9%
	>24.9	480	29.8%
Presenting Skin Diagnosis	Tumor-BN	238	23.9%
	MISC	336	29.8%
	Acne	243	23.9%
	ECZ	492	20.7%
	Hair Ds	46	30.4%
	INF	274	20.8%
	PIG-MISC	83	19.3%
	PIG-VIT	41	22%
	PSO	109	23.9%
	ROS	27	25.9%
	Scars	24	16.7%
	Tumor-D/IS/M	104	26%
Hyperhidrosis Subtypes	No HH	1580	14.3%
	HH (total)	437	57.4%
	PPH	130	48.5 %
	AH	96	64.6%
	GFH	91	61.5%
	LOHH	120	58.3%
HH Severity Score	Mild	247	49.4%
	Moderate	92	63.0%
	Severe	98	72.4%

Subjects		Total	Night Sweating %
Negative Impact	HH with No NI	214	40.2%
	HH with Mild NI	118	71.2%
	HH with Mod. NI	47	68.1%
	HH with Severe NI	58	84.5%
Stress Symptoms	No Anx. or Dep.	1709	19.9%
	Anx. only	38	44.7%
	Dep. only	91	38.5%
	Anx. and Dep.	179	47.5%

Abbreviations: AH: axillary hyperhidrosis; Anx.: anxiety; BMI: body mass index; Chi-Van: Chinese from Vancouver; Chi-Sha: Chinese from Shanghai; Dep.: depression; ECZ: eczematous conditions; GFH: generalized or facial hyperhidrosis; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; LOHH: late onset hyperhidrosis; MISC: miscellaneous; Mod: moderate; NI: negative impact; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PPH:P plantar hyperhidrosis; PSO: psoriasis; ROS: rosacea; SSEA: South and Southeast Asian; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors

3.4.1.1 Night sweating in Different Genders

Among the demographic factors in this study, no significant difference was observed between males and females in association with NS after controlling the results for age, BMI, ethnicity, presenting skin diagnosis, HH and anxiety/depression variables (table 3-45).

Table 3-45: The Association between Gender and Night Sweating

Outcome	Gender	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	Male	24.7%	Reference		Reference	
	Female	22.9%	0.366	0.90 (0.7-1.1)	0.224	0.86 (0.7-1.1)

The total number of males: 826, total number of females: 1190. The results on the adj. P-value and adj. OR columns are adjusted for ethnicity, age, BMI and presenting skin diagnosis, HH and anxiety and depressions. Abbreviations: Adj.: adjusted; NS: night sweating; OR: odds ratio

3.4.1.2 Night Sweating in Different Ethnicities

Both Chi-Van ethnicity (p-value: 0.003 and OR: 0.56 [0.4-0.8]) and Chi-Sha ethnicity (p-value<0.001 and OR: 0.40 [0.3-0.6]) are less correlated with NS compared to the reference group, Caucasian ethnicity, after adjusting the results for other variables including age, gender, BMI, presenting skin diagnosis, HH and anxiety/depression (table 3-46).

Table 3-46: The Association between Ethnicity and Night Sweating

Outcome	Ethnicity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	Caucasian	38.6%	Reference		Reference	
	SSEA	27.4%	0.046	0.60 (0.4-1.0)	0.140	0.65 (0.4-1.2)
	Other	34.9%	0.680	0.85 (0.5-1.5)	0.433	0.77 (0.4-1.5)
	Chi-Sha	18.7%	<0.001	0.37 (0.3-0.5)	<0.001	0.40 (0.3-0.6)
	Chi-Van	20.7%	<0.001	0.42 (0.3-0.6)	0.003	0.56 (0.4-0.8)

The total number of Caucasians: 355, the total number of patients from Chi-Sha: 1010, the total number of patients from Chi-Van: 483, the total number of patients from SSEA: 106 and the total number of patients from other ethnicities: 63. The results on the adj. P-value and adj. OR columns are adjusted for gender, age, BMI and presenting skin diagnosis, HH and anxiety and depression. Abbreviations: Adj.: adjusted; Chi-Sha: Chinese from Shanghai; Chi-Van: Chinese from Vancouver; NS: night sweating; OR: odds ratio; SSEA: South and Southeast Asian

3.4.1.3 Night Sweating in Different Age groups

Compared to over 60 y/o age group, age group <30 y/o (p-value: 0.043 and OR: 1.54 [1.05-2.3]), is significantly higher associated with NS, after controlling the effect of other variables (gender, ethnicity, BMI, presenting skin diagnosis, HH and anxiety/depression) in the multivariate logistic regression analysis (table 3-47).

