Psychodermatology: Challenges, Prevalence and Therapeutic Options

by

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Abstract

Psychodermatology is specialized field of medicine that encompasses the skin-mind interaction and the conditions associated with it. Psychodermatology poses ongoing challenges for healthcare practitioners. There are notable gaps in knowledge that impede clinicians' ability to provide comprehensive treatment within this niche area. These include the inadequacy of specialized services mainly stemming from the scarcity of prevalence data, the lack of clinical trials and guidelines discerning treatment options, and referral system complications. To address these gaps, this thesis aimed to enhance our comprehension of the prevalence and treatment of psychodermatologic conditions and identify the challenges faced by dermatologists in their management.

The research objectives encompassed four distinct studies. Firstly, the thesis sought to estimate the frequency of psychodermatologic conditions in Alberta, Canada. To achieve this, a chart review was conducted on administrative health data to determine the prevalence of these conditions in dermatology clinics. The findings revealed that 28.6% of patients visiting dermatology clinics were concurrently dispensed psychotropic medications, indicating a potential presence of psychodermatologic conditions. This study provided a valuable estimation of the prevalence of these conditions in the region, shedding light on the potential burden they place on both the healthcare system and the population.

The second study, conducted through a systematic review, aimed to explore the global prevalence of primary psychodermatologic conditions (PPDs). The scarcity of existing data in this area necessitated a comprehensive analysis to gather and evaluate the available literature. The study highlighted that the pathologic and subclinical forms of primary psychodermatologic conditions had a minimum prevalence of 0.3%, and the most common condition in the general

population was pathologic skin picking, with a prevalence range of 1.2% to 11.2%. These findings underscored the wide-ranging prevalence of psychodermatologic conditions and emphasized the need for further research to better understand their true burden on populations worldwide.

The third study aimed to investigate the efficacy of pharmacologic interventions in managing PPDs. Through a comprehensive analysis of existing literature and clinical trials, the study aimed to discern the effectiveness of various therapeutic options available to healthcare practitioners. The study mapped out seven distinct classes of pharmacologic interventions and evaluated their effectiveness across five psychodermatologic conditions. This investigation provided valuable insights into which medications showed more promising effectiveness for specific conditions, facilitating more informed treatment decisions for clinicians. The study also highlighted the existing gaps in evidence/

Finally, to gain a deeper understanding of the challenges faced by dermatologists when treating psychodermatologic conditions, the fourth study involved surveying Canadian dermatologists' perceptions, practice patterns, and difficulties encountered in their clinical practice. The results indicated that most dermatologists had less than optimal comfort levels in managing these conditions and initiating psychopharmacological therapy. A majority of dermatologists advocated for a multidisciplinary approach. The study also emphasized the importance of more training opportunities for residents and specialists to better equip healthcare providers in managing psychodermatologic conditions effectively. The research outcomes from the four studies led to the establishment of a multidisciplinary psychodermatology clinic at Kaye Edmonton Clinic in Alberta, Canada, the Skin Health Clinic (Psychodermatology). Preliminary

findings from the clinic's first year of operation (2021-2022) revealed valuable insights into patient demographics, diagnoses, and treatment modalities.

In conclusion, this thesis presents a comprehensive exploration of psychodermatology, shedding light on the prevalence, treatment options, and challenges faced by healthcare practitioners. The findings highlight the potential benefits of a multidisciplinary approach to improve patient care. Through continued research and integration of mental health support, the field of psychodermatology can further advance and enhance the overall well-being and outcomes of patients with psychodermatologic conditions.

Preface

Some of the research conducted for this thesis forms part of an international research collaboration, led by Professors Esther Fujiwara and Professor Marlene Dytoc at the University of Alberta. All the tables and figures in this thesis are created by myself in collaboration of the co-authors of my research studies. All the tables and figures in this thesis are created by myself in collaboration of the co-authors of my research studies. The data analysis in chapter II were supported by Alberta Health Services Data & Analytics. The systematic reviews in chapters III and IV were supported by University of Alberta library services. Chapters II and V of this thesis received research ethics approval from the University of Alberta Research Ethics Board, Project Name "Psychodermatology: Improving quality of care", Pro00092486, 7/4/2019.

Chapter II of this thesis has been published as Turk T, Dytoc M, Youngson E, Abba-Aji A, Mathura P, Fujiwara E. Estimated frequency of psychodermatologic conditions in Alberta, Canada. Journal of Cutaneous Medicine and Surgery. 2021 Jan;25(1):30-7. Chapter III has been published as Turk T, Liu C, Straube S, Dytoc M, Hagtvedt R, Dennett L, Abba-Aji A, Fujiwara E. The global prevalence of primary psychodermatologic disorders: a systematic review. Journal of the European Academy of Dermatology and Venereology. 2022 Dec;36(12):2267-78. Chapter IV has been published as Turk T, Liu C, Fujiwara E, Straube S, Hagtvedt R, Dennett L, Abba-Aji A, Dytoc M. Pharmacological Interventions for Primary Psychodermatologic Disorders: An Evidence Mapping and Appraisal of Randomized Controlled Trials. Journal of Cutaneous Medicine and Surgery. 2023 Mar;27(2):140-9. Chapter V has been published as Turk T, Fujiwara E, Abba-Aji A, Mathura P, Dytoc M. Psychodermatology in Canada: a national survey assessment of dermatologists' perception, practice patterns, and challenges. Journal of Cutaneous Medicine and Surgery. 2021 May;25(3):249-56. In all four studies, I conceptualized the studies,

formulated the research questions, designed the overall methodology, and with support from my supervisors and collaborators, I analyzed the data, drafted the initial manuscript, and carried out all revisions until publication. Specifically, for data collection, analysis, and synthesis of the results for the study in chapter II, I received help from Erik Youngsen, Data Analytics, Alberta Health Services, and for both systematic reviews in chapters III and IV, I collaborated with health librarian Liz Dennett, University of Alberta and Chaocheng ("Harry") Liu, whom I share first authorship for the study in chapter IV.

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Amidst the challenges and uncertainties, my uncle, Dr. Samer Aldandashi, treated me like his son. His generosity in hosting me during my stay in Canada provided a safe haven where I could immerse myself in my work, free from distractions. I am grateful for his support, which created an environment conducive to creativity and focused learning.

I would like to acknowledge Tara Checknita and Dr. Allen Chan for their unwavering support and responsiveness. I am deeply indebted to my supervising committee members, Dr. Adam Abba-Aji and Dr. Andrew Greenshaw, whose valuable inputs and constructive critiques significantly enhanced the quality of this work. Their collective expertise and guidance have left an indelible mark on this research. Also, to my friend, Theresa Dusonchet, whose presence in my life made it a lot sweeter.

Lastly, I want to recognize the profound impact of the war in Syria on my life. The adversity and hardships I faced during this time have made me more resilient, resourceful, and determined. The resilience I developed amidst the turmoil has undoubtedly shaped the person I am today and influenced the trajectory of this research. In memory of the struggles endured by my homeland, its people, and all the friends and family members who we lost along the way, I dedicate this achievement to all those who have shown unwavering resilience in the face of adversity.

My deepest gratitude goes out to all these remarkable individuals and circumstances that have played a pivotal role in making this thesis a reality. Their support, love, and belief in me have been the cornerstones of my success. Together, they have made this journey truly unforgettable and have instilled in me the belief that with determination and a strong support system, anything is possible.

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List of Abbreviations:

SPD: Skin Picking Disorder

TTM: Trichotillomania

CI: Confidence Interval

OCDR: Obsessive-Compulsive Related Disorders

BFRB: Body-focused Repetitive Behaviors

INF a: Interferon Alpha

CNS: Central Nervous System

ASD: Autism Spectrum Disorder

BDNF: Brain-Derived Neurotrophic Factor

SSRIs: Selective Serotonin Reuptake Inhibitors

TCAs: Tricyclic Antidepressants

CBT: Cognitive-behavioral Therapy

DBT: Dialectical Behavior Therapy

ADHD: Attention-Deficit Hyperactive Disorder

AHS: Alberta Health Services

ICD-9: International Classification of Disease – 9

PIN: Pharmaceutical Information Network

DIN: Drug Identification Number

ATC: Anatomical Therapeutic Chemical Classification.

PPD: Pimary Psychodermatologic Disorder

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analyses

DSM: Diagnostic and Statistical Manual of Mental Disorders

RCT: Randomized Clinical Trial

NAC: N-acetylcysteine

DP: Delusional Parasitosis

HRT: Habit Reversal Training

MGH-HPS: Massachusetts General Hospital Hairpulling Scale

PITS: Psychiatric Institute Trichotillomania Scale

CGI-I: Clinical Global Impression-Improvement

CGI-S: Clinical Global Impression-Severity of Illness

SPTS: Skin Picking Treatment Scale

NE-YBOCS: Yale-Brown Obsessive-Compulsive Scale Modified for Neurotic Excoriation

SP-SAS: Skin Picking Symptom Assessment Scale

BPRS: Brief Psychiatric Rating Scale

CDA: Canadian Dermatology Association

GP: General Practitioner

PD: Psychodermatology

I. CHAPTER 1 - Introduction

This thesis addresses psychodermatologic conditions, exploring the intricate and fascinating interplay between the mind and the skin. In the following, I give an overview on the definition, classification, prevalence, etiology and treatments of psychodermatologic conditions. The aim of this section is to highlight the challenges in the field of psychodermatology and preface the studies that I conducted in my PhD to address some of these challenges, mainly address the gaps in knowledge on prevalence and therapeutic options.

1.1. Definition and Classification in Psychodermatology

Psychodermatology encompasses the interplay between the cutaneous and neuropsychiatric systems where emotional or psychological factors significantly contribute to the onset, exacerbation, or maintenance of skin conditions, or vice versa (Misery, 1996). Psychodermatologic conditions are characterized by the bidirectional relationship between the mind and the skin, with emotional stressors and psychological factors manifesting as skin symptoms, or skin conditions triggering psychological distress (Koo & Lee, 2003). Psychodermatology emphasizes the connection between mental health and skin health, acknowledging the impact of stress, anxiety, depression, and other psychological factors on skin disorders such as psoriasis, eczema, acne, and dermatitis (Koo & Lee, 2003). This interdisciplinary field highlights the importance of comprehensive evaluation and treatment approaches that address both the physical and psychological aspects of dermatological symptoms.

Although there is no universal consensus on clinical categorization of psychodermatologic conditions, they are often grouped into three broader categories: 1) primary psychiatric disorders

(e.g., delusional parasitosis) where the origin of the skin symptoms is a psychiatric condition, 2) secondary psychiatric disorders (e.g., vitiligo-induced anxiety) where skin conditions trigger psychiatric symptoms, and 3) psychophysiologic disorders where there is a bidirectional relationship between the skin and mental health disorders (e.g., depression and psoriasis interplay) (Koo & Lee, 2003). Alternative classifications categorize conditions based on their assumed psychiatric etiology (i.e., psychodermatologic conditions due to depression, delusions, anxiety or obsessive-compulsive behavior) (Koo & Lee, 2003). The debate around classifications mainly arises from the fact that there is no consensus on the best approach to these conditions and the fact that it is still unclear how skin and psyche interact (Ferreira & Jafferany, 2021). Also, some conditions such as psychogenic pruritus, an itch sensation primarily caused or intensified by psychological factors, are difficult to group into the proposed classifications and are often standalone diagnoses. Unlike other psychodermatologic disorders, psychogenic pruritus has no apparent skin abnormalities, but can coexist with other skin conditions, acting as both a primary and secondary psychodermatologic disorder (Misery et al., 2018). Thus, patients may experience psychogenic itch in response to an existing skin condition, or it may arise as an independent disorder triggered by psychological factors (Misery et al., 2018). This dual nature of psychogenic pruritus makes it difficult to categorize and distinguish from other psychodermatologic conditions.

In 2021, Ferreira and Jafferany conducted a review of previously proposed classifications, emphasizing their limitations in failing to encompass the psychiatric consequences of dermatologic treatments and vice versa (Ferreira & Jafferany, 2021). Additionally, they highlighted that existing classifications tended to group unrelated disorders, such as dysesthesias and delusional infestation, together, potentially leading to an overpsychologizing of certain

syndromes. Moreover, these classifications overlooked the inclusion of treatment side effects and disregarded the significant impact of stress or psychological factors on exacerbating various dermatologic disorders, potentially giving rise to secondary psychiatric disorders. Furthermore, the classifications tended to group different psychodermatoses into the same groups, introducing ambiguity. Consequently, Ferreira and Jafferany proposed a new and more refined classification system, suggesting that psychodermatological disorders could be categorized into three distinct groups: a) *Primary PD disease*: In cases where a primary dermatosis is present (e.g., alopecia areata and atopic dermatitis); b) *Primary PD illness*: When skin symptoms manifest, with or without secondary self-induced skin lesions (such as excoriations), but without an underlying primary dermatosis (e.g., delusional parasitosis and psychogenic pruritus); c) *Secondary PD disorder*: Secondary dermatologic diseases caused by psychiatric medications or secondary psychiatric illness due to dermatologic medications, i.e., drug-induced reactions that bridge the domains of dermatology and psychiatry (e.g., lithium-induced acne and isotretinoin-induced mood disorders).

1.2. Prevalence of Psychodermatologic Conditions

Psychodermatologic conditions are prevalent in dermatology practice; it is estimated that every third patient in dermatology clinics has psychological factors affecting the course or management of their skin lesions (Bolognia, Schaffer, Duncan, & Ko, 2014; Locala, 2009). However, these conditions are frequently overlooked, unreported and/or unaccounted for in the management plan. This may be a result of the lack of understanding and training, as well as the paucity of targeted protocols that precisely outline the proper therapeutic approach to these patients (Thompson, 2014). Other challenges that have been reported to hinder the optimization of care

for patients with these conditions include the lack of specialized multidisciplinary treatment facilities, referral system complications, and challenges related to patients' limited insight into their conditions and therefore difficulties with compliance with psychiatric (i.e., non-dermatological) treatment (Gupta & Voorhees, 1990; Thompson, 2014). As a result, there is a paucity of data on the prevalence of these conditions.

Studies have reported varying prevalence rates for few psychodermatological disorders. For instance, trichotillomania, an impulse control disorder involving hair-pulling, affects 0.5-3.9% of the general population (Grant, Dougherty, & Chamberlain, 2020; Grzesiak, Reich, Szepietowski, Hadryś, & Pacan, 2017; Thomson, Farhat, Olfson, Levine, & Bloch, 2022). Delusional infestations, such as delusional parasitosis, have an estimated prevalence of 1-5 per 100,000 individuals (Bailey et al., 2014). Neurotic excoriations, where individuals repetitively scratch their skin due to emotional distress, have been reported in 25-30% of dermatology patients (Spitzer et al., 2022). Moreover, body dysmorphic disorder, which involves an obsessive preoccupation with perceived flaws in appearance including skin manifestations, affects up to 1-2% of the population (Buhlmann et al., 2010). The varying prevalence rates in different settings (general population versus dermatology clinics versus psychiatry patients, etc.) and the inadequacy of reports on some conditions such as psychogenic pruritus (Shevchenko, Valdes-Rodriguez, & Yosipovitch, 2018) may be attributed to underreporting, misdiagnosis, stigma, limited research focus, and the complexity of diverse clinical presentations that lead to inappropriate referrals to different clinicians.

Unclear prevalence rates for psychodermatologic conditions can have several negative outcomes for healthcare practitioners. For instance, prevalence data help healthcare practitioners understand the likelihood of encountering these conditions in their practice, whether it is

dermatology settings, psychiatric settings or family medicine (Lowell, Froelich, Federman, & Kirsner, 2001). Without this knowledge, there is a risk of misdiagnosis or delayed diagnosis, as the conditions might be overlooked or mistaken for something else (Lowell et al., 2001; Musalek, Hobl, & Mossbacher, 2001). Another consequence of the paucity of prevalence data is inappropriate resource allocation and training of healthcare professionals (Cimmino & Hazes, 2002). Further, prevalence data can guide research and development efforts (Cimmino & Hazes, 2002). Researchers prioritize studying more prevalent conditions to understand their causes, develop effective treatments, and improve patient outcomes. Lastly, knowing the prevalence rates for these conditions can help policymakers identify public health priorities, allocate funding, develop preventive strategies, and implement healthcare policies (Cimmino & Hazes, 2002). Therefore, it is imperative to narrow the gaps in prevalence data for psychodermatologic conditions including primary, secondary and psychophysiologic conditions.

To address the aforementioned challenges and gain a comprehensive understanding of the prevalence of psychodermatologic conditions, this thesis comprises two studies (see chapters II and III) (Turk, Dytoc, et al., 2021; Turk et al., 2022). Given the lack of any prevalence studies from Canada, and the absence of centralized databases that capture these conditions, my first study (chapter II) (Turk, Dytoc, et al., 2021) is a cross-sectional analysis of prevalence estimates of potential psychodermatologic conditions in Alberta, Canada based on administrative health care data. The second study (see chapter III) (Turk et al., 2022) entails a systematic review, focusing on identifying prevalence rates for primary psychodermatologic conditions, as available from the extant literature on different populations (e.g., general population, dermatology patients, psychiatry patients, etc.). Together, these two studies aimed to increase our understanding of the prevalence of psychodermatologic conditions, in order to shed light on the global burden of these

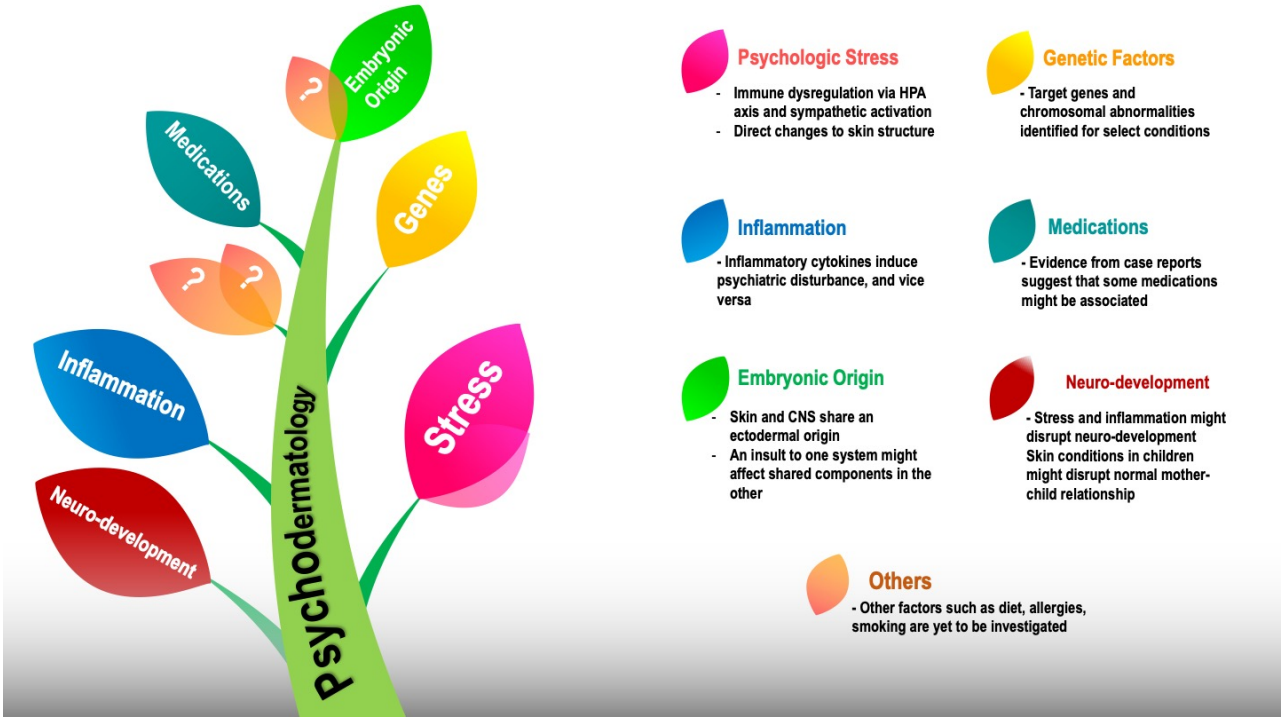
disorders and to offer insights for healthcare planning, policy development, and improved patient care.

1.3. Pathophysiology and Potential Causes of Psychodermatologic Conditions

There are several hypotheses to explain possible mind-skin interactions underlying psychodermatologic conditions (see Figure I.1). The main hypotheses focus on the role of hormones (e.g., cortisol), neuropeptides (e.g., substance P) and neurotransmitters (e.g., acetylcholine) in orchestrating interactions between the CNS and the skin (Jafferany, 2011). The changes in these factors can result from internal elements (e.g., genetic susceptibility, systemic inflammation) and external triggers (e.g., stress, medications, toxins, pollutants, allergens and trauma), causing or exaggerating the release of inflammatory mediators such as cytokines, interleukins and other inflammatory proteins that ultimately result in psychodermatologic conditions (Jafferany, 2007; Misery, 1996). Additional theories focus on neurodevelopmental factors and the role of medications.

Advancing our understanding of these etiologies holds significant promise for identifying potential risk factors that contribute to the development of psychodermatologic conditions (e.g., early life stressors, family history of mental health disorders, etc). This knowledge may allow for a better understanding of who might be more susceptible to these conditions, which, in turn, helps better estimate their prevalence in the population. Additionally, it may help in developing personalized and effective prevention and treatment strategies. Early identification of risk factors and targeted interventions can potentially avert or mitigate the development of psychodermatologic disorders. Further, gaining the understanding of the etiological factors is of paramount importance as it complements and forms the foundation of my

PhD research focused on enhancing the comprehension of prevalence and treatment options for psychodermatological conditions.



Note: HPA: hypothalamic-pituitary-adrenal; CNS: Central Nervous System

Figure I.1: *Etiological factors in psychodermatologic conditions*

1.3.1. Stress Hypothesis

Reports have long pointed to the negative impact of stress on the homeostasis of the skin and its sequelae of cutaneous lesions (Garg et al., 2001) and stress is still the most commonly reported trigger of psychodermatologic conditions. Many clinical studies highlight the role of stress in the development or treatment resistance of certain dermatoses such as psoriasis, atopic dermatitis, vitiligo, acne, and alopecia areata (Choe et al., 2018). Conversely, several epidemiological studies found high rates of psychiatric comorbidities such as body dysmorphia, anxiety and depression in patients with chronic dermatologic disorders that are associated with

significant stress (Picardi & Pasquini, 2007).

Stress can be defined as a physiological and psychological response to a perceived threat or challenge (Sapolsky, 2004). When an individual encounters a stressor (a stimulus or situation perceived as stressful), the body and brain activate a series of responses to cope with the perceived threat (Kimyai-Asadi & Usman, 2001). Acute or chronic stress may disrupt the homeostatic status of the neuroendocrine and/or immunologic systems (Jafferany, 2011; Locala, 2009). The human body responds to stress through activating the hypothalamic-pituitary-adrenal axis and the sympathetic system (Jafferany, 2011). Consequently, the immune response drifts towards humoral immunity leading to an increase in inflammatory responses. Terminal nerve endings in the skin respond by releasing neuromodulators such as substance P, Gastrin-releasing peptide, Neuropeptide Y, Neurotensin, Neurokinin, and Bradykinin, which have a variety of effects on local inflammatory processes in the skin (Arck, Slominski, Theoharides, Peters, & Paus, 2006; Jafferany, 2011). This neuroimmune reaction may trigger or exaggerate psychodermatologic disorders.

In addition, stress can directly impact the skin and alter its components and structure locally. This includes impairing stratum corneum's cohesion, disrupting skin barrier's integrity, reducing the antimicrobial properties of the skin, delaying wound healing, dysregulating epidermal innate immunity (Choe et al., 2018; Garg et al., 2001; Lin et al., 2014; O'Sullivan, Lipper, & Lerner, 1998; Orion & Wolf, 2012; Panconesi & Hautmann, 1996). These changes are thought to contribute to the onset, progression, or exacerbation of various skin disorders.

1.3.2. Genetic Hypothesis

The role of genetic factors in psychodermatology has been supported by findings from several familial and twin studies. In a report of four generations of a South African family, members of

the family suffered from Skin Picking Disorder (SPD), Trichotillomania (TTM) and severe nail biting with no evidence of other psychiatric disorders (Khumalo, Shaboodien, Hemmings, Moolman-Smook, & Stein, 2016). A larger-scale study on SPD in a British twin sample (female twins, n= 2,191), found genes to account for 40% [95% confidence interval (CI) 19-58%] of the variance of the skin picking behavior, while environmental factors and measurement errors accounted for the remaining variance. In a similar study on body dysmorphic symptoms (female twins, n= 3544), genes accounted for 44% of the variance [95% CI 36-50%] (Benedetta Monzani et al., 2012), and another twin study on trichotillomania TTM (n= 68) found a heritability estimate of 78% (Novak, Keuthen, Stewart, & Pauls, 2009). It is notable that all these symptoms can be classified under Obsessive-Compulsive Related Disorders (OCRDs), which raises questions about whether genetic susceptibility is specific to this particular spectrum of disorders. Whether genetic susceptibility is specific to individual disorders within this spectrum or can generalize to other psychodermatologic conditions remains to be seen (B. Monzani, Rijsdijk, Harris, & Mataix-Cols, 2014).

Although determining the susceptibility genes that confer risk for psychodermatologic disorders is yet to be accomplished, several condition-specific genes were identified: The SAP90/PSD9-associated protein (SAPAP3) gene for SPD and TTM (Bienvenu et al., 2009; Chattopadhyay, 2012), the Slit and Trk-like 1 (SLITRK1) for TTM (Zuchner et al., 2006), and the genes encoding Dopamine Receptor 1 (DRD1) and Serotonin Receptors (5-HTTLPR and 5-HT2A) for body-focused repetitive behaviors (BFRBs) such as skin picking and hair pulling (Chattopadhyay, 2012). Other examples of genes potentially involved in psychodermatology are highlighted in depression-psoriasis studies. The potential of having psoriasis-depression-specific genes was pointed out in several studies where G-banding and cell cultivation were used to

detect changes in chromosomes 8, 15, 21, 22, and the sex chromosomes in a family with both psoriasis and bipolar disorder (Demirhan et al., 2012). Another study demonstrated the existence of specific tandem repeat polymorphisms in intron 2 of the 5-HTT gene and serotonin receptor-related genes, which may underlie the psychiatric symptoms (i.e., depression, stress and/or anxiety) present in individuals with psoriatic lesions (Aleem & Tohid, 2018; Kleyn et al., 2020). Thus, there is some evidence for a genetic component for some of the bidirectional relationships between psychiatric and skin conditions, in particular in conditions linked to the OCDR spectrum and in psoriasis.

1.3.3. Inflammation Hypothesis

Many psychiatric disorders induce a stress-triggered, glucocorticoid-mediated dysregulation of the immune system and an increase in pro-inflammatory cytokines, which can result in the development or flaring of a skin condition (Bauer & Teixeira, 2019). Conversely, inflammation itself can lead to mood fluctuations (Bauer & Teixeira, 2019). The acute or chronic induction of cytokines seems to be the major driver of inflammation-induced psychiatric symptoms (Bauer & Teixeira, 2019). For example, some findings have shown that if elevated, C-reactive protein and IL-6 can predict future depression, while baseline depressive symptoms do not predict future increase in inflammatory markers (Khandaker, Pearson, Zammit, Lewis, & Jones, 2014; Valkanova, Ebmeier, & Allan, 2013). This is supported by clinical studies on patients taking immune boosters such as patients receiving interferon-alpha for hepatitis C, or IL-2 for cancer and reportedly developing depressive symptoms afterwards (Capuron et al., 2001; Dieperink, Willenbring, & Ho, 2000). IL-2 and Interferon Alpha (INF a) directly increase the enzymatic activity of Indolaminee-2,3- dioxygenase, which increases the conversion of tryptophan to kinurenine and, therefore, reduces synthesis from tryptophan to serotonin. Decreased serotonin

levels and increased kynurenine are thought to produce depressive symptoms (Wichers & Maes, 2004).

In dermatology practice, treating dermatoses using medications that target inflammatory cytokines demonstrated how treating inflammation in patients with skin conditions may improve fatigue and depressive symptoms, with or without affecting the severity of skin and joint lesions (Haugeberg, Hoff, Kavanaugh, & Michelsen, 2020; Skoie, Dalen, & Omdal, 2019; Strober et al., 2018). An important example is a study in which treating psoriasis patients with dual blockade of anti-TNF a and anti-IL17 led to a decrease (-43.8%) in the use of antidepressants and sleep medications in the same patients (Wu et al., 2016). This could be explained by the decrease in systemic inflammation as opposed to the psychological effect of the decrease in the severity of psoriasis. Inflammatory processes in the skin conditions could therefore play a major role in the emergence of and recovery from secondary psychodermatologic conditions. Further, in delusions of parasitosis, which is a primary psychodermatologic condition, several reports documented cases that are associated with infectious (e.g., syphilis, AIDS, tuberculosis) or inflammatory (e.g., multiple sclerosis, encephalitis) conditions (Ansari & Bragg, 2023). Many antipsychotics, including risperidone, the first-line treatment for delusions of parasitosis, have anti-inflammatory properties (Campbell, Elston, Hawthorne, & Beckert, 2019; MacDowell et al., 2013). Therefore, more research on the inflammatory cytokine profiles in patients with delusions of parasitosis seems plausible and might lead to clinically relevant outcomes for patients' workup and therapy.

1.3.4. Medications

Several case reports have linked medications to the development of psychodermatologic conditions e.g., trichotillomania, or psychodermatologic symptoms, e.g., hair pulling. For instance, trichotillomania was reported after taking stimulants like amphetamine or cocaine

(George & Moselhy, 2005; Narine, Sarwar, & Rais, 2013), skin picking was reported with intake of atomoxetine (antidepressant) and clozapine (atypical antipsychotic) (Kasar & Yurteri, 2020; Reddy, Das, & Guruprasad, 2018), and delusions of parasitosis has been documented in conjunction with topiramate (antiepileptic drug/mood stabilizer) (Fleury, Wayte, & Kiley, 2008), ciprofloxacin (antibiotic) (Steinert & Studemund, 2006), amantadine (antiviral) (Swick & Walling, 2005), ketoconazole (antifungal) (Frean, 2010), and phenelzine (antidepressant) (Aizenberg, Schwartz, & Zemishlany, 1991; Ansari & Bragg, 2023). These reports highlight the importance of recognizing and understanding the potential psycho-dermatologic side effects of certain medications, enabling healthcare providers to make informed decisions while prescribing them and ensuring appropriate patient care.

1.3.5. Embryonic Origin Hypothesis

The skin (epidermis, hair, glands, sensory placodes) and the neural tube share an ectodermal origin during embryonic development. Some researchers postulate that mind-skin interactions can be attributed to this shared embryonic origin of the skin and central nervous system (CNS), and that an insult to one of them can result in disturbance in the other (Chen & Lyga, 2014; Paus, Theoharides, & Arck, 2006). Preliminary evidence from animal models suggests that abnormal neural development may influence epidermal differentiation during embryogenesis. Some evidence to support this hypothesis comes from genetic disorders such as Waardenburg syndrome, a series of autosomal dominant auditory–pigmentary disorders where a genetic defect affects several melanocytic proteins that share an embryonic origin from the neural crest (Saleem, 2019). As recently argued by Jameson, Boulton, Silove, Nanan, and Guastella (2023), epidemiological studies also consistently support the positive association between atopic diseases and Autism Spectrum Disorder (ASD), which indicates a potential underlying shared etiological

mechanism. Common molecular factors shared between skin and neural structures, such as Brain-Derived Neurotrophic Factor (BDNF) and filaggrin were highlighted to supported the association between atopy and ASD. Dysregulation of BDNF has been observed in both ASD and atopic conditions, implying a potential role in provoking concurrent morphological and pro-inflammatory changes in the skin and neural tissue. Similarly, loss-of-function mutations in the filaggrin gene have been identified as susceptibility variants for both ASD and atopic dermatitis, further supporting the link between skin and neural system. Those novel insights support the role of shared embryonic origin in the development of psychodermatologic conditions, and reflect on the interplay of various factors such as genetics, inflammation and neurodevelopment.

1.3.6. Developmental Hypothesis

Neurodevelopment is a progressive and dynamic process. Early life adversity can alter the trajectory of neurodevelopment, with significant impact on health later in life (Syed & Nemeroff, 2017). Environmental and biological events in childhood can also contribute to psychodermatologic conditions. The main childhood factors that were reported to disrupt normal development were mother-child detachment, childhood stress, and childhood inflammation (Khandaker et al., 2014; Koblenzer, 1983). Studies have specifically reported that children with infantile skin diseases, such as eczema, often exhibit disturbed mother-child relationships and recurrent psychiatric distress throughout their development (Osman, 2010; Pines, 1980; Pretorius, 2004). However, more longitudinal studies are necessary to solidify if specific childhood experiences and biological events contribute to the development of psychodermatologic conditions later in life.

In summary, the main etiologic hypotheses in psychodermatology revolve around stress, genes, and inflammation. Additionally, there are intriguing arguments and reports concerning the shared embryonic origin of skin and neurons, the potential impact of medications, and early-life neurodevelopment. Given the involvement of multiple systems in these complex conditions, it is unlikely that any single hypothesis can fully explain the interactions between the skin and the mind.

1.4. Treatment of Psychodermatologic Conditions

In this section, I outline common (e.g., antidepressants) and more unique (e.g., N-Acetylcysteine) therapeutic options for treating psychodermatologic conditions. A multifaceted approach is often recommended, addressing both the physical symptoms and the psychological aspects that accompany them (Thompson, 2014).

1.4.1. Pharmacological Treatment

Pharmacological treatment plays a crucial role in the therapeutic armamentarium for psychodermatologic conditions (Torales et al., 2020). For instance, selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and other psychotropic medications have demonstrated efficacy in alleviating both the psychological and dermatological symptoms associated with these conditions (Torales et al., 2020). SSRIs, such as fluoxetine and sertraline, are commonly prescribed due to their serotonergic modulation and ability to improve mood and reduce anxiety, which can subsequently influence the course of dermatological disorders (Eskeland, Halvorsen, & Tanum, 2017). TCAs, such as amitriptyline and doxepin, exhibit both antidepressant and antipruritic properties, making them particularly effective in managing conditions characterized by chronic itch, such as atopic dermatitis and prurigo nodularis (Park &

Koo, 2013). The use of systemic corticosteroids, immunosuppressants, and biologic agents may also be warranted in specific cases to target inflammation and modify immune responses associated with dermatological manifestations.

Using pharmacologic treatments to manage psychodermatologic conditions comes with significant challenges, especially concerning the lack of understanding about the safety and efficacy of specific medications for different psychodermatologic conditions (Torales et al., 2020). There is currently no consensus on which pharmacologic treatments are safe and effective for particular conditions, leading to a gap in our knowledge (Goldin, 2021). For instance, in controlled trials, medications like fluoxetine, a selective serotonin receptor inhibitor, have shown promising results in patients with skin picking disorder, but have not demonstrated similar improvement in those with trichotillomania (M. R. Bloch, Elliott, Thompson, & Koran, 2001; van Minnen, Hoogduin, Keijsers, Hellenbrand, & Hendriks, 2003). The reasons behind such contradictory outcomes are unclear, leaving practitioners with uncertainties about which treatments to prescribe for specific psychodermatologic conditions. The complexity of medication regimens, potential side effects, and the influence of psychological factors on patients' compliance further contribute to the limitations of pharmacological treatments (Chung, Ng, Koh, Peh, & Liu, 2012; Harth, Gieler, Kusnir, & Tausk, 2008). Moreover, it remains unknown whether patients' compliance with certain medications can be influenced by factors such as efficacy, safety, time required for symptom relief, and potential drug-drug interactions (Chung et al., 2012; Torales et al., 2020).

Thus, the lack of standardized treatment guidelines, likely resulting from a combination of diagnostic confusion and a paucity of controlled trials, poses a considerable obstacle for clinicians when determining the most appropriate therapeutic options for patients with

psychodermatologic conditions (Thompson, 2014; Torales et al., 2020). My doctoral research aimed to address part of this issue by examining the extant literature on pharmacologic treatments. To limit the scope and study variability, I focused on primary psychodermatologic disorders (see Chapter IV). These conditions are less ambiguously diagnosed as being psychiatric in nature, and they are particularly challenging to treat in dermatologist practice. Thus, I conducted a systematic review of the extant controlled clinical trials in primary psychodermatologic conditions to better understand which medications are effective and safe for which of these conditions (Turk et al., 2023).

1.4.2. Non-pharmacologic Treatments

It is crucial to note that pharmacologic treatments alone may not adequately address the psychosocial and environmental factors that can affect psychodermatology patients (Jaspers, 1996) and multiple non-pharmacologic treatments have been explored in psychodermatology. Non-pharmacological interventions form an integral component of the management of psychodermatologic conditions and encompass various psychotherapeutic and psychosocial approaches (Fried, 2002). Cognitive-behavioral therapy (CBT) is widely recognized as an effective intervention, focusing on modifying maladaptive thought patterns and behaviors that contribute to the maintenance of both psychological distress and dermatological symptoms (Revankar et al., 2022). CBT techniques, including cognitive restructuring, relaxation training, and behavioral activation, have been shown to reduce psychological distress, improve coping mechanisms, and enhance treatment outcomes in conditions such as psoriasis, acne, and chronic itch (Revankar et al., 2022). Similarly, dialectical behavior therapy (DBT) incorporates mindfulness-based practices, emotion regulation, and interpersonal effectiveness training to address emotional dysregulation and promote adaptive coping strategies, which were used as part

of the treatment of some psychodermatologic conditions such as trichotillomania and skin picking disorder (Jafferany & Patel, 2019; Keuthen et al., 2011; Madan, Davidson, & Gong, 2023). In addition, supportive counseling, psychoeducation, and stress management techniques are often used by psychologists to enhance patient understanding, encourage treatment adherence, and address psychosocial factors that may influence disease severity and course (De Zoysa, 2013). However, implementing non-pharmacological treatments can be challenging due to limited accessibility, particularly in rural areas or among marginalized populations, availability of trained professionals, and patient adherence (Fried, 2002). Since the commitment and motivation required from patients to engage in psychotherapeutic processes may vary, ongoing support and reinforcement are often necessary to facilitate lasting behavioral changes (Fried, 2002). In addition to the challenges associated with specific treatment modalities, the management of psychodermatologic conditions faces broader systemic and societal challenges. Stigma and misconceptions surrounding mental health and dermatological disorders can lead to delays in seeking appropriate care and contribute to patient distress (Dimitrov & Szepietowski, 2017). Promoting awareness, reducing stigma, and educating the public about the bidirectional relationship between the mind and the skin are crucial steps in improving treatment-seeking behaviors and overall outcomes.

To summarize, treatment of psychodermatologic conditions includes pharmacological (dermatologic and psychiatric) and non-pharmacological interventions. Both are essential for psychodermatology patients, and they complement each other in providing comprehensive care. It is currently challenging for clinicians to choose one over the other, or to tailor a hybrid approach. This difficulty mainly stems from the difficulty in diagnosing some of these conditions as well as the current immaturity of evidence base that would support specific interventions for

each of the conditions, while taking into consideration the intervention's safety profile, the severity of the condition and the patient's insight into their condition.

1.4.3. Additional Challenges in Daily Clinical Practice

The treatment landscape for psychodermatologic patients is fraught with complex challenges that clinicians face in their daily practice. A major reported hurdle lies in the difficulty to accurately diagnose these conditions, as symptoms often manifest with overlapping features, making it challenging to distinguish between purely dermatological issues and those with underlying psychological components (Lopes, Vide, Antunes, & Azevedo, 2018; Mohandas, Srinivasan, Ravenscroft, & Bewley, 2018). For example, skin manifestations and behaviors like hair pulling and skin picking may exacerbate during periods of heightened stress, complicating the diagnosis and treatment process (Hajcak, Franklin, Simons, & Keuthen, 2006). An additional significant challenge arises from the limited insight exhibited by patients regarding their conditions, especially when patients solely focus on the visible skin manifestations without addressing the potential emotional triggers. Due to the stigma and fear around mental health, patients might reject psychotropic medications, choosing to pursue solely dermatological treatments without addressing the underlying psychological factors (Gupta & Gupta, 2014). Another obstacle comes from navigating the referral system for psychodermatology patients which can be cumbersome (Nguyen et al., 2015). The integration of dermatology and psychiatry services is not always straightforward, and the absence of clear pathways for referrals may result in delayed access to appropriate care (Nguyen et al., 2015; Thompson, 2014).