Table 3-47: The Association between Age and Night Sweating

Outcome	Age (y/o)	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	=> 60	17.8%	Reference		Reference	
	<30	26.1%	0.004	1.64 (1.2-2.3)	0.043	1.54 (1.05-2.3)
	30-59	23.8%	0.026	1.45 (1.1-2.0)	0.072	1.40 (0.95-2.0)

The total number of patients in =>60 y/o age group: 332, the total number of patients in age group <30 y/o age group: 712, the total number of patients in 30-59 y/o age group: 973. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, BMI and presenting skin diagnosis, HH and anxiety and depression. Abbreviations: Adj.: adjusted; NS: night sweating; OR: odds ratio; y/o: years old

3.4.1.4 Night Sweating in Different BMIs

After considering all the other variables in this study, obese patients with BMI over 24.9, didn't show a statically meaningful difference in association with NS compared to non-obese patients (table 3-48).

Table 3-48: The Association between BMI and Night Sweating

Outcome	BMI	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	<= 24.9	21.9%	Reference		Reference	
	>24.9	29.8%	<0.001	2.16 (1.7-2.8)	0.587	1.08 (0.8-1.4)

The total number of patients with BMI<= 24.9: 1476, the total number of patients in with BMI> 24.9: 452. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and presenting skin diagnosis, HH and anxiety and depression. Abbreviations: Adj.: adjusted; BMI: body mass index; NS: night sweating; OR: odds ratio

3.4.1.5 Night Sweating in Different Presenting Skin Diagnoses

No presenting skin diagnoses showed a significantly higher association with NS than benign

tumors, after controlling the results for the effect of other variables including gender, age, BMI, ethnicity, HH and anxiety/depression (table 3-49).

Table 3-49: The Association between Presenting Skin Diagnosis and Night Sweating

Outcome	Skin Disease	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	Tumor-BN	23.9%	Reference		Reference	
	MISC	29.8%	0.149	1.34 (0.9-2.0)	0.822	0.95 (0.6-1.5)
	Acne	23.9%	1.0	1.00 (0.6-1.6)	0.258	1.36 (0.8-2.3)
	ECZ	20.7%	0.373	0.83 (0.6-1.2)	0.305	1.27 (0.8-2.0)
	Hair Ds	30.4%	0.457	1.39 (0.6-2.9)	0.347	1.48 (0.7-3.3)
	INF	20.8%	0.455	0.83 (0.5-1.3)	0.514	1.19 (0.7-2.0)
	PIG-MISC	19.3%	0.470	0.76 (0.4-1.5)	0.851	1.07 (0.5-2.1)
	PIG-VIT	22.0%	0.937	0.89 (0.4-2.1)	0.259	0.59 (0.2-1.5)
	PSO	23.9%	1.0	0.99 (0.6-1.7)	0.518	1.23 (0.7-2.3)
	ROS	25.9%	1.0	1.11 (0.4-2.9)	0.560	0.72 (0.2-2.1)
	Scars	16.7%	0.613	0.64 (0.2-2.0)	0.444	0.62 (0.2-2.1)
	Tumor-D/IS/M	26.0%	0.794	1.11 (0.6-1.9)	0.632	1.16 (0.6-2.1)

The total number of patients with Tumor-BN: 238, the total number of patients with acne: 243, the total number of patients with ECZ: 492, the total number of patients with Hair Ds: 46, the total number of patients with INF: 273, the total number of patients with PIG-MISC: 84, the total number of patients with PIG-VIT: 41, the total number of patients with PSO: 109, the total number of patients with ROS: 27, the total number of patients with scars: 24, the total number of patients with MISC skin problems: 336 and the total number of patients with Tumor-D/IS/M: 104. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, HH and anxiety and depression. Abbreviations: Adj.: adjusted; ECZ: eczematous conditions; Hair Ds: hair disorders; HH: hyperhidrosis; INF: infections; MISC: miscellaneous; NS: night sweating; OR: odds ratio; PIG-MISC: miscellaneous pigmentation disorders; PIG-VIT: vitiligo related pigmentation disorders; PSO: psoriasis; ROS: rosacea; Tumor-BN: benign tumors; Tumor-D/IS/M: dysplastic/ in-situ/ metastatic tumors

3.4.2 Night Sweating in Patients with or without Hyperhidrosis

Patients with HH are about 7 times more likely to have NS than patients without HH, after adjusting the OR and the p-value for other variables in this study (table 3-50).

Table 3-50: The Association between Presence of Hyperhidrosis and Night Sweating

Outcome	Hyperhidrosis	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	No HH	14.3%	Reference		Reference	
	HH (total)	57.4%	<0.001	8.07 (6.3-10.3)	<0.001	6.91 (5.3-8.9)

The total number of patients with HH: 437 and the total number of the patients without HH: 1580. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and anxiety and depression. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; NS: night sweating; OR: odds ratio

3.4.2.1 Night Sweating in Hyperhidrosis Subtypes

All HH subtypes compared to the population without HH are significantly more correlated with NS, after controlling the results for the effect of gender, age, BMI, ethnicity, presenting skin diagnosis and anxiety/depression (table 3-51).

Table 3-51: Association between HH Subtypes and Night Sweating

Outcome	Hyperhidrosis	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	No HH	14.3%	Reference		Reference	
	PPH	48.5%	<0.001	5.62 (3.8-8.3)	<0.001	4.89 (3.3-7.3)
	AH	64.6%	<0.001	10.90 (6.9-17.5)	<0.001	7.85 (4.9-12.7)
	GFH	61.5%	<0.001	9.56 (6.0-15.4)	<0.001	8.24 (5.1-13.2)
	LOHH	58.3%	<0.001	8.37 (5.6-12.6)	<0.001	7.96 (5.2-12.1)

The total number of patients with PPH: 130, the total number of patients with AH: 96, the total number of patients with GFH: 91, the total number of patients with LOHH: 120 and the total number of the patients without HH: 1580.

The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and anxiety and depression. Abbreviations: Adj.: adjusted; AH: axillary hyperhidrosis; GFH: generalized or facial hyperhidrosis; HH: hyperhidrosis; LOHH: late onset hyperhidrosis; NS: night sweating; OR: odds ratio; PPH: palmar and plantar hyperhidrosis

3.4.2.2 Night Sweating in Different Hyperhidrosis Severities

Figure 3-4 shows, as HH severity increases from mild to severe, the prevalence of NS grows.

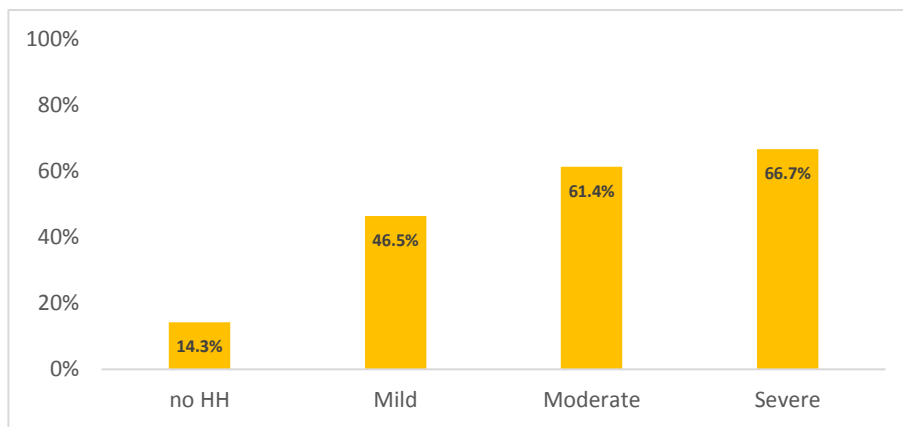


Figure 3-4: Prevalence of Night Sweating in Different Severities of Hyperhidrosis

After controlling the results for all the variables in this study, including age, BMI, gender, ethnicity, presenting skin diagnosis, all severities of HH (including severe, moderate and mild) are more associated with NS than no HH group (table 3-52).

Table 3-52: The Association between Hyperhidrosis Severity and Night Sweating

Outcome	HH Severity	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	No HH	14.3%	Reference		Reference	
	Mild	46.5%	<0.001	5.84 (4.3-7.9)	<0.001	5.43 (4.0-7.3)
	Moderate	61.4%	<0.001	10.20 (6.4-16.5)	<0.001	8.96 (5.6-14.3)
	Severe	66.7%	<0.001	15.71 (9.7-26.0)	<0.001	12.14 (7.2-20.4)

The total number of patients with mild HH: 247, the total number of patients with moderate HH: 92, the total number of patients with severe HH: 98 and the total number of the patients without HH: 1580. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and anxiety and depression. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; NS: night sweating; OR: odds ratio

3.4.2.3 Night Sweating in Different Negative Impacts from Excessive Sweating

In an increasing trend, the patients with more negative impact scores show higher prevalence of NS (figure 3-5).

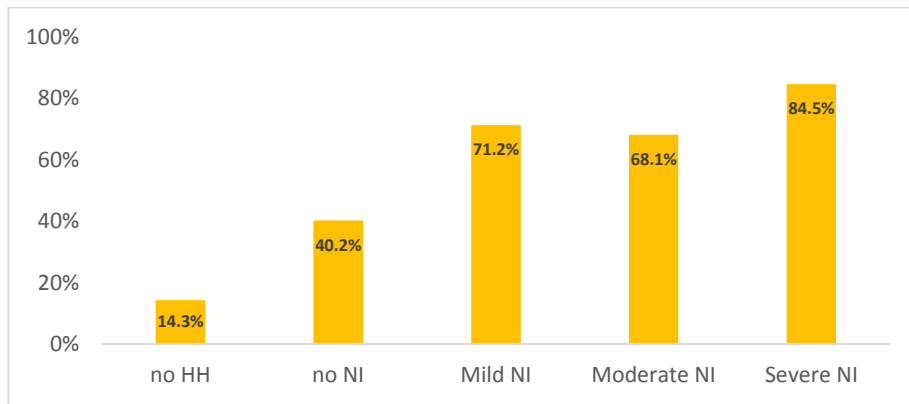


Figure 3-5: Prevalence of Night Sweating in HH Patients with Different Negative Impact Severities

The association between NI and NS is also assessed after including all the other variables and adjusting the result for their effects (table 3-53).