The complexities of these disorders and potential side effects associated with psychotropic medications may also create uncertainty among clinicians when deciding on

appropriate treatment (Jafferany, Stamu-O'Brien, Mkhoyan, & Patel, 2020; Weber, Recuero, & Almeida, 2020). Clinicians, including dermatologists and general practitioners, may not feel confident in prescribing and monitoring psychotropic medications to address psychodermatologic conditions (Weber et al., 2020). These uncertainties may lead to variations in practice patterns, with some clinicians relying solely on dermatological treatments, potentially overlooking the potential benefits of a more comprehensive, multidisciplinary approach that incorporates both dermatology and psychiatry (Jafferany, Ferreira, Abdelmaksoud, & Mkhoyan, 2020; B. Shah & Levenson, 2018; Torales et al., 2020). Finally, patient adherence to treatment regimens is also known to pose a challenge in daily practice as patients may find it difficult to comply with prescribed therapies due to ongoing emotional distress, limited insight into their condition, or the chronic nature of the disorder (Ali, Brodell, Balkrishnan, & Feldman, 2007; Thompson, 2014).

Comprehending all these challenges and their impact on clinicians' practices in psychodermatology is pivotal in devising interventions that address them most effectively. Canada faces unique limitations in psychodermatology services, and a systematic review of the epidemiological characteristics, clinical experiences, and challenges in this domain is yet to be conducted. The unique challenges include the complex referral system that may delay patients' visits to specialist, the paucity of specialized psychodermatologic multidisciplinary services and the inadequacy of data on prevalence and treatment guidelines. This lack of knowledge regarding challenges and the current state of psychodermatology treatment in Canada likely reduces the quality of care. As part of my doctoral work, I conducted a comprehensive nationwide survey to assess Canadian dermatologists' attitudes towards psychodermatology, their practice patterns, and the obstacles hindering the delivery of optimal care (Turk, Fujiwara, Abba-Aji, Mathura, &

Dytoc, 2021), outlined in Chapter V. The aim of this study was to characterize psychodermatological practice in Canada and uncover potential strategies to enhance dermatologists' confidence and competence in managing psychodermatologic conditions.

1.5. Thesis objectives

Psychodermatology poses ongoing challenges for healthcare practitioners, necessitating further exploration and investigation. Currently, there exist notable gaps in knowledge that impede clinicians' ability to deliver optimal care within this specialized field. To begin, we first need to enhance our comprehension of the prevalence of psychodermatologic conditions to improve their identification and diagnosis. Secondly, we need a better understanding of the many factors that complicate treatment of these conditions in dermatological practice. Many pharmacological treatments exist, but the efficacy of these treatments even for the easier to identify primary psychodermatologic conditions has not been systematically explored. Therefore, I conducted four studies aimed at determining the prevalence of psychodermatologic conditions, investigate the efficacy of some of the therapeutic options available for managing these conditions, and identify the challenges faced by dermatologists when treating patients. Specifically, I conducted a chart review on administrative heath data to estimate frequency of psychodermatologic conditions in Alberta, Canada (Chapter II) (Turk, Dytoc, et al., 2021). Through systematic reviews, I explored the global prevalence of primary psychodermatologic conditions (Chapter III) (Turk et al., 2022) and the efficacy of pharmacologic interventions for primary psychodermatologic conditions (Chapter IV) (Turk et al., 2023). Finally, in order to identify the concrete challenges faced by dermatologists in treating these conditions and to generate actionable recommendations for improving care, I surveyed the perceptions, practice patterns and challenges that Canadian dermatologist report when they treat patients with psychodermatologic conditions (Chapter V) (Turk, Fujiwara, et al., 2021).

II. CHAPTER 2 - Estimated Frequency of Psychodermatological Conditions in Alberta, Canada

Turk, T., Dytoc, M., Youngson, E., Abba-Aji, A., Mathura, P., & Fujiwara, E. (2021). Estimated frequency of psychodermatologic conditions in Alberta, Canada.

Journal of Cutaneous Medicine and Surgery, *25*(1), 30-37.

2.1. Abstract

Background: Psychodermatological disorders are difficult to identify and treat. Knowledge about the prevalence of these conditions in dermatological practice in Canada is scarce. This hampers our ability to address potential gaps and establish optimal care pathways. **Objectives:** To provide an estimate of the frequencies of psychodermatological conditions in dermatological practice in Alberta, Canada. **Methods:** Two administrative provincial databases were used to estimate the prevalence of potential psychodermatological conditions in Alberta from 2014 to 2018. Province-wide dermatology claims data were examined to extract relevant ICD-9 codes as available. Claims were linked with pharmacy dispensation data to identify patients who received at least one psychoactive medication within 90 days of the dermatology claim. **Results:** Of 243,963 patients identified, 28.6% had received at least one psychotropic medication (mean age: 47.9 years; 67.5% female). Rates of concurrent psychotropic medications were highest for pruritus and related conditions (46.7%), followed by urticaria (44.5%) and hyperhidrosis (32.8%). Among patients with psychotropic medications, rates of antidepressants were highest (56.3%), followed by anxiolytics (37.1%). Across billing codes, besides hyperhidrosis (71.2%), diseases of hair (61.4%) and psoriasis (59.1%) had the highest rates of antidepressant dispensations. Patients with atopic dermatitis had the highest rates for anxiolytic prescriptions (54.3%). **Conclusion:** In a five-year window, more than a quarter of the identified dermatology patients in Alberta received at least one psychotropic medication, pointing to high rates of potential psychodermatological conditions and/or concurrent mental health issues in dermatology. Diagnostic and care pathways should include a multidisciplinary approach to better identify and treat these conditions.

2.2. Introduction

Psychodermatological conditions are multi-faceted disorders with skin- and mind-related components. While there is no universal consensus on the categorization of these illnesses, a differentiation into primary psychodermatological disorders where the psychiatric disorder is the primary aetiology of the skin condition (e.g., delusions of parasitosis), secondary psychodermatological disorders in which psychiatric distress develops as a consequence of disfiguring skin lesions (e.g., illness anxiety disorder), psychophysiologic disorders where exacerbations are known to be triggered by emotional factors (e.g., psoriasis) and psychogenic pruritus has been proposed (Koo & Lee, 2003). Other classifications categorize conditions based on the nature of the underlying or accompanying mental health (i.e., skin-disorders with depressive, delusional, anxiety-related or obsessive-compulsive symptomatology) (Koo & Lee, 2003).

The frequency of psychodermatological conditions and psychiatric comorbidites in dermatology practice is high. It has been estimated that every third patient in dermatology clinics should be evaluated for psychological distress (Bolognia et al., 2014; Gupta & Voorhees, 1990; Korabel, Dudek, Jaworek, & Wojas-Pelc, 2008). In 2017, an Indian study reported a high prevalence of depression (36.3%, n=146) and anxiety (18.4%, n=74) among dermatology outpatients (Raikhy, Gautam, & Kanodia, 2017). In addition, a nationwide population-based study in Taiwan found that 11.5% (n= 17086) of psoriasis patients have major depression disorder (Hu, Chen, & Tu, 2019). Suicidal ideation has been reported in a study from Italy in 8.6% of outpatients with skin conditions, with 7.2% of those with psoriasis and 5.6% of those with acne (Picardi, Mazzotti, & Pasquini, 2006), exceeding rates in the general population (Gupta & Gupta, 2003). A small study reported that the rate of psychosomatic disorders in acne

vulgaris patients is (30%, n=22) (Gupta & Gupta, 1998). For patients with alopecia areata, a survey-based study reported a lifetime prevalence of one or more psychiatric disorder of (74%, n=22) (Colon, Popkin, Callies, Dessert, & Hordinsky, 1991). Furthermore, a national survey on children's health in the United States of America reported a lifetime prevalence of Attention-Deficit Hyperactive Disorder (ADHD) in patients with atopic dermatitis of (12.6%, n= 959) (Yaghmaie, Koudelka, & Simpson, 2013).

Healthcare delivery to patients with psychodermatological conditions can be challenging and the outcomes of approaching psychodermatoses can be unsatisfying. Challenges include shortfalls in the referral and reporting systems, as well as a lack of mental health training of primary healthcare providers in dermatology (Hu et al., 2019; Ocek et al., 2015; Thompson, 2014). Other challenges are patient-centred and mainly include patients' limited insight into the psychological aspects of their skin condition, and consequently, limited compliance with psychological or psychiatric referrals, consultations, and therapy (Thompson, 2014). In addition, specialized psychodermatological treatment facilities jointly addressing the dermatological and psychological needs of these patients are not widely available, despite evidence for the benefits of multidisciplinary treatment models (R. B. Shah, 2018).

In Canada, psychodermatology practice is limited and currently there are no studies reporting the prevalence of psychodermatological conditions in a Canadian population. The lack of knowledge about prevalence and baseline characteristics of patients with potential psychodermatological conditions limits our ability to establish and scale appropriate interventions to provide optimal care to these patients. The current report is an estimation of the frequencies of psychodermatological conditions in Alberta, Canada, highlighting important

figures for healthcare providers to inform future endeavours in this underappreciated field of medicine.

2.3. Material and Methods

2.3.1. Data sources

The study was a retrospective review of provincial summary data, analysed by Alberta Health Services (AHS) (E.Y.), and approved by the University of Alberta Research Ethics Board (Pro00092486). Two administrative databases (the Practitioner Claims Database and the Pharmaceutical International Network Database) were accessed through AHS with support from the Alberta Strategy for Patient Oriented Research Support Unit Data Platform to derive our cohort of patients.

2.3.2. Practitioner Claims Database

The Practitioner Claims Database captures physician billing claims for the approximately 4.3 million residents of Alberta and includes visit dates, physician specialty, patient gender, age and the International Classification of Disease (ICD-9) diagnostic codes per visit. For the current study, only claims submitted by dermatologists were reviewed. Claims data were used to identify patients who were coded as having a dermatological condition by using specific ICD-9 codes we selected (see Table II.1), covering dermatology visits between January 1, 2014 and Dec 31, 2018. As can be seen in Table II.1, we chose to include several skin disorders with known psychodermatological characteristics (e.g., pruritus and related, atopic dermatitis, psoriasis) as well as broader classes of potentially relevant skin conditions (acne, eczema) and ill-defined skin disorders (ICD-9 code 709.8). We also included hyperhidrosis (780.8), included in ICD-9 code 780: “Signs, Symptoms and Ill-defined Conditions”. Finally, we included mental health-related billing codes, summarized into two larger classes: psychotic conditions and select non-psychotic

mental disorders (see Table II.1). By including mental health billing codes, we aimed to find the number of cases who were clearly identified by dermatology as primary psychiatric patients such as those with delusions of parasitosis, dysesthesia and neurotic excoriations. Patients who met the criteria for multiple conditions were separately counted under each code, but contributed only once to the total number of patients across all conditions.

Table II.1: *Billing codes obtained from the Physicians Claim Database*

Short label (ICD-9 codes)	**ICD-9 Label and description**
Skin and Subcutaneous Tissue-specific Conditions	
Atopic dermatitis (691.*)	**Atopic dermatitis and related conditions:** Atopic dermatitis and other related conditions
Eczema (692.*)	**Contact dermatitis and other eczema:** Eczematous disorders (except for contact dermatitis of eyelids, dermatitis due to ingested substances, eczema of external ear, perioral dermatitis)
Psoriasis (696.*)	**Psoriasis and similar disorders:** Psoriasis and similar disorders including psoriatic arthropathy and other types of psoriasis, parapsoriasis, pityriasis rosea, pityriasis rubra pilaris, other and unspecified pityriasis
Pruritis and related (698.*)	**Pruritus and related condition:** Pruritis ani, pruritis of genital organs, prurigo, lichenification and lichen simplex chronicus, dermatitis factitia (artefacta) and other unspecified pruritic conditions.

Short label (ICD-9 codes)	ICD-9 Label and description
Diseases of hair (704.*)	**Diseases of hair and hair follicles:** Alopecia, hirsutism, variations in hair colour, unspecified diseases of hair and hair follicles (except trichiasis of eyelid, madarosis, syphilitic alopecia)
Acne (706.*)	**Diseases of sebaceous glands:** Acne and diseases of sebaceous glands including sebaceous cyst, seborrheic keratosis and seborrhoea (except for acne rosacea, capiliti and sicca)
Urticaria (708.*)	**Urticaria** Allergic, idiopathic, urticaria due to cold and heat, dermatographic, vibratory, cholinergic, and other/ unspecified urticarias
Other skin diseases (709.8)	**Other diseases of skin** Skin conditions not classified elsewhere
Mental Health-Related Disorders	
Psychotic (290.* to 299.*)	**Organic and other psychotic conditions:** Senile and presenile, alcoholic, drug-induced, transient and chronic, schizophrenic, affective, paranoia-related, nonorganic, childhood and unspecified psychoses.

Short label (ICD-9 codes)	ICD-9 Label and description
Mental Health (300.*, 304.*, 306.*, 307.*, 308.*, 309.*, 312.*, 316.*)	**Select non-psychotic mental disorders:** 300.*: Neurotic disorders (300.*, e.g., anxiety, phobia, hysteria, obsessive-compulsive disorder 304.*: Drug dependence, 306.*: Physiological malfunction arising from mental factors (includes tissue/skin damage of mental origin) 307.*: Special symptoms or syndromes not elsewhere classified (includes tics, stereotypies) 308.*: Acute reaction to stress 309.*: Adjustment reaction 312.*: Disturbance of conduct not elsewhere classified (may include trichotillomania) 316.*:Psychic factors associated with diseases classified elsewhere
Signs, Symptoms and Ill-defined Conditions	
Hyperhidrosis (780.8)	–

2.3.3. Pharmaceutical Information Network (PIN) Database

The Pharmaceutical Information Network (PIN) database captures prescription drug dispensations from community pharmacies, including the date of dispensation, quantity of drug

dispensed, drug identification number (DIN), and the corresponding Anatomical Therapeutic Chemical (ATC) classification. The PIN database was used to derive whether a dispensation for any psychotropic medication from one of five major classes co-occurred within 90 days before or after the claim. Table II.2 lists the ATC medication classes that were included in this study.

Table II.2. *Psychotropic medications and their Anatomical Therapeutic Chemical (ATC) codes, accessed through the PIN database.*

Class	**Drugs**
N03 Antiepileptics	N03AA Barbiturates and derivatives
N03A Antiepileptics	N03AB Hydantoin derivatives
	N03AC Oxazolidine derivatives
	N03AE Benzodiazepine derivatives
	N03AF Carboxamide derivatives
	N03AX Other antiepileptics
N05A Antipsychotics	N05AA Phenothiazines with aliphatic side-chain
	N05AB Phenothiazines with piperazine structure
	N05AC Phenothiazines with piperidine structure
	N05AD Butyrophenone derivatives
	N05AE Indole derivatives
	N05AF Thioxanthene derivatives
	N05AG Diphenylbutylpiperidine derivatives
	N05AG02 pimozide

Class	Drugs
	N05AH Diazepines, oxazepines, thiazepines and oxepines
	N05AL Benzamides
	N05AN Lithium
	N05AX Other antipsychotics
N05B Anxiolytics	N05BA Benzodiazepine derivatives
	N05BB Diphenylmethane derivatives
	N05BC Carbamates
	N05BD Dibenzo-bicyclo-octadiene derivatives
	N05BE Azaspirodecanedione derivatives
	N05BX Other anxiolytics
N05C Hypnotics and Sedatives	N05CA Barbiturates, plain
	N05CB Barbiturates, combinations
	N05CC Aldehydes and derivatives
	N05CD Benzodiazepine derivatives
	N05CE Piperidinedione derivatives
	N05CF Benzodiazepine related drugs
	N05CH Melatonin receptor agonists
	N05CM Other hypnotics and sedatives
	N05CX Hypnotics and sedatives in combination, excl. barbiturates
N06A Antidepressants	N06AA Non-selective monoamine reuptake inhibitors

Class	Drugs
	N06AB Selective serotonin reuptake inhibitors
	N06AF Monoamine oxidase inhibitors, non-selective
	N06AG Monoamine oxidase A inhibitors
	N06AX Other antidepressants
N06B Psychostimulants, agents used for ADHD and nootropics	N06BA Centrally acting sympathomimetics
	N06BC Xanthine derivatives
	N06BX Other psychostimulants and nootropics

All billing claims by a dermatologist that met the criteria for included ICD-9 codes were initially retained for all patients, and it was evaluated at each claim date whether one of the medications of interest were dispensed within 90 days. A patient was considered to meet the diagnostic and medication criteria if they had any visit along with a relevant drug dispensation within 90 days.

2.4. Results

We identified a total of 243,963 unique patients with at least one of the included ICD-codes in the claims database. Of these, 69,786 (28.6%) had received at least one psychotropic medication within 90 days of their visit. Patients on medications had a mean age of 47.9 years (SD = 19.8), and we observed a female predominance of 67.5%. Figure II.1 illustrates the frequencies of patients with the included ICD-9 codes along with percentages of patients with concurrent psychotropic drug dispensations. During the period of five years, few patients were billed by dermatologists for having mental health-related disorders; 30 patients were billed for psychotic conditions (ICD-9: 290.* - 299.*) and 199 for other psychiatric conditions as listed in Table II.1

(ICD-9: 304, 306 – 309, 312, 316). Of these, 60% and 66.8% were on psychotropic medications, respectively. Note that included in the category of non-psychotic mental disorders (ICD-9: 300s), 22 patients were identified as having psychogenic pruritus (ICD-9: 306.3), 19 (86.4%) with a psychotropic prescription within 90 days. For patients taking concurrent psychotropic medications, the median number of identified conditions per patient was 1. However, 9595 patients (13.7%) had multiple conditions. Across the included dermatological conditions, rates of concurrent psychotropic medications were highest for pruritus and related (ICD-9 689: 46.7%, n=4297), followed by urticaria (ICD-9 708: 44.5%, n=2324) and hyperhidrosis (ICD-9 780.8: 32.8%, n=860).

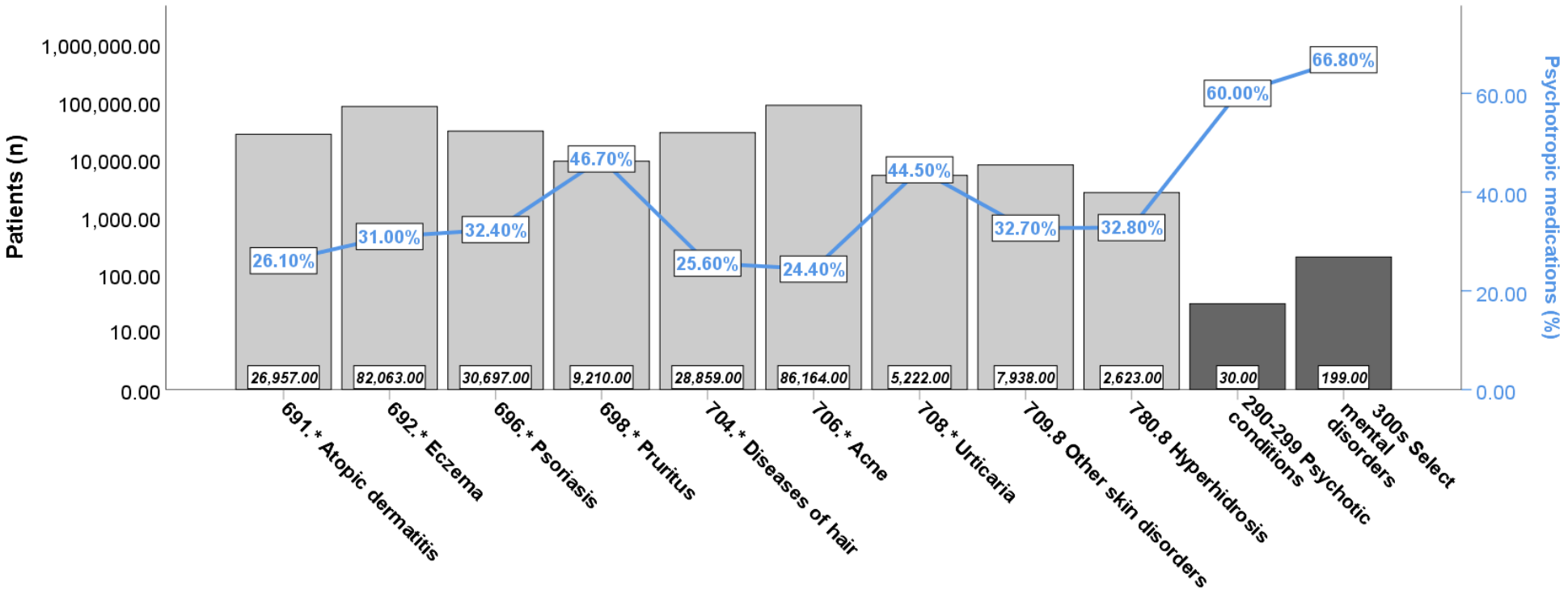


Figure II.1: *Number of patients with dermatological billing records across conditions; percentages of patients with concurrent psychoactive drug dispensations*

The breakdown of the prescribed psychoactive medications (Figure II.2) within the dermatological codes showed that prescription rates were highest for antidepressants overall. Patients with hyperhidrosis most frequently dispensed a prescription of antidepressants (71.2%), followed by patients with diseases of hair (61.4%) or psoriasis (59.1%). Prescriptions for anxiolytic were highest in patients with urticaria (65%), followed by those with atopic dermatitis (54.3%). Patients with psoriasis had the highest rates of prescriptions of hypnotics/sedatives (29%), while patients with pruritus and related conditions had the highest prescription rates of antiepileptic/mood stabilizing medications (32.3%). The median number of medications per patient was 1, but 38.1% of patients received two or more psychoactive medications.