Table 3-53: The Association between Hyperhidrosis Negative Impact and Night Sweating

Outcome	HH Negative Impact	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	No HH	14.3%	Reference		Reference	
	HH with No NI	40.2%	<0.001	4.02 (2.9-5.5)	<0.001	3.84 (2.8-5.3)
	HH with Mild NI	71.2%	<0.001	14.76 (9.5-23.3)	<0.001	14.09 (9.0-22.0)
	HH with Moderate NI	68.1%	<0.001	12.75 (6.6-25.8)	<0.001	11.98 (6.1-23.4)
	HH with Severe NI	84.5%	<0.001	32.5 (15.5-76.3)	<0.001	29.03 (12.9-65.3)

The total number of HH patients with no NI: 214, the total number of HH patients with mild NI: 118, the total number of patients with moderate NI: 47, the total number of HH patients with severe NI: 58 and the total number of the patients without HH: 1580. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and anxiety and depressions. Abbreviations: Adj.: adjusted; HH: hyperhidrosis; NI: negative impact; NS: night sweating; OR: odds ratio

3.4.3 Night Sweating in Patients with and without Anxiety/Depression

As depicted in figure 3-6, patients with stress symptoms, including anxiety, depression or both, illustrate higher prevalence of NS than patients without any anxiety or depression.

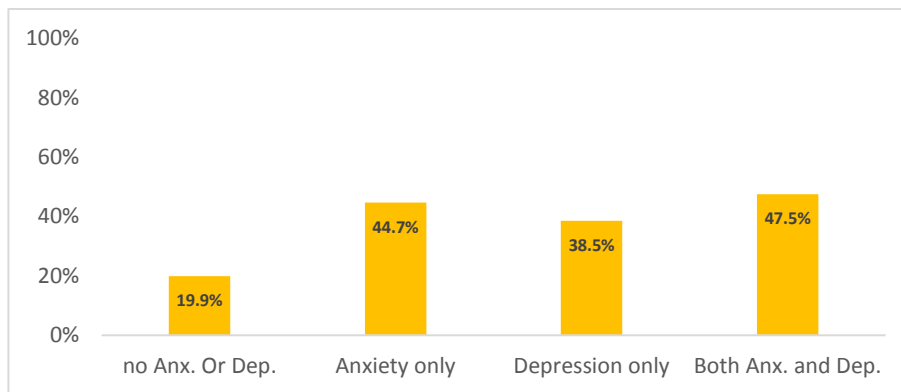


Figure 3-6: Prevalence of Night Sweating in Patients with Stress Symptoms

Anxiety (p-value: 0.017, OD: 2.43 [1.2-5.0]), depression (p-value: 0.028, OD: 1.76 [1.1-2.9]) or both anxiety and depression (p-value< 0.001, OD: 1.94 [1.3-2.8]) groups are significantly more correlated with NS than no anxiety or depression group, after controlling the results for other variables in this study (table 3-54).

Table 3-54: The Association between Anxiety/Depression and Night Sweating

Outcome	Anxiety and Depression	Prevalence	P-value	OR	Adj. P-value	Adj. OR
NS	No Anx. or Dep.	19.9%	Reference		Reference	
	Anx. only	44.7%	<0.001	3.26 (1.6-6.6)	0.017	2.43 (1.2-5.0)
	Dep. only	38.5%	<0.001	2.51 (1.6-4.0)	0.028	1.76 (1.1-2.9)
	Anx. and Dep.	47.5%	<0.001	3.64 (2.6-5.0)	<0.001	1.94 (1.3-2.8)

The total number of the patients with no Anx. or Dep.: 1709, the total number of the patients with Anx. only: 38, the total number of the patients with Dep. only: 91 and the total number of the patients with both anxiety and depression: 179. The results on the adj. P-value and adj. OR columns are adjusted for gender, ethnicity, age and BMI, presenting skin diagnosis and HH. Abbreviations: Adj.: adjusted; Anx.: anxiety; Dep.: depression; NS: night sweating OR: odds ratio

Chapter 4: Discussion

4.1 True Prevalence of Hyperhidrosis and Demographic Characteristics

The prevalence of primary HH has been the subject of examination by several groups. This ranges from 2.8% in the United States [73], 4.4 % PPH in Fuzhou, China [74], to 16.3 % in Germany [52] and 12.8% in Japan [32]. Possible reasons for the wide variation may include differences in study methods, precise definitions used, ethnic composition of the study subjects, age, gender and the environment. Our study is the first to examine prevalence of hyperhidrosis involving multiple ethnicities and multiple centers in the same setting and using the same study method and diagnostic criteria. This showed very similar prevalence of total hyperhidrosis in Shanghai and Vancouver.

This study is the second population-based study on HH prevalence in North America. For the assessment of HH prevalence, we excluded the patients who presented with HH and therefore, the prevalence of HH represents the true prevalence in the population. The prevalence of HH (>17%) in our study is much higher than 2003 US study [73] and shows how intensely it has been underreported (p-value <0.001, OR: 7.84 [6.5-9.5]). The high burden of the disease indicates the importance of cautious selection of HH patients vs. non-HH ones for future genetic or epidemiologic studies, as many patients with HH do not report their excessive sweating unless they are asked for it.

Further examinations revealed differences in the prevalence of different severities of HH according to age, sex, ethnicity, and body weight in dermatology outpatients.

After controlling the effect of other variables including age, ethnicity, BMI and presenting skin diagnosis and comparing to male age group in our study, we discovered that gender has a relative

impact of hyperhidrosis prevalence and presentation. Males are more likely to develop PPH and GFH, whereas females are more likely to develop LOHH and there is no difference in AH mild primary HH presentation between genders. LOHH may partially be explained by menopausal hormonal changes as it reaches the highest incidence at 30-59 y/o, age group. It is yet unknown why moderate and severe PPH is more common in men.

After controlling the effect of other variables including gender, ethnicity, BMI and presenting skin diagnosis and comparing to >60 y/o age group, we found that total primary HH is about 13 times higher in patients younger than 30 y/o and about 5 times higher in patients 30-59 y/o. After dividing the HH into different severity groups, this increase was more seen in moderate to severe PPH for <30 y/o age group (about 7.5 times). The reasons for the decreased prevalence with age is not clear, but this potentially suggests that primary hyperhidrosis is not a life-long condition.

In the majority of the cases, primary hyperhidrosis becomes milder or even resolves with age.

This may explain that most people seeking treatments for hyperhidrosis are those younger than 30 years of age. It is at present unknown what physiological /psychosocial aspects of biological age influences manifestations of hyperhidrosis. Instead the prevalence of either moderate and severe or mild LOHH is significantly less in <30 y/o age group, compared to >60 y/o age group.

The hyperhidrosis association with ethnic origin was one of the first to be observed in early hyperhidrosis literature. Cloward asserted that PPH mostly affects South-East Asians [75].

However, this was not formally investigated in a non-biased fashion that involves multi-ethnicity previously. Our results showed no difference in the prevalence of PPH between different ethnic groups.

Our study showed that the total primary hyperhidrosis in Chinese population from Vancouver is slightly lower than that of Caucasians. In fact, while PPH, GFH and LOHH are similar among all

ethnic groups at all severities of sweating, Caucasians have much higher chances of developing moderate and severe AH than the Chinese subjects.

The impact of obesity or increased BMI on primary HH has not been investigated previously.

The intuition is that increased body weight may cause higher incidences of hyperhidrosis.

However, our data showed that, after considering the other contributing factors for primary HH, BMI does not play an important role in the prevalence of primary HH in general, or in specific anatomic subtypes of primary HH at any severity level of sweating. The biggest impact of increased BMI is on the prevalence of LOHH, with those having $BMI > 24.9$ are more than twice likely to develop moderate to severe LOHH than those who are not obese.

We also examined the potential impact of the presenting concerns of the subjects have on the prevalence of hyperhidrosis. In general, the presenting diagnoses do not influence prevalence of HH, with potential exception of vitiligo and scar formation disease, which seem to be more likely than the benign tumors to develop moderate to severe PPH. Future speculation about the cause and the details is recommended. Another interesting finding of our study was that patients with acne develop less mild PPH than the control group. However, these observations need to be further confirmed in future studies.

The impact of geographical locations on the prevalence of hyperhidrosis has not been investigated previously. Our study took place in two cities located on opposite sides of the Pacific Ocean. However, the prevalence of primary hyperhidrosis in the Chinese subjects is quite similar, suggesting that geographical locations do not seem to influence development of HH.

4.2 Relationship between Hyperhidrosis and Psychological Comorbidities in the Presence of Other Variables

The other important aim of this study was to investigate the correlation between mental stress symptoms and HH. Both anxiety and depression were found to be more common in patients with HH and among all the variables; HH has the most powerful impact on the stress symptoms. Furthermore, our study demonstrated that the HH-associated increase in anxiety and depression prevalence was independent of other variables, including gender, BMI, age, ethnicity, and presenting diagnosis and considering all these variables doesn't affect the significant association between HH and anxiety or depression.

The mechanism for the strong association between HH and the prevalence of depression and anxiety is, at present, unknown. Sweating is an important manifestation of anxiety [76].

However, more than 70% of people with HH did not report symptoms of anxiety or depression, suggesting that primary HH is not simply a manifestation of anxiety or depression. Yet, we highly recommend the screening for anxiety and depression in all the patients who present with HH or are found to have HH incidentally.