Patients billed for psychotic and non-psychotic mental health conditions expectedly had higher rates of concurrent psychoactive medications. Of patients with psychotic conditions (n=18), 61.1% were prescribed antidepressants and 55.6% were taking anxiolytics, followed by antipsychotics (33.3%). Among patients with a billing code for one of the non-psychotic mental disorders included here (ICD-9: 300s; see Table II.1), antidepressants (69.9%) and anxiolytics (48.9%) were more frequent compared to other classes of medications such as antipsychotics (31.6%), and hypnotics and sedatives (29.3%). Psychogenic pruritus, which is the only psychodermatological condition that was explicitly diagnosed in 19 cases (ICD9: 306.3; n=19) and was subsumed in our larger ICD-9 300.* class, had high rates of concurrent prescriptions of antidepressants (68.4%), anxiolytics (63.2%), but also high rates of antipsychotics (57.9%) and antiepileptic/mood stabilizing medications (52.6%)

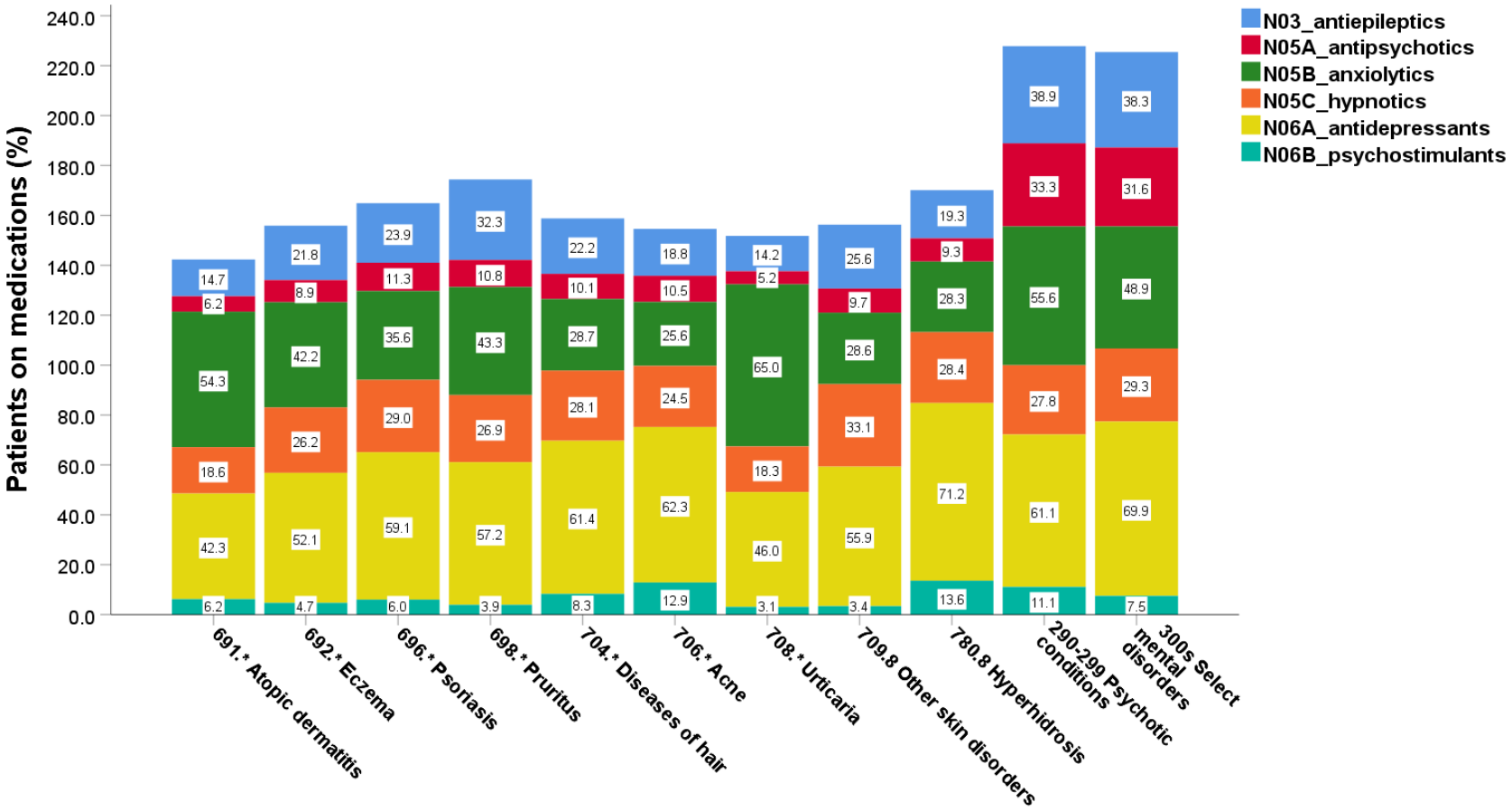


Figure II.2: *Summary of medications types at the time of dermatological treatment visits across the targeted billing codes*

2.5. Discussion

Our province-wide retrospective study of patients in dermatological care in Alberta, Canada showed more than a quarter of dermatology patients in Alberta were concurrently prescribed psychotropic medications, implying high rates of psychodermatological and/or concurrent mental health conditions in dermatology. Our results are compatible with previously reported estimates (Bolognia et al., 2014; Gupta & Voorhees, 1990; Korabel et al., 2008). Owing to the nature of the available databases, the frequency of psychodermatological conditions could be overestimated since dermatological and prescriptions of concurrent psychotropic medications may have been independent of each other. Conversely, the frequency of psychodermatological conditions could be even higher considering that we included only those dermatology patients who indeed dispensed a prescribed psychotropic medication, i.e., we could not capture patients who may have opted to forgo psychiatric treatments. Despite these uncertainties, to our knowledge, this report is the first estimation of the prevalence of potential psychodermatological conditions in Canada. Given the current lack of knowledge about these conditions in Canada, these numbers represent a starting point from which to raise awareness for the common co-occurrence of skin and mental disorders and eventually enhance the quality of care in psychodermatology.

The use of antidepressants has previously been emphasized in dermatology practice, especially for the treatment of dermatitis artefacta, neurotic excoriations, trichotillomania, cutaneous body image disorders and several secondary psychodermatological conditions like psoriasis- and atopic dermatitis-induced depression (Gupta & Gupta, 2001). In our population, they were the most commonly prescribed psychoactive medication; in most of the included categories, more than 50% of patients dispensed an antidepressant prescription within 90 days of

their visit to dermatology, with high rates also in atopic dermatitis (42.3%) and urticaria (46%). Within the dermatological billing codes, the highest percentages were found in patients with hyperhidrosis (71.2%), diseases of hair (61.4%), and psoriasis (59.1%). In dermatology, antidepressants are sometimes favourable due to their antihistaminic, anticholinergic and anti-inflammatory effects rather than their antidepressant or anxiolytic actions, which might contribute to the high rates of using these medications (Eskeland et al., 2017). This is most prominent in hyperhidrosis patients where antidepressants can be used for their anticholinergic effects, which decrease sweating. However, the high rates of antidepressant prescriptions still raise questions. Canada is among the countries with the highest antidepressant prescription rates worldwide, and studies have raised concerns about the overuse of antidepressants for unapproved indications such as fatigue, chronic pain and insomnia (J. Wong et al., 2017). Further studies are needed to investigate indications for antidepressant prescriptions in patients with dermatological conditions, and to distinguish and guide their use for disorders with primary psychiatric aetiology (e.g., body dysmorphic disorder) from those with primary cutaneous insult (e.g., psoriasis).

Anxiolytics were the second most commonly encountered family of medications, with highest rates in atopic dermatitis. Several studies from Denmark reported elevated rates of anxiety in atopic dermatitis patients compared to the general population and other dermatological conditions such as psoriasis (Egeberg, Andersen, Gislason, Skov, & Thyssen, 2017; Thyssen et al., 2018). Based on data from the Danish National Patient Register, Thyssen et al. found that nearly one-third of patients with moderate-to-severe atopic dermatitis dispensed a prescription of anxiolytics within 5 years of their assessment (32.1%, n=1370). Similar to our observation, anxiolytic prescription rates in atopic dermatitis was also higher in their population compared to antidepressants (20.4%, n=870) (Thyssen et al., 2018). A recent meta-analysis emphasized the

importance of considering anxiety, depression and suicide ideation in atopic dermatitis (Ronnstad et al., 2018). In dermatology, antiepileptics are mainly used for chronic pruritus and neurotic excoriations (Scheinfeld, 2003), with gabapentin being the most common antiepileptic in dermatological practice although more studies are needed on its use in psychodermatology (Muñoz & Koo, 2006). In our population, highest rates of antiepileptic prescriptions were found under primary mental health disorders (ICD9: 290-299, 300s; see Table II.2), which include psychogenic pruritus.

Other classes of psychoactive medications were less frequently encountered in our population and in the literature. In dermatology, antipsychotics are most commonly used to treat delusions of parasitosis, a rare disorder compared to other psychodermatological conditions, especially some of the secondary psychodermatological conditions like psoriasis-induced depression (Gupta, Vujcic, Pur, & Gupta, 2018). Dermatologists may also lack experience or confidence to initiate therapy with antipsychotics; only 3% of 40 dermatologists in an online survey in Boston, USA reported confidence in prescribing these medications, which might contribute to the low rates of these medications in our population (Gee, Zakhary, Keuthen, Kroshinsky, & Kimball, 2013).

Our results highlight several challenges in psychodermatology, one of which is under-reporting. The percentages of conditions billed by dermatologists to be clearly psychodermatological or mental health-related (e.g., psychogenic pruritus), were strikingly low. For example, over five years, only a population of 19 patients with psychogenic pruritus was identified in Alberta. Although claims data may overestimate these gaps in reporting given that diagnostic information would be more precisely documented in individual patient charts than in billings, it is also possible that dermatologists are not sufficiently trained and experienced to

diagnose mental health conditions. It would be desirable in future studies examine more in-depth diagnostic information from individual medical records rather than through billings. However, even as it stands, the current numbers represent a starting point from which assessment and improvement of quality of care for psychodermatological conditions can be planned to establish informed interventions. It would also be advisable that existing specialized psychodermatology clinics report the epidemiological characteristics of these conditions.

As already alluded to, our study has some limitations. First, we were restricted to rely on claims data to gather ICD-9 codes, using case definitions that have not been validated clinically. Furthermore, many billing records only provided the first 3 digits of the ICD-9 codes which means that we could not capture specific conditions such as delusions of parasitosis (psychotic diseases; ICD9 =290.* to 299.*), trichotillomania (diseases of hair; ICD9 =704.*), and dysesthesia and vulvodynia/vestibulodynia (Mental Health; ICD9 =300s.*). This may have led to over- or under-capturing of certain conditions. Secondly, the pharmacological data captured drugs that were dispensed, so we were unable to capture prescriptions that were not filled, which may lead to underestimations of reported cases. In conclusion, our results suggest that for a substantial proportion of dermatology patients, a multidisciplinary approach including dermatological and mental health services could be beneficial. There is a need for further population-based studies and better or specialized reporting systems to bridge the potential gaps.

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III. CHAPTER 3: Global Prevalence of Primary Psychodermatologic Disorders: A Systematic Review

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3.1. Abstract

The management of primary psychodermatologic disorders (PPDs) (i.e., psychiatric disorders with dermatologic presentation) is challenging. The scarceness of reported prevalence hinders the development of coordinated interventions to improve healthcare delivery. This review aimed to explore the global prevalence of PPDs. The review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses statement. Of the 4632 identified publications, 59 were included. Five PPDs were investigated from the included studies: delusional parasitosis (n=9), skin picking disorder (n=26), trichotillomania (n=26), tanning dependence (n=5), and repetitive nail biting (n=6). Delusional parasitosis was rare in the general population (prevalence ranging from 0.0002% to 0.03%), with higher rates in the psychiatric settings (outpatient=0.5%; inpatient=0.1%). Other pathologic or subclinical forms of PPDs had a minimum prevalence of 0.3% (median=7.0%; mean=17.0%). The distribution of the prevalence rates was highly skewed, with large differences based on the study setting (e.g., dermatologic settings, psychiatric settings, and general population). The most common condition was pathologic skin picking (prevalence, 1.2%–11.2%) in the general population. Its rates were higher in the psychiatric settings (obsessive-compulsive disorder, 38.5%; Tourette syndrome, 13.0%; body dysmorphic disorder, 26.8%–64.7%). The prevalence of trichotillomania in the general population ranged from 0.6% to 2.9%, while that of pathologic tanning and nail biting could not be ascertained as the studies were mainly in students (range; 12.0%–39.3% and 3.0%–10.1%, respectively). In conclusion, PPDs are common, especially in the dermatologic and psychiatric settings. Further population-based studies are needed to determine more accurate prevalence rates.

3.2. Introduction

Psychodermatology represents the interaction between the neuropsychiatric and cutaneous systems of the human body (Basavaraj, Navya, & Rashmi, 2010). Primary psychodermatologic disorders (PPDs) (i.e., psychiatric disorders with dermatologic symptoms) include delusional parasitosis, trichotillomania, pathologic skin picking disorder, etc.(Jafferany, 2007). Although studies have shown that patients with PPDs have significantly reduced quality of life(Al-Imam, 2016; Flessner & Woods, 2006; Odlaug, Kim, & Grant, 2010), these conditions are frequently underdiagnosed. A better understanding of these conditions and their management, especially in dermatologic settings where, is needed (Jafferany, Ferreira, et al., 2020). Thus, knowing the prevalence of these conditions in daily practice will aid in the planning and delivery of care. The prevalence of all psychodermatologic conditions in dermatology practice is estimated to be 30.0%–40.0% (Koo & Lee, 2003; Korabel et al., 2008; Turk, Dytoc, et al., 2021).

In a 2018 narrative review that summarized available data on the epidemiology of PPDs, the scarceness of population-based studies and lack of precise prevalence estimates of these disorders were highlighted (Krooks, Weatherall, & Holland, 2018). Currently, there is no systematic review assessing the prevalence and incidence of PPDs in the general population or in specific clinical settings (dermatologic or psychiatric). The objective of this systematic review was to explore the prevalence and incidence of PPDs.

3.3. Methods

The Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement was followed(Moher, Liberati, Tetzlaff, Altman, & Group, 2009). Medline, EMBASE, PsycInfo, and Scopus were searched on October 10, 2019 (full search strategy, Appendix S1) (Larney et

al., 2013). No language or date restrictions were imposed. References of the included studies were also searched.

Two reviewers independently screened titles and abstracts and completed full-text review, quality assessment, and data extraction (Appendix S1). Disagreements were resolved through discussions within the team. The focus of the review was pathologic processes in various PPDs. Studies were considered if they evaluated any PPD including delusional parasitosis, skin picking disorder, trichotillomania, tanning dependence, psychogenic pruritus, psychogenic purpura, skin manifestations of obsessive-compulsive disorder, phobias, body dysmorphic disorder, and dermatitis artefacta. Studies reporting subclinical behaviors related to PPDs were also considered given a spectrum of the severity of clinical symptoms in PPDs (Appendix 1). The four target behaviors were hair pulling, skin picking, nail biting, and tanning with no age limits for the study participants. Studies were required to report either the prevalence (point, period, or lifetime) or incidence rates or provide sufficient data for the calculation of the same. Review articles and case reports were excluded.

Meta-analyses were attempted using random effects in R and R Studio in the 'metaprop' package. Statistical heterogeneity was assessed using tau^2 test and I^2 statistics. Descriptive analyses using percentages and ranges were conducted with Microsoft Excel.

3.4. Results

Overall, 4632 abstracts were screened. Of the 270 potentially relevant full texts reviewed, 59 were included in the final analysis (See Figure III.1- PRISMA flow diagram). Of all PPDs, the following five were investigated: delusional parasitosis (n=9), skin picking disorder, also known

as neurotic excoriations (n=26), trichotillomania (n=26), tanning dependence (n=5), and repetitive nail biting (n=6).

For the attempted meta-analysis, studies were categorized based on the type of setting or population into four categories: general population, psychiatric setting, dermatologic setting, and students. However, significant heterogeneity was noted across all four categories, failing to achieve a reasonable minimum for the number of studies with comparable characteristics (see Appendix S2 for definitions of the study settings and attempted meta-analysis outcomes).

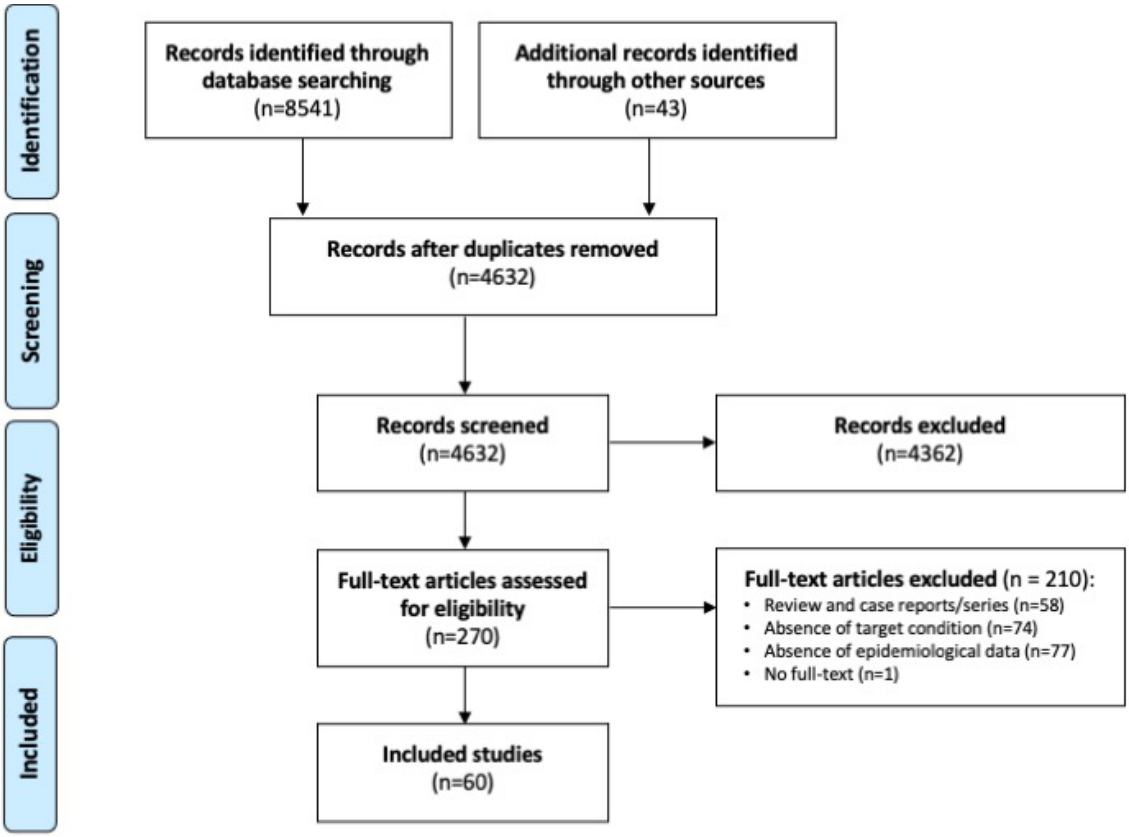

Figure III.1: *Flow diagram illustrating the screening and identification of relevant studies.*

Despite high heterogeneity and extreme differences in reported prevalence rates, the minimum prevalence rate was 0.3% for the mostly identified PPDs and less extent their

associated subclinical behaviors. This estimate was derived from all comparable studies (characteristics; skin picking, hair pulling, tanning, and nail biting), except for delusional parasitosis where the studies were extremely heterogeneous (Table III.1). The mean and median prevalence rates were 17.0% and 7.0%, respectively, and the overall prevalence of pathologic or subclinical forms of PPDs for the identified studies was approximately 1.0%. The different mean and median rates indicate substantial variation across the studies. In terms of quality assessment using a rating scheme modified from the Oxford Center of Evidence-Based Medicine (Appendix S1, Table S1), all studies were cross-sectional and were accordingly rated ‘4’ (Table III.1, Table III.2, Table III.3 and Appendix S1).