Currently, it is unknown if anxiety and depression in HH patients affect their long-term prognosis or response to therapies. Previously, it was found that PPH patients with coexisting symptoms of sweating in the axillae that undergo an endoscopic thoracic sympathectomy (ETS) have a higher incidence of post-ETS compensatory hyperhidrosis compared with those that experience sweating in the palms and feet alone [77]. Interestingly, we showed that HH patients with sweating involving the more central anatomic sites, such as the axillae, trunk, or face, have a higher incidence of anxiety and depression.

It would be of interest to examine whether the compensatory hyperhidrosis patients experience

following ETS is influenced by coexisting anxiety or depression.

Besides the HH factor (including subtypes, severity and NI score from HH), ethnicity is also important in presenting stress symptoms as patients with Chinese ethnicity, whether from Vancouver or Shanghai, show less anxiety or depression when compared to Caucasians.

We also found that not only HH is an important skin disease in the presence of stress symptoms, but also patients with psoriasis suffer more from anxiety and depression in comparison with benign tumors, after all the other variables are studied together in a multivariate logistic regression analysis. Similarly, patients with skin infection diseases showed higher prevalence of depression.

Also, night sweating is not a negligible factor in the presence of anxiety or depression. Around 40% of the patients who have severe NS suffer from anxiety or depression. NS, besides HH, NI score, ethnicity and presenting skin disease shows a significant effect on anxiety and depression when considering all the studied variables.

Other variables in this study, including gender, age and BMI, didn't show significant association with the anxiety or depression according to the results of the multivariate logistic regression analysis.

It is unknown whether the management of HH-associated anxiety or depression would impact the treatment success of HH. For instance, in our study, HH severity was also directly associated with higher prevalence of anxiety and depression. It is possible that treating moderate and severe HH promptly would efficiently reduce the associated mental symptoms. Patients who reported to have higher NI scores suffered more from anxiety and depression. Thus, NI scores could be used to select patients for stress management therapies in conjunction with excessive sweating treatment.

Further studies are needed to examine how coexisting depression and anxiety in patients with HH influences their treatment decisions and affects their response to various HH therapies.

4.3 Relationship between Night-time Sweating and Hyperhidrosis as Well as Other Demographic Factors

In the last part of our study, we investigated the correlation between NS and HH. We previously, in the second part of the study, found that both HH and NS affect presence of anxiety and depression.

Also NS is believed to be an exclusion criterion for HH and it is rarely seen in patients with primary HH [22], therefore we also focused on the effect of HH and other variables on NS.

NS is a very common disorder, which is easily ignored by the patients. About one fourth of our study population suffered from NS in general, although variations in NS prevalence were seen according to different stratifications according to different studies [78, 79].

After considering the effect of all the variables on NS prevalence, we illustrated that BMI does not play a role in NS prevalence although Melby showed that BMI might affect night sweating [80]. Similar to BMI, gender is not a contributing factor in the presence of NS.

Including all the variables, HH has the highest correlation with NS. About 57.4% of the patients with HH reported sweating during sleep compared to patients without HH among who only 14.3% suffered from NS. The results of the multivariate regression analysis show that among all the subtypes, patients with GFH experience more episodes of night sweating. Also as the HH symptoms and the negative impacts get severer, the signs of NS become more common.

Therefore, we suggest a review on NS in order to change the diagnosis criteria for HH.

Similar to HH, age and ethnicity also affect the presence of NS. Prevalence of NS decreases by

increasing the age. NS is more common in Caucasians (about 39%) than in Chinese ethnicities from Canada or China (about 19%). These similarities between the factors, which affect both the HH and NS prevalence, indicate the common pathophysiological pathways between the two. The correlation between stress symptoms and NS was also discussed and investigated in the discussion of the second part of this study and the results of this part of the study also confirm the association of NS with both anxiety and depression. Also the reported NI from sweating has a positive correlation with NS prevalence and shows that people who suffer more from HH and are psychologically affected by excessive sweating, experience more episodes of night sweating. It is still unknown if day-time or night-time sweating cause psychological symptoms or opposite[81], but we suggest further studies with parallel therapy for anxiety or depression in patients who suffer from HH and evaluate the consequent impacts. Although the trend for NS prevalence is clearly decreasing by age, another study after excluding the menopausal aged women with hot flushes is recommended for getting more accurate results by eliminating the most important cause of NS [82].

4.4 Conclusion

In summary, this is the first multi-ethnic and intercontinental study of hyperhidrosis prevalence and demographical profile. We found the more than 17% of people in dermatology clinics suffer from HH. This study revealed that primary hyperhidrosis is mainly the disease of the young people, whereas late onset hyperhidrosis is primarily the disease of the older age groups. PPH and GFH seem to have similar prevalence in the three ethnic groups investigated whereas AH is highest in Caucasians compared to Chinese. Contrary to common beliefs, increased body weight does not play a role in the development of primary HH although it is a major risk factor

for developing LOHH.