Table III.1 *Characteristics, prevalence and incidence rates, and quality assessment of studies on delusional parasitosis – studies are ordered by population type/setting (A - general population and children; B - psychiatric settings)*

Study	Study Setting/Population	Location, year	Diagnosis method	Sample size	Prevalence per 100,000 person-years	Prevalence (%)	Incidence (%)
Kohorst, Bailey, Andersen, Pittelkow, and Davis (2018)	A – General Population	United States, 2010	Screening for DP using ICD-9 criteria	Age- and sex-specific estimates of the US population in 2010	27.3	0.03	-
Pearson et al. (2012)	A – General Population	United States, 2006-2008	Self-reported emergence of fibers/materials from the skin accompanied by skin lesion and/or disturbing skin sensation, evaluated by research staff	2,850,606	3.7	0.004	-
Bailey et al. (2014)	A – General Population	United States, 1976-2010	Screening for DP using ICD-9 criteria	144,000	-	-	0.002
Lepping, Baker, and Freudenmann (2010)	A – General Population	United Kingdom, 2008	Individual dermatologists reporting positive cases using a survey	Total catchment area of about 36.5 million	0.5 3-year window	0.5 3-year window	-
Trabert (1993)	A – General Population (primary care settings)	Germany, NR	Individual dermatologists reporting positive cases using a survey	-	4.2	0.004 §	0.0008
Trabert (1991)	A – General Population (primary care settings)	Germany, NR	Individual dermatologists reporting positive cases using a survey	-	0.2 §	0.0002 §	-
Hebbar, Ahuja, and Chandrasekaran (1999)	B – Psychiatry (Outpatient)	India, 1994-1997	Retrospective chart review to identify DP using ICD-10	4,234	496 4-year window	0.5 4-year window	-
Srinivasan, Suresh, Jayaram, and Fernandez (1994)	B – Psychiatry (Outpatient)	India, 1987-1990	Interview conducted by a psychiatrist	4,200	452 4-year window	0.5 4-year window	-
Marneros, Deister, and Rohde (1988)	B – Psychiatry (inpatient)	Germany,1950-1979	Retrospective chart review	40,029	70.0 30-year window	0.1 30-year window	-

§ Dissertations with no available full texts

Quality of all included studies was rated as 4 (Medicine, 2022) case series or cross-sectional studies (see Appendix S1 for details)

NR = not reported; DP = Delusional Parasitosis; ICD = International Classification of Disease

Table III.2 *Characteristics, prevalence rates and quality assessment of studies on subclinical and clinical/pathologic skin picking – studies are ordered by population type/setting (A - general population and children; B - psychiatric settings; C - dermatologic settings; D - students) then according to their sample size*

Study	Study setting/Population	Location, year	Diagnosis method	Sample size	Prevalence (%)	
					Pathologic Skin Picking	Subclinical Skin Picking
Machado et al. (2018)	A – General Population	Brazil, NR	Skin Picking Stanford Questionnaire	7639	3.4*	-
Keuthen, Koran, Aboujaoude, Large, and Serpe (2010)	A – General Population	United States, 2004	Phone interview - criteria: (1) picking resulting in noticeable skin damage, (2) picking not attributable to a medical condition or hearing voices, (3) picking-related distress, and (4) either school or work absences or interference with social functioning	2511	16.6**	-
Benedetta Monzani et al. (2012)	A – General Population	Not defined	The Skin Picking Scale	2481	1.2*	-
Leibovici et al. (2015)	A – General Population	Israel, 2012-2014	Questionnaires and scales screening for skin picking disorder, and assessing the severity of perceived stress, depression, obsessive-compulsive disorder, body dysmorphic disorder	2145	5.4**	-
Hayes, Storch, and Berlanga (2009)	A – General Population	United States, NR	The Skin Picking Scale and the Skin Picking Impact Scale	354	5.4*	62.7*
Selles et al. (2015)	A – Children	El Salvador, NR	Repetitive Body-Focused Behavior Scale; Behavioral Assessment System for Children	315	8.3*	24.8*
Hayes et al. (2009)	A – General Population	United States, NR	The Skin Picking Scale and the Skin Picking Impact Scale	222	11.2*	-
Greenberg et al. (2018)	B – Psychiatry (Tourette Syndrome)	United States and Canada, NR	Self-report screening questionnaire on body-focused repetitive behaviors	811	13.0**	-

Study	Study setting/Population	Location, year	Diagnosis method	Sample size	Prevalence (%)	
					Pathologic Skin Picking	Subclinical Skin Picking
Grant, Menard, and Phillips (2006)	B – Psychiatry (BDD)	United States, NR	Clinician-led assessment	176	36.9*	44.9*
Karakus and Tamam (2011)	B – Psychiatry (outpatient)	Turkey, 2006-2008	Clinician-led assessment	124	10.5*	-
Phillips, Menard, Fay, and Weisberg (2005)	B – Psychiatry (BDD)	United States, 1993	DSM-IV criteria for skin picking	123	26.8*	44.0*
Conceicao Costa et al. (2012)	B – Psychiatry (obsessive-compulsive disorder)	Brazil, 2003-2009	Clinician-led assessment	109	38.5*	-
Marron et al. (2020)	B – Psychiatry (BDD with concurrent acne)	Spain, NR	Body Dysmorphic Disorder Questionnaire	43	64.7*	-
Marron et al. (2020)	C – Dermatology (acne)	Spain, NR	Body Dysmorphic Disorder Questionnaire	202	58.9*	-
Dixon and Snorrason (2019)	C – Dermatology	United States, 2018	The Skin Picking Scale – Revised	237	21.9*	45.1*
Houghton, Alexander, Bauer, and Woods (2018)	D – Students (psychology)	United States, 2014-2017	Questionnaire designed by study authors	4435	5.7*	23.9*
Leibovici et al. (2014)	D –Students (multidisciplinary)	Israel, 2012-2013	Skin Picking Stanford Questionnaire	2176	3.0*	-
Odlaug et al. (2013)	D –Students (multidisciplinary)	United States, 2011	A voluntary questionnaire based on DSM-5 criteria	1916	4.2*	-
Hajcak et al. (2006)	D – Students (psychology)	United States, 2004	The Skin Picking Scale	1,324	5.2*	28.8*
Prochwicz, Kałużna-Wielobób, and Kłosowska (2016)	D – Students (high school and university)	Poland, NR	Skin Picking Scale & Skin Picking Impact Scale	534	7.6*	46.0*
Martínez-Aguayo et al. (2017)	D – Students (medicine and kinesiology)	Chile, NR	Questionnaire designed by study authors	440	4.5*	28.0*
Teng, Woods, Twohig, and Marcks (2002)	D –Students (psychology)	United States, NR	DSM-IV criteria for BFRB and the Habit Questionnaire	439	2.7*	-

Study	Study setting/Population	Location, year	Diagnosis method	Sample size	Prevalence (%)	
					Pathologic Skin Picking	Subclinical Skin Picking
Yeo and Lee (2017)	D – Students (elementary or middle school)	South Korea, 2016	Skin picking scale-revised	410	15.6*	66.8*
Tamam, Paltaci, and Keskin (2017)	D –Students (medicine)	Turkey, NR	Structured Clinical Interview for DSM-IV & modified version of the Minnesota Impulse Disorders Interview	277	2.2**	-
Calikusu, Kucukgoncu, Tecer, and Bestepe (2012)	D –Students (multidisciplinary)	Turkey, 2009-2010	Questionnaire designed by study authors adopting criteria from the medical literature	245	2.0*	87.8*
Siddiqui, Naeem, Naqvi, and Ahmed (2012)	D –Students (medicine)	Pakistan, 2010	Self-administered questionnaire designed by the authors & the Habit Questionnaire	210	9.0*	-
Bohne et al. (2002)	D –Students (psychology)	Germany, NR	The Skin Picking Inventory, Body Dysmorphic Disorder Questionnaire, Maudsley Obsessive-Compulsive Inventory & Beck Depression Inventory	133	4.6*	91.7*
Keuthen et al. (2000)	D – Students (psychology)	United States, NR	Skin Picking Inventory	105	3.8*	78.1*

*Period/point prevalence

**Lifetime prevalence

^^Quality of all included studies was rated as 4 (Medicine, 2022): case series or cross-sectional studies (see Appendix S1 for details)

BDD = Body Dysmorphic Disorder, BFRB = Body-Focused Repetitive Behavior, DSM = Diagnostic and Statistical Manual of Mental Disorders, SP = Skin Picking, NR = Not Reported

Table III.3 *Characteristics, prevalence rates and quality assessment of studies on: a) hair pulling and trichotillomania; b) subclinical and pathologic tanning; c) subclinical and pathologic tanning – studies are ordered by population type/setting (A - general population and children; B - psychiatric settings; C - dermatologic settings; D - students) then according to their sample size*

Study	Population type/Settings	Location, year	Diagnosis method	Sample size	Prevalence %	
Hair Pulling					Trichotillomania	Subclinical Hair Pulling
D. C. Duke, Bodzin, Tavares, Geffken, and Storch (2009)	A – General Population	United States, NR	Florida Hair Pulling Scale-Revised	830	0.6*	6.5*
King et al. (1995)	A – General Population (adolescents ≥ 17 years old)	Israel, NR	Clinician-led assessment	794	-	0.5* 1.0**
Selles et al. (2015)	A – Children	El Salvador, NR	Repetitive Body-Focused Behavior Scale; Behavioral Assessment System for Children	315	2.9*	10.5*
Phillips et al. (2005)	A – General Population	United States, NR	Structured Clinical Interview for DSM-IV	200	2.5*	-
Malhotra, Grover, Baweja, and Bhateja (2008)	B – Psychiatry (children in outpatient clinic)	India. 2000-2005	Clinician-led assessment	1610	1.2*	-
Greenberg et al. (2018)	B – Psychiatry (Tourette Syndrome)	United States and Canada, NR	Self-report screening questionnaire on Body-Focused Repetitive Behaviors	811	3.8**	-
Grant, Levine, Kim, and Potenza (2005)	B – Psychiatry (inpatient)	United States, NR	The Minnesota Impulsive Disorders Interview for screening. Positively screened individuals were evaluated by Structured Clinical Interview for DSM-IV	204	3.4* 4.4**	-
Al-Refu (2013)	C – Dermatology (children)	Jordan, 2009-2013	Clinician-led assessment	2800	7.0*	-
Conti et al. (2016)	C – Dermatology (children)	Italy, 2009	Clinician-led assessment	2640	0.3*	-
Cortes, Mardones, and Zemelman (2015)	C – Dermatology (children with hair loss)	Chile, 2007-2010	Retrospective review of patients' charts	345	5.2*	-
Sharma et al. (2019)	C – Dermatology (children with hair loss)	India. 2015-2016	Clinician-led assessment	300	1.0*	-

Study	Population type/Settings	Location, year	Diagnosis method	Sample size	Prevalence %	
Moneib et al. (2017)	C – Dermatology (children with hair loss)	Egypt, 2013-2014	Clinician-led assessment	255	3.1*	-
Houghton et al. (2018)	D – Students (psychology)	United States, 2014-2017	Questionnaire designed by study authors	4435	0.7*	4.8*
Christenson, Pyle, and Mitchell (1991)	D – Students (multidisciplinary)	United States, 1989	DSM-III-R criteria	2534	0.6**	2.5**
Hajcak et al. (2006)	D – Students (psychology)	United States, 2004	The Massachusetts General Hospital Hairpulling Scale	1,324	1.2*	11.0*
Odlaug et al. (2013)	D – Students (multidisciplinary)	United States, 2006	Modified Minnesota Impulse Disorder Interview, consistent with DSM-IV-TR	791	3.9**	-
McCarley, Spirrison, and Ceminsky (2002)	D – Students (multidisciplinary undergraduates)	United States, NR	Questionnaire based on DSM-IV-TR criteria	635	2.0**	-
D.C. Duke, Keeley, Ricketts, Geffken, and Storch (2010)	D – Students (multidisciplinary)	United States, NR	Florida Hair Pulling Scale	527	-	9.7*
Rothbaum et al. (1993) (Data Set 1)	D – Students (multidisciplinary)	United States, NR	Questionnaire designed by study authors	490	1.2*	9.8*
Grzesiak et al. (2017)	D – Students (medicine)	Poland, NR	Clinician-led assessment	339	2.4**	3.5**
Dubose and Spirrison (2006)	D – Students (multidisciplinary)	United States, NR	Modified Hair Pulling Inventory based on DSM-IV	314	0.3*	8.3*
Hansen, Tishelmian, Hawkins, and Doepke (1990)	D – Students (multidisciplinary)	United States, NR	Questionnaire designed by study authors	286	-	22.4*
Tamam et al. (2017)	D – Students (medicine)	Turkey, 2011-2012	Structured Clinical Interview for DSM-IV (SCID-I) & modified version of the Minnesota Impulse Disorders Interview (MIDI)	277	1.4*	-

Study	Population type/Settings	Location, year	Diagnosis method	Sample size	Prevalence %	
Woods, Miltenberger, and Flach (1996)	D – Students (multidisciplinary)	United States, NR	The Habit Questionnaire, Trait version of the State-Trait Anxiety Inventory & Pennebaker Inventory of Limbic Languidness	246	-	3.2*
Karakus and Tamam (2011)	D – Students (multidisciplinary)	Turkey, NR	Structured Clinical Interview for DSM-IV	226	6.2**	-
Rothbaum et al. (1993) (Data Set 2)	D – Students (multidisciplinary)	United States, NR	Questionnaire designed by study authors	221	0.9*	13.1*
Siddiqui et al. (2012)	D – Students (medicine)	Pakistan, 2010	Self-administered questionnaire designed by the authors & the Habit Questionnaire	210	13.3*	-
Tanning					Pathologic Tanning	Subclinical/Excessive Tanning
Harrington et al. (2011)	A – General Population (tanning salon customers)	United States, NR	Self-reported questionnaire designed using CAGE and DSM-IV criteria	100	33.0*	4.0*
Blashill et al. (2016)	A – General Population (females who occasionally do indoor tanning)	United States, NR	Questionnaire designed by study authors, the Behavioral Addiction Indoor Tanning Screener, the Perceived Stress Scale, the Seasonal Pattern Assessment Questionnaire, and the Dysmorphic Cancer Questionnaire	74	-	43.0*
Marron et al. (2020)	B – Psychiatry (BDD with concurrent acne)	Spain, NR	Body Dysmorphic Disorder Questionnaire	43	-	30.2*
Marron et al. (2020)	C – Dermatology (acne)	Spain, NR	Body Dysmorphic Disorder Questionnaire	202	-	17.8*
Ashrafioun and Bonar (2014)	D – Students (psychology)	International, 2011	Excessive tanning DSM criteria, modified Tanning CAGE items	533	12.0*	31.0*
Mosher and Danoff-Burg (2010)	D – Students (psychology)	United States, NR	Questionnaire designed by study authors & the revised Obsessive-Compulsive Inventory	421	39.3**	36.6**
Nail Biting					Clinical/ Pathologic Nail Biting	Subclinical Nail Biting

Study	Population type/Settings	Location, year	Diagnosis method	Sample size	Prevalence %	
Selles et al. (2015)	A – Children	El Salvador, NR	Repetitive Body-Focused Behavior Scale; Behavioral Assessment System for Children	315	7.3*	34.6*
Houghton et al. (2018)	D – Students (multidisciplinary)	United States, 2014-2017	Questionnaire designed by study authors	4435	3.0*	33.5*
Teng et al. (2002)	D – Students (multidisciplinary)	United States, NR	The Habit Questionnaire & DMS IV criteria for BFRB	439	-	6.3*
Hansen et al. (1990)	D – Students (multidisciplinary)	United States, NR	Questionnaire designed by study authors	286	-	63.6*
Woods et al. (1996)	D – Students (multidisciplinary)	United States, NR	The Habit Questionnaire, State-Trait Anxiety Inventory & Pennebaker Inventory of Limbic Languidness	246	10.1*	34.3*
Siddiqui et al. (2012)	D – Students (medicine)	Pakistan, 2010	Self-administered questionnaire designed by study authors & the Habit Questionnaire	210	6.2*	-

*Period/point prevalence, **lifetime prevalence

^^ Quality of all included studies was rated as 4 (Medicine, 2022): case series or cross-sectional studies (see Appendix 1 for details)

BDD = Body Dysmorphic Disorder, CAGE = Cut-Annoyed-Guilty-Eye, BFRB = Body-Focused Repetitive Behavior, DSM = Diagnostic and Statistical Manual of Mental Disorders, CAGE=. NR = Not Reported

3.4.1. Delusional Parasitosis

Nine studies investigated the prevalence and/or incidence of delusional parasitosis. The characteristics, prevalence, and incidence rates are listed in Table III.1. The prevalence of delusional parasitosis in the general population was estimated to range from 0.0002% to 0.03%. The rates were significantly higher in the psychiatric settings where the prevalence from one inpatient and two outpatient studies were 0.1% and 0.5%, respectively. The incidence was reported in only two studies; 0.002% per person-year in a period between 1976 and 2010 (Bailey et al., 2014), and 0.0008% with no specified timeframe (Trabert, 1993).

3.4.2. Skin Picking and Neurotic Excoriations

Twenty-six studies investigated the prevalence of pathologic skin picking, and 13 of them reported the prevalence of skin picking as a subclinical, repetitive behavior (Table III.2).

Figure III.2 illustrates the prevalence of subclinical and pathological skin picking. Eight studies examined the prevalence of subclinical skin picking (lowest rate, 23.9%; highest rate, 91.7%) in university students, and another two in the general population (lowest rate, 24.8%; highest rate, 62.7%) (Hayes et al., 2009; Selles et al., 2015). For studies on pathologic skin picking, the range varied based on the clinical setting (Figure III.2). The highest prevalence rates were observed in the psychiatric settings, with differences across specific psychiatric disorders such as obsessive-compulsive disorder (38.5%) (Conceicao Costa et al., 2012), Tourette syndrome (13.0%) (Greenberg et al., 2018), and body dysmorphic disorder (26.8%–64.7%) (Grant et al., 2006; Marron et al., 2020; Phillips et al., 2005). In the general adult population, the prevalence was generally much lower, ranging from 1.2% to 16.6%(Keuthen et al., 2010; Benedetta Monzani et al., 2012). None of the studies reported any incidence.

The most common site of skin picking was the face, followed by the upper extremity (mostly fingers, hands, and/or cuticles) or the scalp (Bohne et al., 2002; Calikusu et al., 2012; Hayes et al., 2009; Prochwicz et al., 2016). The most common cutaneous trigger was acne (Bohne et al., 2002; Calikusu et al., 2012; Prochwicz et al., 2016). Frequent picking (≥5 times per day) was reported in 11.0% (n=28) of a population of university and high school students in a study (Prochwicz et al., 2016) and in 32.1% (n=340) of university students in another study (Houghton et al., 2018). A markedly higher percentage (56.5%, n=126) of frequent picking was reported in individuals with pathologic skin picking which emphasizes the pathologic nature of the condition (Houghton et al., 2018). The duration of skin picking per episode was investigated in one study on university students (Bohne et al., 2002), and 43.6% (n=58) of them endorsed picking for 1–10 minutes per episode. In another study on students (Calikusu et al., 2012), 56.3% (n=138) reported that their episodes lasted less than one minute. In a study by Prochwicz et al. (2016) 69.9% (n=172) of the students endorsed picking for "less than a couple of minutes." None of the studies compared the duration of episodes between subclinical and pathologic skin picking.