Among all the presenting skin diseases, HH and psoriasis are correlated with mental stress diagnoses, including anxiety and depression. All HH subtypes were associated with increased anxiety and depression. Anxiety and depression are also found to be more common in patients with Caucasian ethnicity and presenting NS symptoms. On the other hand, gender, BMI and age do not affect anxiety or depression.

Contrary to what's believed about the rareness of NS in HH patients [22], NS is much more common in HH patients and HH is the only skin condition which is associated with NS. Similar to HH, NS is less commonly seen in Chinese ethnicity and it decreases as the age increases. BMI and gender factors do not affect NS prevalence. Negative impact of sweating might be a very important question to ask as the patients with severer NI, experience higher prevalence of NS and stress symptoms. Therefore, it is suggestive of a common physiological pathway between HH and NS.

4.5 Limitations of the Study

This study is limited in some aspects; the data were gathered according to patients' self-reports and the sample size was relatively small in some groups after stratification for gender, ethnicity and age and different skin diseases. Further, being outpatient clinics, the subjects with severe medical conditions affecting mobility may be underrepresented thus not investigated in this study. The female population in the general population is just slightly higher than male [83], whereas in Dermatology Clinics we have much higher representation of females. The proportion of Caucasians in the Vancouver general population is about 40.6% [84], however only 30% of our study population consists of Caucasians. This difference is due to the referral pattern of the

attending dermatologists. However, since the presenting diagnosis of HH was excluded from the HH prevalence calculations, we do not believe this aspect to have any major impact on our conclusion.

Due to small number of patients with HH, we did not specify if there is any difference in the prevalence of anxiety, depression or NS between the patients who refer due to HH or found to have HH incidentally. Also due to the sample size, we didn't stratify the patients with anxiety or depression according to severity of stress symptoms.

The medications that cause NS were not excluded but since the prevalence of patients taking medication was not significantly different between HH and non-HH, we do not think it is of very much concern. We just focused on English articles. To stop making the questionnaire very long, we didn't ask about room temperature and sleeping habits.

4.6 Future Plans

In the future, we would want to find out the differences in the pattern of HH and its associating factors among patients who presented with HH and the patient who presented with other skin conditions but were found to have HH incidentally after they filled out the questionnaire.

We are also planning to do a review study on night sweating in the future by asking more details about the pattern of night sweating.

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83. Female Population, a Slim Female Majority.
84. Projections of the Diversity of the Canadian Population.

Appendices

Appendix A

Patients' Questionnaire in English

Office Use Only			
Chart No: _____	BMI: _____	Skin Type: _____	Diagnosis: _____

1. Today's date: _____ Postal Code: _____
2. Ethnic origin: _____ Height: _____
3. Country of birth: _____ Body weight: _____
4. Sex: Female (___), Male (___) Age (yrs) _____
5. Your current occupation: _____ Your last occupation (if retired) _____
6. What is the **main problem** that brought you in today? (List **one problem only**)

7. Do any **family members** have the same condition? (List their relationship to you below):

8. Have you been diagnosed with the following **medical conditions**? (Please use "✓" to answer)

Medical Conditions	Yes	No	Details (if "yes")	MD
Diabetes				
Hypertension				
Hyperlipidemia				
Thyroid disease				
Depression				
Anxiety				
• Psoriasis				
• Atopic dermatitis (eczema)				
• Melasma				
• Rosacea				
• Acne				
• Vitiligo				
• Hyperhidrosis				
• Alopecia areata				
• Andro-genetic alopecia				
• Skin cancers				
Other medical or skin diagnoses				

9. Are you currently taking any **drugs /or medicines** prescribed by a doctor? (If yes, list them)

10. Are you **allergic to any drugs**? (If yes, list the **drug names** and **types of reactions** below)

11. How many people live in your home? (including yourself) _____
12. How many toilets are there in your home? _____
13. In the past two weeks, have you taken medicines for depression / anxiety? Yes ___; No ___
14. In the past two weeks, how often are you bothered by the following stress symptoms?
(0 = not at all; 1 = in less than half of the days; 2 = in more than half of the days; 3 = nearly every day)

Stress Symptoms	Frequency			
1) Having little interest or pleasure in doing things	0	1	2	3
2) Feeling down, depressed, or hopeless	0	1	2	3
3) Having trouble falling or staying asleep; Or opposite Sleeping too much	0	1	2	3
4) Feeling tired, or having little energy	0	1	2	3
5) Having poor appetite; Or opposite Eating too much	0	1	2	3
6) Feeling bad about yourself, or thinking that you are a failure, or feeling having let yourself or family down	0	1	2	3
7) Having trouble concentrating on things (such as reading the newspaper or watching television)	0	1	2	3
8) Moving or speaking so slowly that other people could have noticed; Or opposite, being so fidgety or restless that you have been moving around a lot	0	1	2	3
9) Having thoughts that you would be better off dead, or having thoughts of hurting yourself	0	1	2	3
10) Feeling nervous, anxious, or on edge	0	1	2	3
11) Not able to stop worrying	0	1	2	3
12) Worrying too much about various things	0	1	2	3
13) Having trouble relaxing	0	1	2	3
14) Being so restless that it is hard to sit still	0	1	2	3
15) Becoming easily annoyed or irritable	0	1	2	3
16) Feeling afraid as if something awful might happen	0	1	2	3
17) Sweating for no obvious reasons on hands, feet, armpits or face (That is, sweating even when not feeling nervous, doing physical activities, or being in a hot environment)	0	1	2	3
18) Sweating at night or during sleep	0	1	2	3
19) Your sweating having a negative impact on you	0	1	2	3