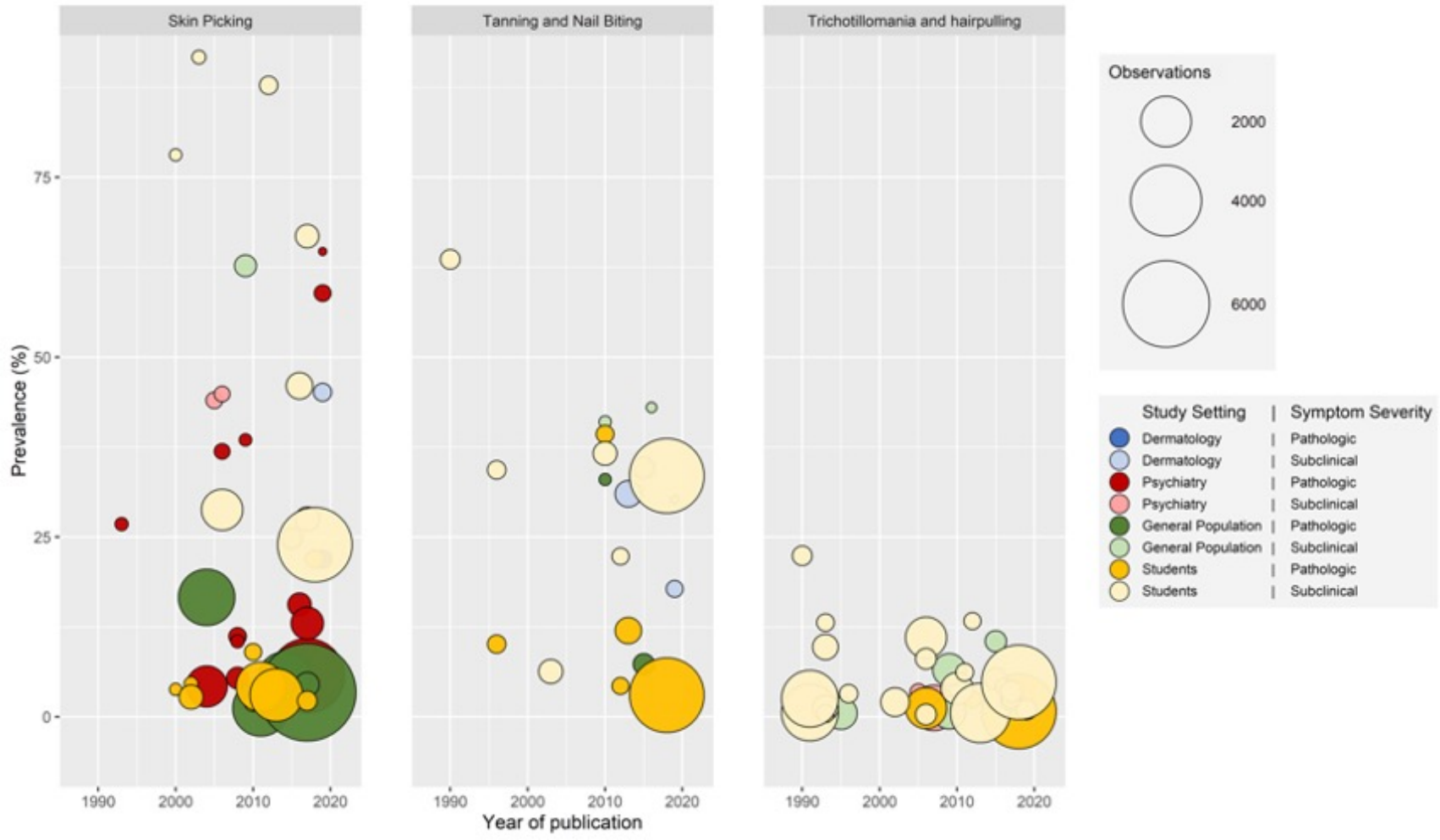

Figure III.2 *Prevalence of pathologic and subclinical forms of the primary psychodermatologic disorders and related subclinical behaviors examined in the included studies*

3.4.3. Hair Pulling and Trichotillomania

Hair pulling was examined as a subclinical behavior in 12 studies and as a pathologic condition (trichotillomania) in 22 studies (Table III.3 and Figure III.2). The prevalence of hair pulling ranged between 2.5% (Christenson, Pyle, et al., 1991) and 22.4% (Hansen et al., 1990), with these extremes from studies on university students. Only two of the 12 studies investigated hair pulling in the general adult and pediatric populations (prevalence; 6.5% (D. C. Duke et al., 2009) and 13.3%(Selles et al., 2015), respectively). For trichotillomania (Figure III.2), the prevalence ranged between 0.3% (Dubose & Spirrison, 2006) and 6.2% (Karakus & Tamam, 2011), again with extremes from studies on university students. Of the 22 studies, three assessed the prevalence of trichotillomania in the general population, reporting rates of 0.6%, 2.5%, and 2.9% (Table III.3). None of these studies reported any incidence.

The most common site of hair pulling was the scalp, followed by the eyebrows. Five studies reported the duration of hair pulling, three of which reported an average of 4–4.5 years. The most commonly reported comorbid condition was anxiety disorder. Other secondary parameters such as the frequency and duration of hair pulling episodes, the number of pulled hairs, and the triggers of hair pulling were inconsistently reported across the studies.

3.4.4. Excessive Tanning and Nail Biting

Five studies investigated tanning behavior (see Table III.3), and all of them reported on subclinical tanning behavior, while three reported on pathologic tanning. The prevalence of subclinical tanning ranged from 17.8% in patients with acne (Marron et al., 2020) to 43.0% in a community-based female population (Blashill et al., 2016). The prevalence of pathologic tanning ranged from 12.0% to 39.3%, with both extremes from studies on university students. Figure III.2 illustrates the prevalence of tanning-related skin conditions in different study settings.

Additional outcomes included one study on pathologic tanning, which reported no difference in prevalence between genders and equal endorsement of indoor and outdoor tanning in those with the condition(Ashrafioun & Bonar, 2014). Another study reported “looking good” as the most common reason for subclinical tanning (Harrington et al., 2011).

Six studies examined nail biting (Table III.3), including subclinical, repetitive nail biting behavior (n=6), and more severe pathologic forms of nail biting (n=4), with outcomes illustrated in Figure III.2. The prevalence of subclinical nail biting ranged from 6.3% to 63.6% in two student cohorts (Hansen et al., 1990; Teng et al., 2002). One study reported the prevalence of subclinical nail biting in a pediatric population as 34.6% (Selles et al., 2015). For pathologic nail biting, the prevalence ranged between 3.0% (Houghton et al., 2018) and 10.1% (Woods et al., 1996) in two student cohorts. In a general population study, the prevalence was 7.3% (Selles et al., 2015). None of these studies reported any incidence.

3.5. Discussion

Overall, the prevalence rates of five PPDs were identified: delusional parasitosis, skin picking disorder, trichotillomania, pathologic tanning, and pathologic nail biting. The average prevalence was approximately 1.0%, but variable depending on the study population and the severity of the condition. Incidence was not reported for any of the identified conditions, except for delusional parasitosis. The evidence derived from this systematic review strongly suggests that further research is warranted to accurately determine the prevalence or incidence of PPDs.

Based on studies on the general population identified in our analysis, delusional parasitosis was the least common of the identified PPDs (Table III.1). Pathologic skin picking is the most common PPD, with similar estimates of point/period prevalence among the general population (1.2%–11.2%) and in the younger student population (2.0%–9.0%). The prevalence rates for pathologic skin picking were high in the psychiatric settings (10.5%–38.5%) and even higher in dermatologic settings (21.9%–58.9%). The highest estimate (64.7%) was observed in individuals receiving care for concurrent body dysmorphic disorder and acne. Therefore, screening for skin picking disorders might be important in primary care and dermatologic settings for any patient with suspicious cutaneous lesions and potential psychological distress. Trichotillomania showed a similar trend of higher prevalence rates in the psychiatric and dermatologic settings compared with the general population. There is, therefore, a need for more studies in the general population, particularly on pathologic tanning and nail biting. Furthermore, the prevalence or incidence of several PPDs including psychogenic pruritus, dermatitis artefacta, and psychogenic purpura were not identified in our review, which may be attributed to the lack of multidisciplinary psychodermatology services and databases capturing these conditions. More importantly, patients with these conditions typically present to dermatologists but may decline

referrals to psychiatrists(Patel & Jafferany, 2020), which may lead to erroneous or missed diagnoses.

Another challenge is the variation in symptom severity in several disorders. Apart from delusional parasitosis in which the clinical symptoms were clearly defined, the clinical presentation of skin picking, hair pulling, tanning, and nail biting falls on a spectrum, ranging from subclinical repetitive behavior to severe pathologic manifestations that affect patients' functioning or cause impairment. Our results showed that the prevalence of mild repetitive symptoms was generally higher than that of the severe pathologic ones. Although challenging, it is important for clinicians to determine where the symptoms lie on the spectrum and how the clinical courses progress.

Naturally, when assessing patients with PPDs, dermatologists may focus on the cutaneous presentations, while psychiatrists would concentrate on the underlying psychiatric disorders. This may create a discrepancy in terminologies, diagnostic tools, and management plans. Skin picking disorder and trichotillomania have been recently defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (2013). Delusional parasitosis falls under the delusional disorder somatic type in the DSM-5 (code: 297.1). Pathologic nail biting is one form of a "body-focused repetitive behavior disorder" (DSM-5 code: 300.2), but the definition of "repetitive" is unclear and is operationalized differently among different studies. For instance, in our sample of studies on skin picking, Keuthen et al. used a criteria modified from the DSM-IV trichotillomania criteria to identify skin picking in the general population (Keuthen et al., 2010), Machado et al. used a version of the Skin Picking Stanford Questionnaire modified based on Keuthen et al.'s survey (Keuthen et al., 2010; Machado et al., 2018), whereas Odlauge et al. conducted a survey based on DSM-5 criteria (Odlaug et al., 2013). In the identified tanning

studies, symptoms were not diagnosed based on DSM-5 criteria but by ad-hoc questionnaires developed by the authors of each study (Table III.3). Furthermore, it is currently unclear whether pathologic tanning should be considered as a behavioral addiction or a body-focused repetitive behavior (Ashrafioun & Bonar, 2014; Kourosh, Harrington, & Adinoff, 2010). A multidisciplinary approach is known to increase the quality of care for psychodermatologic disorders, which points to the need for common terminologies and efforts to achieve standardized categorization and diagnostic criteria in psychodermatology. Furthermore, in studies where self-reported questionnaires were the main tools of measurement, response rates and recall bias may impact the accuracy of the reported prevalence rates (Tarrant, Manfredo, Bayley, & Hess, 1993). Whether self-reported symptoms are as accurate as clinician-rated assessments is debated (Wongpakaran et al., 2014), and there is a lack of studies comparing these two options in PPDs. In addition, most identified studies were case series and small-scale cross-sectional studies (Table III.1 and Table III.2). Large-scale, population-based studies that use standardized clinical assessment tools may increase the accuracy of future prevalence estimates.

This review has several limitations. Gray literature was not explored, implying that unpublished data might have been missed. Furthermore, there was a significant heterogeneity in the included literature in terms of diagnostic methods, populations studied, and definitions of the conditions. The field of psychodermatology is evolving, and the definitions of psychodermatologic disorders have not been fully established. Therefore, the initial search may have omitted some studies on conditions such as onychophagia (nail eating) and pathologic lip biting that are yet to be clearly defined in current diagnostic criteria.

PPDs were common, with a minimum prevalence of 0.3%, median of 7.0%, and mean of 17.0% for any pathologic or subclinical form in our identified studies. The distribution of the prevalence rates across the identified studies was highly skewed, with large differences based on the study setting and population types (e.g., dermatologic settings, psychiatric settings, and general population). More population-based studies and studies that follow standardized diagnostic criteria are needed for the accurate determination of the prevalence and incidence of these conditions.

IV. CHAPTER 4: Pharmacological Interventions for Primary Psychodermatologic Disorders: An Evidence Mapping and Appraisal of Randomized Controlled Trials.

Turk, T.*, Liu, C.*, Fujiwara, E., Straube, S., Hagtvedt, R., Dennett, L., Abba-Aji, A., Dytoc, M. (2023). Pharmacological Interventions for Primary Psychodermatologic Disorders: An Evidence Mapping and Appraisal of Randomized Controlled Trials. *: shared first-authorship

Journal of Cutaneous Medicine and Surgery, *27*(2), 140-149.

Key Points

Question: What medications have been investigated through randomized clinical trials (RCTs) for primary psychodermatologic disorders (PPDs) and how effective and safe are they?

Findings: Limited RCT-derived evidence supports the use of antidepressants in trichotillomania, pathologic skin picking (PSP), pathologic nail biting and dermatitis from compulsive hand washing, antipsychotics in trichotillomania and delusional parasitosis, and N-acetyl cysteine in trichotillomania and PSP.

Meaning: More research is warranted to establish standardized international clinical guidelines on pharmacotherapy in psychodermatology. However, current evidence is important for clinicians and researchers to make informed decisions when approaching PPDs.

4.1. Abstract

Importance: The lack of clinical guidelines for treatment of primary psychodermatologic disorders (PPDs) hinders providing optimal care to patients. Identifying the areas with sufficient clinical evidence for specific pharmacological interventions for PPDs is crucial for providers when managing patients with PPDs. **Objective:** We aim to identify, appraise, and summarize the currently available evidence about the safety and effectiveness of pharmacological management of PPDs through randomized controlled trials (RCTs). **Evidence Review :** We followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRIMSA) statement and the Global Evidence Mapping Initiative guidance. We searched Medline, Embase, Psycinfo, Cochrane and Scopus in November 2020. Two reviewers independently completed article review, data extraction and quality assessment. **Findings:** After screening 2618 unique abstracts, full texts of 83 were reviewed and 21 RCTs were eventually included. Five PDDs were identified: trichotillomania (n=12 studies), pathologic skin picking (n=5), nail biting (n=2), delusional parasitosis (n=1), and dermatitis from compulsive hand washing (n=1). Seven different classes of medications were investigated: SSRIs (i.e., fluoxetine, sertraline, and citalopram), tricyclic antidepressants (i.e., clomipramine and desipramine), antipsychotics (i.e., olanzapine and pimozide), anticonvulsant (i.e., lamotrigine), N-acetylcysteine (NAC), inositol, and milk thistle. Our findings showed RCT-derived evidence supporting the use of antidepressants in trichotillomania (sertraline, clomipramine), pathologic skin picking (fluoxetine), pathologic nail biting and dermatitis from compulsive hand washing (clomipramine or desipramine); antipsychotics in trichotillomania (olanzapine) and delusional parasitosis (pimozide); N-acetyl cysteine in trichotillomania and skin picking. **Conclusions and Relevance:** Few pharmacotherapies for primary psychodermatologic conditions are assessed through

controlled trials in the literature. This manuscript serves as a roadmap for researchers and clinicians to reach informed decisions with current evidence, and to build on it to establish guidelines in the future.

4.2. Introduction

Psychiatric disorders that present with dermatologic symptoms are often referred to as "primary psychodermatologic disorders", for example, delusional parasitosis (Jafferany, 2007; Koo & Lee, 2003). These are different from "secondary psychodermatologic disorders", dermatologic conditions with secondary or accompanying psychiatric symptoms, for example, acne vulgaris causing increased anxiety (Jafferany, 2007; Koo & Lee, 2003). Primary psychodermatologic disorders (PPDs) present with a skin complaint that has a primary psychiatric origin (Koo & Lee, 2003). The most commonly reported PPDs are delusional parasitosis (DP), trichotillomania (TTM), neurotic excoriations, excessive nail biting, tanning dependence, psychogenic pruritus, and dermatitis artefacta (Greenberg et al., 2018; Jafferany, 2007; Keuthen et al., 2010; Koo & Lee, 2003).

The clinical management of PPDs is challenging, especially for dermatologists who often are the first to see patients with PPDs (Patel & Jafferany, 2020). Treatment challenges include patients' limited insight into the nature of their condition and, hence, frequent reluctance to consider psychological and psychiatric interventions (Hafi et al., 2020; Jafferany, Ferreira, et al., 2020; Ocek et al., 2015). An additional challenge includes dermatologists' insufficient training and time to treat psychiatric conditions (Hafi et al., 2020; Jafferany, Ferreira, et al., 2020; Ocek et al., 2015). The lack of clinical guidelines for dermatologists on best practices for PPDs (Patel & Jafferany, 2020) is particularly challenging in this context. Few PPDs have been investigated systematically, including skin picking disease and trichotillomania. A meta-analysis from 2016

found that selective serotonin reuptake inhibitors (SSRIs) and an anticonvulsant (lamotrigine) were the only medications for PDDs investigated in controlled trials and showed potential benefits for skin picking (Selles, McGuire, Small, & Storch, 2016). A meta-analysis on trichotillomania found that several pharmacological treatments demonstrated efficacy in single trials (Farhat et al., 2020). Reproducing and validating the outcomes of these trials was recommended (Farhat et al., 2020). For delusional parasitosis, the currently available evidence is mostly derived from case series and small-scale uncontrolled trials (Reich, Kwiatkowska, & Pacan, 2019). Although the most commonly reported medications are pimozide and risperidone, there is a lack of consensus on the dosage of antipsychotics for delusional parasitosis (Reich et al., 2019). The effectiveness of pharmacological interventions for treatment of PPDs, compared to psychotherapy, or the combination of medications and psychotherapy has been debated in the literature with little consensus (Koo & Lee, 2003; J. W. Wong & Koo, 2013). Consequently, clinicians and researchers are currently left with inadequate guidance on how to best approach and investigate PPDs (Massoud, Alassaf, Ahmed, Taylor, & Bewley, 2021). This can affect the quality of care and the conduct of targeted research to enhance psychodermatology practice.

Evidence mapping is a research method used to systematically describe the availability and extent of scientific evidence (Bragge et al., 2011). The aim is to identify gaps and determine the sufficiency of current evidence to support informed decision making, and to pinpoint specific areas of need for future research and interventions (Bragge et al., 2011). In this evidence mapping project, we aim to identify, appraise, and summarize the currently available evidence about the pharmacological management of PPDs through randomized controlled trials (RCTs). Our aim is to identify the areas with sufficient clinical evidence for specific pharmacological interventions for PPDs, and to give an overview of investigated medications and regimens.

4.3. Methods

A protocol was developed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRIMSA) statement (Moher et al., 2009) and the Global Evidence Mapping Initiative (Bragge et al., 2011).

4.3.1. Search Strategy and Data Sources

Team members (TT, CL and LD) created a list of psychodermatology terms and a health sciences librarian (LD) conducted searches in Medline (Ovid MEDLINE(R) ALL), Embase (Ovid interface), Psycinfo (Ovid Interface), Cochrane Trials database (CENTRAL) (Wiley Interface) and Scopus in November 2020. The search strategy combined an exhaustive list of subject headings and keywords for primary psychodermatological conditions (see Appendix S3 for the full search strategy). The search was limited to randomized controlled trials (RCTs) using the Glanville et al. RCT filter (Glanville, Lefebvre, Miles, & Camosso-Stefinovic, 2006). No language or date restrictions were applied. The reference lists of included studies (Table IV.1 and Table IV.2) were also searched for additional studies.

4.3.2. Studies Selection

Two reviewers (TT and CL) independently screened titles and abstracts of retrieved studies to identify potentially relevant ones. They completed full-text review independently using pre-defined inclusion/exclusion criteria. Disagreements were first resolved between the two reviewers and then by the discussion among the research team.

Controlled clinical trials were included if they evaluated any pharmacological intervention for the following PDDs: Delusional parasitosis, neurotic excoriations (skin picking

disorder or dermatillomania), trichotillomania, tanning dependence, psychogenic pruritus, psychogenic purpura, dermatitis artefacta, and skin manifestations of obsessive-compulsive disorder, phobias, or body dysmorphic disorder. There was no limitation on the age of study participants.

4.3.3. Data Extraction and Quality Assessment

Two reviewers (TT and CL) independently extracted data. Details extracted included: study year, geographical location, psychodermatologic condition, population age and gender, details of the interventions and controls, clinical effectiveness as measured by the study using standardized criteria or validated scales, and side effects. For assessing the quality of identified studies, two reviewers working independently conducted a quality assessment using the rating scheme endorsed by JAMA Dermatology, which was modified from the Oxford Centre of Evidence-based Medicine (Medicine, 2022). The rating scheme is as follows: Properly powered and conducted randomized clinical trial; systematic review with meta-analysis = 1; Well-designed controlled trial without randomization; prospective comparative cohort trial =2; Case-control studies; retrospective cohort study =3; Case series with or without intervention; cross-sectional study =4; Opinion of respected authorities; case reports =5.

4.4. Results

A total of 2618 unique studies were identified from the search and 83 of them were subjected to full-text review after the initial screening. Among the 83 studies, 62 studies were excluded for various reasons, and 21 met the pre-defined inclusion and exclusion criteria for data analysis (Figure IV.1). Figure IV.2 demonstrates the mapping of current evidence on all identified medications and studies, along with sample sizes and clinical outcomes.

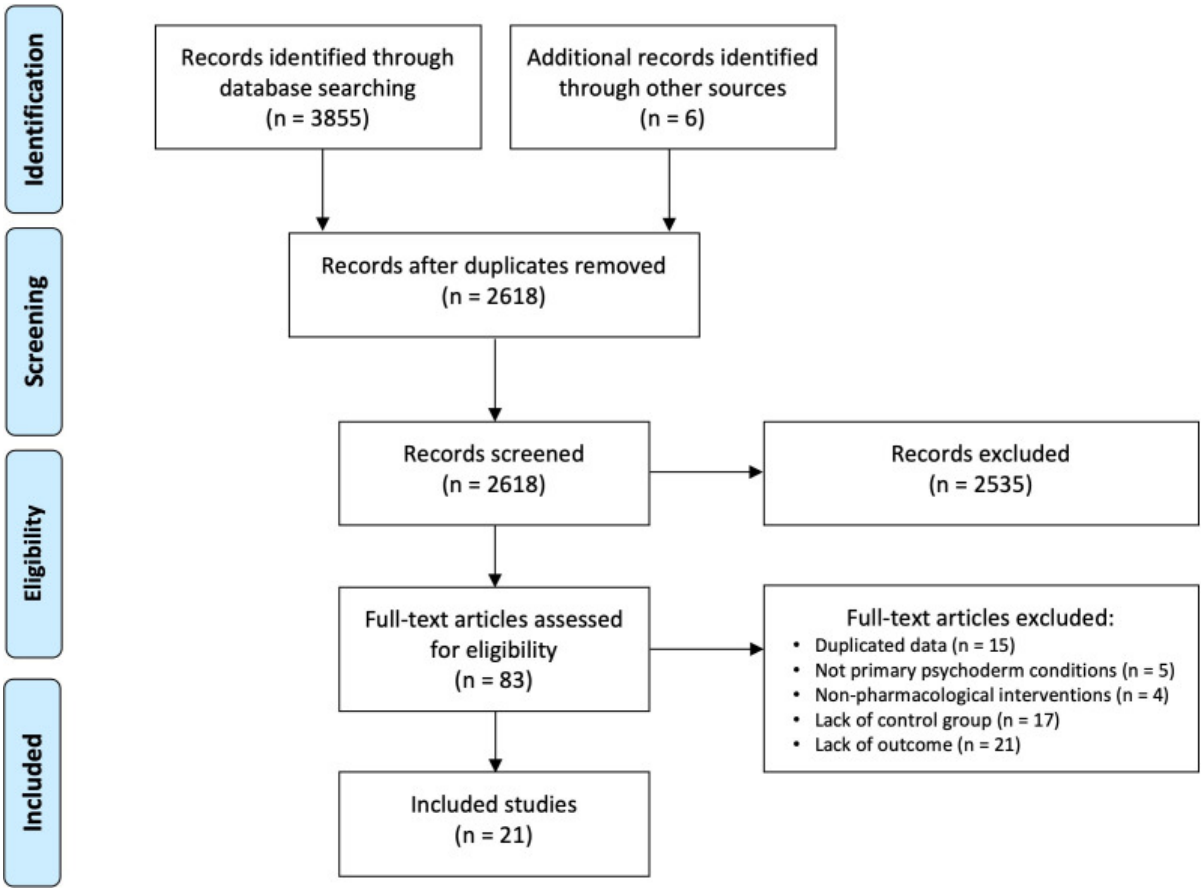

Figure IV.1 *Study Selection for Data Analysis.*

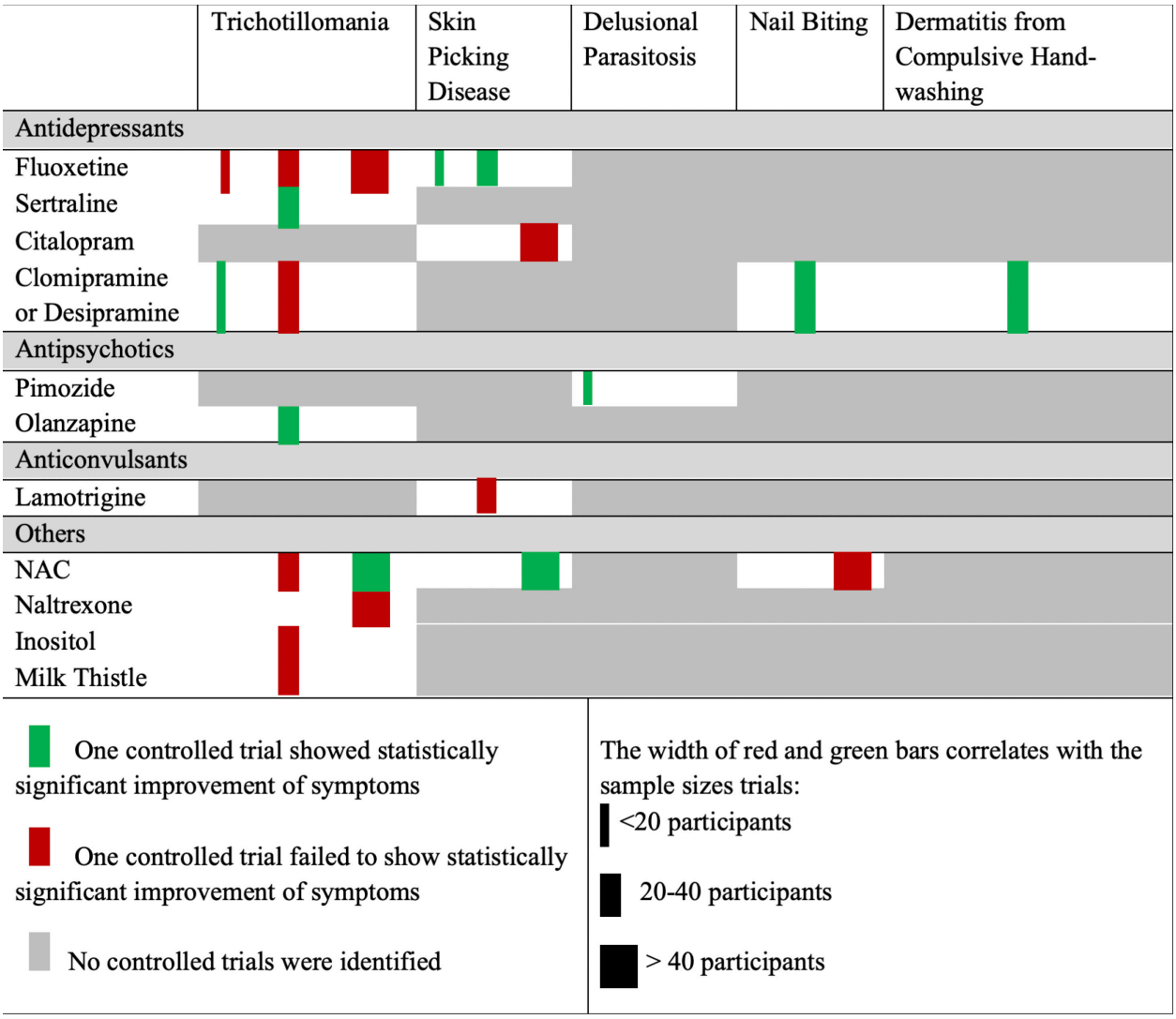

Figure IV.2 *Evidence Mapping of Controlled Trials on the Pharmacological interventions for Primary Psychodermatologic Disorders.*

4.4.1. Study Characteristics

Among the 21 studies published from 1982 to 2019, 16 were conducted in the US, one in Canada, one in the Netherlands, one in Denmark, and two in Iran. Five PDDs were identified: trichotillomania (n=12 studies), skin picking (n=5), nail biting (n=2), delusional parasitosis (n=1), and dermatitis from compulsive hand washing (n=1). Seven different classes of medications were investigated: SSRIs (i.e., fluoxetine, sertraline, and citalopram), tricyclic

antidepressants (i.e., clomipramine and desipramine), antipsychotics (i.e., olanzapine and pimozide), anticonvulsant (i.e., lamotrigine), N-acetylcysteine (NAC), inositol, and milk thistle. Table IV.1 and Table IV.2 summarize the characteristics of all studies, the investigated outcomes measures and clinical outcomes. Table IV.2 also provides a summary of safety and side effects for the investigated interventions.

Table IV.1 *Study Characteristics and Outcome Measures*

Condition	Study (Country)	Study design	Intervention	Comparison group	Enrolled participants	Dropout (n)	Relevant outcome measures
TTM	Christenson, Mackenzie, Mitchell, and Callies (1991)(USA)	18-week cross-over double-blind placebo-controlled trial (6 weeks trials of fluoxetine and placebo, separated by a 5-week washout)	Fluoxetine (20-80 mg/d)	Placebo	16 (8 on fluoxetine; 15 females)	1	1) Number of hair-pulling episodes per week 2) Estimated number of hairs pulled per week 3) Counted number of hairs pulled per week 4) Subject rating of severity of the urge to pull 5) Subject rating of the severity of additional hair pulling

Condition	Study (Country)	Study design	Intervention	Comparison group	Enrolled participants	Dropout (n)	Relevant outcome measures
	Streichenwein and Thornby (1995)(USA)	31-week double-blind, placebo-controlled crossover trial (2-week washout, then two 12-weeks trials separated by a 5-week washout)	Fluoxetine (20-80 mg/d)	Placebo	23 (20 females)	7	1) Number of hair-pulling episodes per week 2) Estimated number of hairs pulled per week 3) Counted number of hairs pulled per week 4) Subject rating of severity of the urge to pull 5) Subject rating of the severity of additional hair pulling
	van Minnen et al. (2003)(Netherlands)	12-week randomized, waiting-list controlled study	Fluoxetine (60 mg/d)	Waiting list or behavioral therapy	43 (38 females; age 31.9 ± 11.5)	3	1) MGHHS 2) Severity of hair loss (video ratings) 3) SCL-90
	Dougherty, Loh, Jenike, and Keuthen (2006)(USA)	22-week double-blind trial	Sertraline (50-200 mg/d) and HRT (dual modality)	Sertraline or HRT (single modality)	26	2	1) MGH-HPS 2) CGI 3) TTMIS 4) PITS

Condition	Study (Country)	Study design	Intervention	Comparison group	Enrolled participants	Dropout (n)	Relevant outcome measures
	M. H. Bloch, Panza, Grant, Pittenger, and Leckman (2013)(USA)	12-week randomized double-blinded placebo-controlled add-on trial	NAC (1200 mg BID)	Placebo	39 (NAC group: 14.0 ± 2.4, 17 females; placebo: 13.1 ± 3.1, 17 females)	4	1) MGH-HPS 2) TSC-C,P 3) NIMH-TSS 4) MIST-C
	Grant, Odlaug, and Kim (2009) (USA)	12-week double-blind placebo-controlled study	NAC (1200-2400 mg/d)	Placebo	50 (25 on NAC; 45 females; age 34.3 ± 12.1)	6	1) MGH-HPS 2) PITS 3) CGI
	Swedo et al. (1989) (USA)	10-week double-blind, crossover trial	Clomipramine (180.8 ± 56.0 mg/d) or desipramine (173.1 ± 33.0 mg/d)	Crossover	14 (14 females, age 31.6 ± 7.6)	1	1) Self-rated severity of TTM symptoms 2) TTM-Impairment scale 3) Physician-rated clinical progress
	Ninan, Rothbaum, Marsteller, Knight, and Eccard (2000)(USA)	9-week placebo-controlled randomized parallel-treatment trial	Clomipramine (avg 116.7 mg/d) or CBT	Placebo	23 (10 on clomipramine and 7 on CBT)	7	1) TSS 2) TTMIS 3) CGI-I

Condition	Study (Country)	Study design	Intervention	Comparison group	Enrolled participants	Dropout (n)	Relevant outcome measures
	Van Ameringen, Mancini, Patterson, Bennett, and Oakman (2010) (Canada)	12-week randomized, double-blind, placebo-controlled trial	Olanzapine (10.8 ± 5.7 mg/d)	Placebo	25 (13 on olanzapine; 17 females; age 33.2 ± 9.1)	2	1) CGI-I 2) CGI-S 3) MGH-HPS 4) TTM Y-BOCS
	Grant, Odlaug, Schreiber, and Kim (2014) (USA)	8-week double-blind, place-controlled study	Naltrexone (150 mg/d)	Placebo	51 (25 on naltrexone; 44 females; age 32.7 ± 9.8)	7	1) MGH-HPS 2) NIMH-TTS
	Leppink, Redden, and Grant (2017)(USA)	10-week double-blind, place-controlled trial	Inositol (6-18 mg/d)	Placebo	38 (18 on inositol; 35 females; age 28.9 ± 11.4)	7	1) MGH-HPS 2) NIMH-TTS 3) CGI-S
	Grant, Redden, and Chamberlain (2019) (USA)	12-week double-blind, placebo-controlled crossover study (two 6-weeks trials of milk thistle or placebo, separated by 1-week washout)	Milk thistle (150-300 mg BID)	Crossover	20 (19 females, 16 adults, age 27.9 ± 11.5)	4	1) NIMH-TSS 2) MGH-HPS 3) CGI-I 4) CGI-S

Condition	Study (Country)	Study design	Intervention	Comparison group	Enrolled participants	Dropout (n)	Relevant outcome measures
Skin picking	M. R. Bloch et al. (2001)(USA)	6-week open-label treatment with fluoxetine followed by 6-week double blinded, placebo-controlled trial	Fluoxetine (up to 60 mg/d)	Placebo	Open label phase: 15 (15 females; age 40.7 ± 11.5); double-blinded phase: 8 (4 on fluoxetine)	None	1) Modified Y-BOCS 2) SPTS 3) MGH-SPS
	Simeon et al. (1997)(USA)	10-week double-blind, placebo-controlled, parallel trial	Fluoxetine (avg 55 mg/d)	Placebo	21 (10 on fluoxetine; 16 females; age 34.2 ± 9.9)	4	1) CGI-Improvement scale 2) SPTS 3) VAS of self-rated change
	Arbabi et al. (2008) (Iran)	4-week double-blind, place-controlled trial	Citalopram (20 mg/d)	Placebo	45 with 23 on citalopram (citalopram group: 15 females, age 32.23 ± 10.25; placebo group: 17 female, age 29.29 ± 10.75)	5	1) Y-BOCS 2) GHQ 3) DLQI 4) VAS of skin picking behaviors
	Grant, Odlaug, Chamberlain, and Kim (2010) (USA)	12-week double-blind, place-controlled trial	Lamotrigine (12.5-300 mg/d)	Placebo	32 (29 females; age 32.8 ± 13.3)	7	1) NE-YBOCS 2) Self-rated skin picking scale 3) SP-SAS

Condition	Study (Country)	Study design	Intervention	Comparison group	Enrolled participants	Dropout (n)	Relevant outcome measures
	Grant et al. (2016) (USA)	12-week randomized double-blind trial	NAC (1200-3000 mg/d)	Placebo	66 (35 on NAC; 59 females; age 34.8 ± 11.0)	13	1) NE-YBOCS 2) CGI-Improvement scale 3) CGI-Severity scale
Delusional parasitosis	Hamann and Avnstorp (1982)(Denmark)	16-week double-blinded crossover study	Pimozide (2-7 mg/d)	NA	11 (10 females; average age 65.6)	2	1) Subjective/objective symptoms 2) Global evaluation of disease state 3) BPRS
Nail biting	Leonard, Lenane, Swedo, Rettew, and Rapoport (1991)(USA)	10-week double-blinded crossover study followed by 2-week single-blind placebo treatment	Clomipramine (120 ± 48 mg/d)	Desipramine 135 ± 53 mg/d	25 patients with severe nail biting (19 females; age 37.2 ± 6.3)	11	1) Nail biting severity scale 2) Nail biting impairment scale 3) Clinical progress scale 4) NIMH global assessment scales for anxiety and depression

Condition	Study (Country)	Study design	Intervention	Comparison group	Enrolled participants	Dropout (n)	Relevant outcome measures
	Ghanizadeh, Derakhshan, and Berk (2013) (Iran)	Double-blinded RCT (2 months)	NAC (800 mg/d)	Placebo	42 (21 on NAC; 28 females; age 9.28 ± 2.81 for NAC and 10.76 ± 3.14 for placebo)	17	Nail length
Dermatitis from compulsive hand washing	Katz, Landau, DeVeaugh-Geiss, and Hakkarainen (1990)(USA)	10-week RCT followed by 2-week single-blind placebo treatment	Clomipramine	Placebo	38 (17 on clomipramine; 30 females)	None	1) Skin examination for dermatitis 2) Y-BOCS

BPRS = Brief Psychiatric Rating Scale; CGI = Clinical Global Impression; CGI-I = Clinical Global Impression-Improvement; CGI-S = Clinical Global Impression-Severity of Illness; DLQI = Dermatology Quality of Life Index; GHQ = General Health Questionnaire; MGH-SPS = Massachusetts General Hospital Skin Picking Scale; MGH-HPS = Massachusetts General Hospital Hairpulling Scale; MGHHS = Massachusetts General Hospital Hairpulling Scale; MIST-C = Milwaukee Inventory for Styles of Trichotillomania-Child; NE-YBOCS = Yale-Brown Obsessive-Compulsive Scale Modified for Neurotic Excoriation; NIMH = National Institute of Mental Health; NIMH-TSS = National Institute of Mental Health-Trichotillomania Severity Scale; PITS = Psychiatric Institute Trichotillomania Scale; SCL-90 = Symptom Checklist with 90 items; SP-SAS = Skin Picking Symptom Assessment Scale; SPTS = Skin Picking Treatment Scale; TTMIS = Trichotillomania Impact Scale; TSC-C,P = Trichotillomania Scale for Children-Child and Parent Versions; TSS = Trichotillomania Severity Scale; VAS = Visual Analog Scale; Y-BOCS = Yale-Brown Obsessive-Compulsive Scale

Table IV.2 *Clinical outcomes and side effects*

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
TTM	Christenson, Mackenzie et al. (1991)	Fluoxetine	1) Number of hair-pulling episodes per week 2) Estimated number of hairs pulled per week 3) Counted number of hairs pulled per week 4) Subject rating of severity of the urge to pull 5) Subject rating of the severity of additional hair pulling	Short-term efficacy of fluoxetine in the treatment of TTM was not demonstrated	Nausea (fluoxetine = 5, placebo = 2) Insomnia (fluoxetine = 2) Tremor (fluoxetine = 2) Insomnia (fluoxetine = 2, placebo =4) Dry mouth (fluoxetine = 2) Urinary hesitancy (fluoxetine = 2) Irritability (fluoxetine = 2, placebo = 1) Sedation (fluoxetine = 2) Urticaria (fluoxetine = 1) Hot flashes (fluoxetine = 1) Yawning (fluoxetine = 1) Anorgasmia (fluoxetine = 1) Sweating (fluoxetine = 1) Diarrhea (placebo = 1)