15. If you sweat for no obvious reasons, at what age did this start? _____
16. How severe is the sweating in the following areas? (0 =none; 1 =mild; 2 =moderate; 3 =severe)
Hands ___; Feet ___; Armpits ___; Face ___; Chest/back ___; Other areas ___
17. Would you like to give a saliva sample to help skin research? Yes ____, No ____
18. Your signature: _____

Office Use only: Score (1-9) _____ Score (10-16) _____ HH Score _____

Appendix B

Patient's Questionnaire in Chinese

Basic Information About Your Skin Condition (UBC)

Page | 1

办公专用

表格编号: _____ BMI: _____ 皮肤类型: _____ 诊断: _____

1. 日期: _____ 邮编: _____
2. 民族: _____ 身高: _____
3. 出生地: _____ 体重: _____
4. 性别: 女 (___), 男 (___) 年龄(岁) _____
5. 现在职业: _____ 以往职业 (如果退休的话) _____

6. 你今天看诊的主要问题是什么? (如有多个问题,请只列最主要的一个问题)

7. 你的家庭成员有相同的情况吗? (如果有, 请说明你们的关系):

8. 你有被诊断出以下的疾病 (状况) 吗? (请在后面打√)

疾病 (状况) 名称	是	否	详情 (若果有的话)	备注
糖尿病				
高血压				
高脂血症				
甲状腺疾病				
抑郁				
焦虑				
• 银屑病				
• 异位性皮炎 (或者湿疹)				
• 黄褐斑				
• 酒渣鼻				
• 粉刺 (痤疮)				
• 白癜风				
• 多汗症				
• 斑秃				
• 雄性脱发				
• 皮肤癌				
其他疾病 (包括其他皮肤病)				

9. 请列出你正在服用的所有药物:

(Version Nov 3, 2014)v15

11. 有多少人住在你家里? _____
12. 你家里有多少个卫生间? _____
13. 在过去的两周内, 你有因为抑郁或者焦虑服用过处方药吗? 是___, 否___(请打√)
14. 在过去的两周内, 你是否被以下情绪压力症状所困扰?
(请用○表示发生频率): 0=完全没有; 1=少于一半的时间; 2=多于一半的时间; 3=几乎每天)

情绪压力症状	发生频率			
1) 几乎对做任何事情没有兴趣或者乐趣	0	1	2	3
2) 感到低沉、沮丧, 毫无希望	0	1	2	3
3) 入睡困难, 易醒; 或者相反, 嗜睡	0	1	2	3
4) 感到疲倦或者无精打采	0	1	2	3
5) 食欲不好; 或者相反, 暴饮暴食	0	1	2	3
6) 自我感觉不好, 或者觉得自己是个失败者, 或者觉得自己让自己或者家人失望	0	1	2	3
7) 做事情无法集中注意力 (例如看报纸或者看电视)	0	1	2	3
8) 别人可以察觉到你行动 (或者说话) 迟缓; 或者相反, 你变得烦躁地 或者不知疲倦地到处闲逛	0	1	2	3
9) 有一死了之(或者伤害自己)的想法	0	1	2	3
10) 感到紧张、焦虑、崩溃	0	1	2	3
11) 无法停止担心	0	1	2	3
12) 对不同的事担心过度	0	1	2	3
13) 情绪无法放松	0	1	2	3
14) 感到坐立不安	0	1	2	3
15) 变得容易激怒烦躁	0	1	2	3
16) 担心坏的事情可能会发生	0	1	2	3
17) 在无明显原因的情况下, 双手、腋窝、或者 面部出汗 (就是说, 在没有精神紧张、没有做运动, 没有身处高温环境中也会出汗)	0	1	2	3
18) 夜间或者睡眠中出汗	0	1	2	3
19) 出汗对你产生了负面影响	0	1	2	3

15. 如果你被出汗过多所困扰, 请注明在什么年龄开始发生? _____
16. 请注明在以下部位出汗的严重程度 (0=完全没有; 1=轻微; 2=中等; 3=严重)
双手 ___; 双脚 ___; 腋窝 ___; 面部 ___; 胸/背 ___; 其他部位 _____
17. 你愿意为皮肤研究提供一份唾液样本吗? 愿意 _____, 不愿意 _____
18. 你的签名: _____

办公专用: 分数 (1-9) _____ 分数 (10-16) _____ HH 分数 _____