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
					Headache (placebo = 1) Lightheadedness (placebo = 1) Irregular menses (placebo = 1)
TTM	Streichenwein and Thornby (1995)	Fluoxetine	1) Number of hair-pulling episodes per week 2) Estimated number of hairs pulled per week 3) Counted number of hairs pulled per week 4) Subject rating of severity of the urge to pull 5) Subject rating of the severity of additional hair pulling	Efficacy of fluoxetine in the treatment of TTM was not demonstrated	Nightmares, insomnia, dizziness, irritability, anxiety, feeling of doom (fluoxetine = 22, placebo = 16); Decreased appetite, diarrhea, constipation, nausea, increased weight, abdominal pain, dyspepsia (fluoxetine = 14, placebo 5); Anorgasmia, decreased libido (fluoxetine = 2, placebo = 0); Chest pain (fluoxetine = 0, placebo = 1)
TTM	van Minnen et al. (2003)	Fluoxetine	1) MGHHS 2) Severity of hair loss (video ratings) 3) SCL-90	Behavioral therapy is highly effective for reducing symptoms of TTM in the short term, whereas fluoxetine is not	9 (after 2 weeks): insomnia, drowsiness, fatigue, nausea, dry mouth, dizziness, excessive perspiration, tremor, headache, or delayed orgasm; 7 (end of treatment): insomnia, fatigue, headache, excessive

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
					perspiration, weight loss, delayed orgasm, or anorgasmia
TTM	M. H. Bloch et al. (2013)	NAC	1) MGH-HPS 2) TSC-C,P 3) NIMH-TSS 4) MIST-C	No significant difference between NAC and placebo was found on any of the primary or secondary outcome measures	Nausea (NAC = 6, placebo = 12) Diarrhea (NAC = 1, placebo = 1) Fatigue (NAC = 0, placebo = 2) Insomnia (NAC = 0, placebo = 1) Rash (NAC = 1, placebo = 0) Depression (NAC = 1, placebo = 0) Difficulty swallowing pills (NAC = 2, placebo = 1)
TTM	Grant et al. (2009)	NAC	1) MGH-HPS 2) PITS 3) CGI	NAC demonstrated statistically significant reductions in TTM symptoms measured by MGH-HPS ($p < 0.001$) and PITS ($p = 0.001$)	Nausea (NAC = 0, placebo = 1) Diarrhea (NAC = 0, placebo = 2) Cough (NAC = 0, placebo = 1)
TTM	Dougherty et al. (2006)	Sertraline and HRT (duo modality)	1) MGH-HPS 2) CGI 3) TTMIS 4) PITS	TTM symptoms in duo modality and single modality groups improved, although the dual modality group was much more likely to reach responder status at final evaluation	NR

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
TTM	Swedo et al. (1989)	Clomipramine or desipramine	1) Self-rated severity of TTM symptoms 2) TTM-Impairment scale 3) Physician-rated clinical progress	Clomipramine appears to be effective in the short-term treatment of TTM with significantly improved symptoms	Constipation (clomipramine = 5, desipramine = 6) Dry mouth (clomipramine = 5, desipramine = 8) Tremor (clomipramine = 7, desipramine = 3)
TTM	Ninan et al. (2000)	Clomipramine or CBT	1) TSS 2) TTMIS 3) CGI-I	CBT had a dramatic effect in reducing symptoms of TTM and was significantly more effective than clomipramine ($p = 0.16$) or placebo ($p = 0.26$); no significant difference between the effects of clomipramine and placebo	Tremor (clomipramine = 3) Sedation (clomipramine = 2) Dry mouth (clomipramine = 2) Constipation (clomipramine = 2) Memory difficulty (clomipramine = 1) Nausea (clomipramine = 1) Increased in appetite (placebo = 1)
TTM	Van Ameringen et al. (2010)	Olanzapine	1) CGI-I 2) CGI-S 3) MGH-HPS 4) TTM Y-BOCS	Olanzapine seems to be a safe and effective treatment for TMM with significant improvement from baseline to end point in the TTM-YBOCS ($p < 0.1$) and the CGI-S ($p < 0.001$)	Dry mouth (olanzapine 7, placebo = 0) Fatigue (olanzapine 7, placebo = 0) Increased appetite (olanzapine 6, placebo = 0)

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
					Headache (olanzapine 5, placebo = 4) Weight gain (olanzapine 5, placebo = 1)
TTM	Grant et al. (2014)	Naltrexone	1) MGH-HPS 2) NIMH-TTS	Naltrexone failed to demonstrate significantly greater reductions in hair pulling compared to placebo, but improved cognitive flexibility (p = 0.026)	Few side effects, sedation statistically more frequent in naltrexone group, both groups had elevated liver function testing
TTM	Leppink et al. (2017)	Inositol	1) MGH-HPS 2) NIMH-TTS 3) CGI-S	No significant difference was found in symptom reductions between inositol and placebo groups	Nausea/upset stomach = 4 Stomach pain = 2 Headache = 2 Diarrhea = 2 Gas = 1 Ectopic pregnancy = 1
TTM	Grant et al. (2019)	Milk thistle	1) NIMH-TSS 2) MGH-HPS 3) CGI-I 4) CGI-S	No significant difference was noted for the main outcome measure between milk thistle and placebo, but milk thistle did demonstrate significant improvement on select secondary outcome measures	Nausea/upset stomach/bloating (milk mistle = 4, placebo = 4) Dry mouth (milk mistle = 1) Diarrhea (milk mistle = 1) Insomnia (placebo = 1) Headache (placebo = 1)

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
Skin picking	M. R. Bloch et al. (2001)	Fluoxetine	1) Modified Y-BOCS 2) SPTS 3) MGH-SPS	Patients in treatment group maintained clinically significantly improvement of their skin picking (measured by modified Y-BOCS and MGH-SPS), while in the placebo group, patients returned to baseline symptom severity.	Nervousness and emotional "numbing" = 2 Excessive yawning and sexual dysfunction = 1
Skin picking	Simeon et al. (1997)	Fluoxetine	1) CGI-Improvement scale 2) SPTS 3) VAS of self-rated change	Fluoxetine was significantly superior to placebo according to 2/3 measures (completer analysis) or 1/3 measures (intent-to-treat analysis)	Nervousness/jitteriness (fluoxetine = 7, placebo = 2) Nausea (fluoxetine = 6, placebo = 3) Insomnia (fluoxetine = 6, placebo = 1) Fatigue/low energy (fluoxetine = 5, placebo = 0) Decreased libido (fluoxetine = 5, placebo = 0)
Skin picking	Arbabi et al. (2008)	Citalopram	1) Y-BOCS 2) GHQ 3) DLQI 4) VAS of skin picking behaviors	Treatment group achieved significant improvement in quality of life, general health status and obsession-compulsion severity ($p < 0.05$), but not pathologic skin picking severity	Increased sleep (citalopram = 4, placebo = 1) Nausea (citalopram = 1, placebo = 2) Tremor (citalopram = 1, placebo = 1)
Skin picking	Grant et al. (2010)	Lamotrigine	1) NE-YBOCS	No significant overall differences were noted between lamotrigine and placebo	Incidence and severity of adverse reactions in lamotrigine-treated

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
			2) Self-rated skin picking scale 3) SP-SAS	on the primary and secondary end points, but lamotrigine responders exhibited impaired cognitive flexibility (extradimensional shifting) at baseline compared with lamotrigine nonresponses	subjects consistent with previous studies (details not reported)
Skin picking	Grant et al. (2016)	NAC	1) NE-YBOCS 2) CGI-Improvement scale 3) CGI-Severity scale	NAC treatment was associated with significant improvements in the NE-YBOCS and CGI-Severity scales, but no significant difference for psychosocial functioning	Nausea (NAC = 5, placebo = 1) Dry mouth (NAC = 1) Constipation (NAC = 2) Dizziness (NAC = 1)
Delusional parasitosis	Hamann and Avnstorp (1982)	Pimozide	1) Subjective/objective symptoms 2) Global evaluation of disease state 3) BPRS	10/11 patients improved during pimozide phase with relief of itch ($p = 0.04$) and delusions ($p = 0.03$); BPRS points decreased significantly with pimozide ($p = 0.012$)	Drowsiness, fatigue (pimozide = 5, placebo = 1) Akathisia (pimozide = 2, placebo = 1) Parkinsonism (pimozide = 2, placebo = 1) Depressive reaction (pimozide = 2, placebo = 1)
Nail biting	Leonard et al. (1991)	Clomipramine vs desipramine	1) Nail biting severity scale 2) Nail biting impairment scale	Clomipramine (120 ± 48 mg/d) superior to desipramine (135 ± 53 mg/d) in decreasing nail biting as measured by nail biting severity, nail biting impairment, and clinical progress scales	Dry mouth (clomipramine = 12, desipramine = 8) Fatigue (clomipramine = 10, desipramine = 5)

Condition	Study	Intervention	Relevant outcome measures	Conclusion	Relevant Side effects (number of patients)
			3) Clinical progress scale 4) NIMH global assessment scales for anxiety and depression		Difficulty sleeping (clomipramine = 7, desipramine = 10) Constipation (clomipramine = 6, desipramine = 7) Sweating (clomipramine = 6, desipramine = 5) Dizziness (clomipramine = 5, desipramine = 3)
Nail biting	Ghanizadeh et al. (2013)	NAC	Nail length	Treatment group has significantly increased nail length after the first month ($p < 0.04$), but no difference after 2 months ($p = 0.59$)	Headache, agitation, and social withdrawal (n = 1) Severe aggression (n = 1) Moderate headache (n = 1)
Dermatitis from compulsive hand washing	Katz et al. (1990)	Clomipramine	1) Skin examination for dermatitis 2) Y-BOCS	Significantly more patients in clomipramine group had improvement in their dermatitis ($p < 0.001$); clomipramine significantly improves Y-BOCS, independent of dermatological response ($p < 0.01$)	Note reported

BPRS = Brief Psychiatric Rating Scale
CGI = Clinical Global Impression
CGI-I = Clinical Global Impression-Improvement
CGI-S = Clinical Global Impression-Severity of Illness
CMI = clomipramine

DLQI = Dermatology Quality of Life Index
GHQ = General Health Questionnaire
MGH-SPS = Massachusetts General Hospital Skin Picking Scale
MGH-HPS = Massachusetts General Hospital Hairpulling Scale
MGHHS = Massachusetts General Hospital Hairpulling Scale
MIST-C = Milwaukee Inventory for Styles of Trichotillomania-Child
NE-YBOCS = Yale-Brown Obsessive-Compulsive Scale Modified for Neurotic Excoriation
NIMH = National Institute of Mental Health
NIMH-TSS = National Institute of Mental Health-Trichotillomania Severity Scale
PITS = Psychiatric Institute Trichotillomania Scale
SCL-90 = Symptom Checklist with 90 items
SP-SAS = Skin Picking Symptom Assessment Scale
SPTS = Skin Picking Treatment Scale
TTMIS = Trichotillomania Impact Scale
TSC-C,P = Trichotillomania Scale for Children-Child and Parent Versions
TSS = Trichotillomania Severity Scale
VAS = Visual Analog Scale
Y-BOCS = Yale-Brown Obsessive-Compulsive Scale

4.4.2. Trichotillomania (TTM)

Trichotillomania was the most studied condition with the most diverse pharmacological interventions.

SSRI (fluoxetine and sertraline): Three studies investigated the efficacy of fluoxetine for TTM (Table IV.1, Table IV.2), including an 18-week cross-over double-blind placebo-controlled trial (20-80 mg/d fluoxetine) of 16 patients (93.75% females), a 31-week double-blind, placebo-controlled crossover trial (20-80 mg/d fluoxetine) of 23 patients (87.00% females), and a 12-week randomized, waiting-list controlled study (60 mg/d fluoxetine) of 43 patients (88.4% females). None of the studies demonstrated efficacy of fluoxetine for treating TTM. In a 22-week double-blind trial, 13 patients received single-modality treatment with either sertraline (50-200 mg/d) or with a psychological intervention, i.e., habit reversal training (HRT), and 11 received both modalities. TTM symptoms improved in both groups, but dual therapy was more effective than sertraline alone.

N-acetylcysteine (NAC): There was conflicting evidence regarding the efficacy of NAC for TTM. In 2009, a 12-week randomized double-blinded placebo-controlled add-on trial on 50 patients demonstrated that NAC (1200-2400 mg) led to statistically significant reduction in TTM symptoms measured by the Massachusetts General Hospital Hairpulling Scale (MGH-HPS) ($p<0.001$) and Psychiatric Institute Trichotillomania Scale (PITS) ($p=0.001$). The study showed improvement in 56.0% of participants on NAC versus 16.0% on placebo. Another 12-week randomized double-blinded placebo-controlled add-on trial, however, found no significant difference between NAC (1200 mg BID) and placebo on any of their primary or secondary outcome measures regarding TTM.

Tricyclic antidepressants (clomipramine and desipramine): Thirteen women with severe TTM completed a 10-week double-blind, crossover trial of clomipramine and desipramine. Clomipramine (180.8 ± 56.0 mg/d) was more effective in improving TTM symptoms than desipramine (173.1 ± 33.0 mg/d), demonstrated by TTM-impairment scale and physician-rated clinical progress. In another 9-week placebo-controlled randomized parallel treatment trial comparing clomipramine of average dose of 116.7 mg/d (n=10), cognitive-behavioral therapy (CBT) (n=7), and placebo (n=6), clomipramine was not significantly better at reducing TTM symptoms than placebo.

Olanzapine: A 12-week randomized, double-blind, placebo-controlled trial demonstrated 11 of 13 patients on olanzapine (10.8 ± 5.7 mg/d) responded to treatment, compared to 2 of 12 patients in the placebo group. Outcome measures included pre-to-post-trial scores on the Clinical Global Impression-Improvement (CGI-I) scale ($p<0.001$), the Yale-Brown Obsessive-Compulsive Scale (YBOCS) ($p<0.01$), and the Clinical Global Impression-Severity of Illness (CGI-S) ($p<0.001$).

Naltrexone, inositol, and milk thistle: An 8-week double-blind, placebo-controlled study investigated naltrexone 150 mg/d in 51 patients (86.27% females) with TTM. A 10-week double-blind, placebo-controlled trial studied inositol 6-18 mg/d in 38 patients (92.10% females), and a 12-week double-blind, placebo-controlled crossover study investigated milk thistle 150-300 mg BID in 20 patients (95.00% females). None of the studies demonstrated significant improvement in hair pulling behaviors measured by different assessment tools (see Table V.2 for details).

4.4.3. Skin Picking

Five studies investigated the efficacy of SSRIs, lamotrigine, and NAC for patients with skin picking. Treatment outcomes were measured via various assessment tools. SSRIs and NAC, but not lamotrigine, demonstrated treatment efficacy for improving skin picking.

SSRI (fluoxetine and sertraline): Two studies investigated the efficacy of fluoxetine for skin picking. One study had 15 female patients going through 6-week open-label treatment with fluoxetine (up to 60 mg/d), 8 of the 15 were responders and were enrolled in a 6-week double-blinded, placebo-controlled trial (4 fluoxetine:4 placebo). Patients on fluoxetine maintained clinically significant improvement of their skin picking, measured by modified Y-BOCS and MGH-SPS, while the 4 patients receiving placebo returned to their baseline symptom level. Another 10-week double-blinded, placebo-controlled, parallel trial studied fluoxetine (average 55 mg/d) in 21 patients (76.19% females) with skin picking (10 on fluoxetine and 11 on placebo). Intent-to-treat analysis showed fluoxetine superior to placebo according to one of the three primary outcome measures (i.e., a visual analogue scale of self-rated change). There was no significant improvement in CGI-I or Skin Picking Treatment Scale (SPTS). In a 4-week double-blind, placebo-controlled trial, treatment group of citalopram 20 mg/d (n=23) achieved significant improvement in quality of life, general health status and obsession-compulsion severity ($p<0.05$), but not in pathologic skin picking severity when compared with the placebo group (n=22).

Lamotrigine: In a 12-week double-blind, placebo-controlled trial, 32 patients (90.63%) with skin picking were randomized into a lamotrigine group (n=16) or a placebo group (n=16). No significant overall differences were noted between lamotrigine (12.5-300 mg/d) and placebo in the Yale-Brown Obsessive-Compulsive Scale Modified for Neurotic Excoriation (NE-YBOCS), the Skin Picking Symptom Assessment Scale (SP-SAS), and a number of self-rated skin picking scales. Interestingly, lamotrigine responders exhibited impaired cognitive flexibility (extradimensional shifting) at baseline compared to lamotrigine non-responders.

N-acetylcysteine (NAC): Grant et al. randomized 66 patients (89.39% females) with skin picking into an NAC group (1200-3000 mg/d) or a placebo group. Comparing with placebo (32/35 completed the study), the NAC group (21/31 completed the study) showed significant improvements in the Yale-Brown Obsessive-Compulsive Scale Modified for Neurotic Excoriation (NE-YBOCS), Clinical Global Impression (CGI) Severity scales, but no difference in psychosocial functioning. The treatment was well-tolerated.

4.4.4. Delusional Parasitosis

Pimozide: One double-blinded crossover study assessed the efficacy of pimozide (2-7 mg/d) among 11 patients (90.90% females) with delusional parasitosis. Of the patients, 90.90% improved during the pimozide phase with relief of itch ($p=0.04$) and reduced delusions ($p=0.03$). Additionally, Brief Psychiatric Rating Scale (BPRS) scores decreased significantly with pimozide treatment ($p=0.01$). Two patients did not complete crossover investigation. Increased insomnia, drowsiness, akathisia, parkinsonism, and depressive reaction were reported during the pimozide period.

4.4.5. Nail Biting

Clomipramine vs desipramine: One study recruited 25 patients with severe nail biting (76.00% females). Among 14 students who completed the study, clomipramine (120 ± 48 mg/d) was shown to be superior to desipramine (135 ± 53 mg/d) in decreasing nail biting as measured by Nail Biting Severity Scale, Nail Biting Impairment Scale, and a number of clinical progress scales.

N-acetylcysteine (NAC): One double-blinded randomized control trial recruited 42 children and adolescents (66.67% females) with chronic nail biting. The NAC group (n=14) had significantly

increased nail length after the first month than the placebo group (n=11) ($p<0.04$) but showed no difference after 2 months ($p=0.59$).

4.4.6. Dermatitis from Compulsive Hand Washing

Clomipramine: 38 patients (78.90% females) with dermatitis from compulsive hand washing were randomized into a clomipramine group (n=17) or a placebo group (n=21). At the end of the 10-week treatment with oral clomipramine (dosage was not provided), 65.00% of the patients in the clomipramine group had improvement in their dermatitis assessed by physicians, which is significantly higher than those receiving placebo (29.00%) ($p<0.001$). Independent of dermatological improvement, clomipramine also significantly improved the scores in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), ($p<0.001$).

4.4.7. Quality Assessment

Quality assessment with the Cochrane Risk-of-Bias Tool and a scheme modified from the Oxford Centre of Evidence-based Medicine was completed and it showed overall low risk with various aspects of the included studies (Table IV.3). The percentages of low-risk studies among all included studies were 85.71% and 76.19% for random sequence generation and allocation concealment, respectively. For other aspects of study quality, including blinding of outcome assessment, incomplete outcome data, and selective reporting, the percentage of low-risk studies was 90.48%.

Table IV.3 *Quality Assessment with the Cochrane Risk-of-Bias Tool and JAMA Dermatology Quality Assessment Scheme*

Study ID	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	JAMA Quality Assessment Scheme
Christenson, Mackenzie, et al. (1991)							**1**
Streichenwein and Thornby (1995)							**1**
van Minnen et al. (2003)							**2**
Dougherty et al. (2006)							**2**
M. H. Bloch et al. (2013)							**1**
Grant et al. (2009)							**1**
Swedo et al. (1989)							**1**
Ninan et al. (2000)							**2**
Van Ameringen et al. (2010)							**1**
Grant et al. (2014)							**1**
Leppink et al. (2017)							**1**
Grant et al. (2019)							**1**

Study ID	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	JAMA Quality Assessment Scheme
M. R. Bloch et al. (2001)							1
Simeon et al. (1997)							1
Arbabi et al. (2008)							1
Grant et al. (2010)							1
Grant et al. (2016)							1
Hamann and Avnstorp (1982)							1
Leonard et al. (1991)							1
Ghanizadeh et al. (2013)							2
Katz et al. (1990)							2
Studies with low risk of bias (%)	85.71%	76.19%	90.48%	90.48%	90.48%	90.48%	

4.5. Discussion

Evidence based on RCTs of pharmacological management of primary psychodermatologic disorders is still limited. This can explain the lack of therapeutic guidelines and highlights the need for more studies to establish evidence-based recommendations that can guide clinicians who are managing these conditions, whether they are dermatologists, psychiatrists, or family doctors. Our findings highlight that current pharmacological management of PPDs is largely condition-specific and depends on understanding each diagnosis and its underlying pathophysiology. For instance, trichotillomania has been classified as an impulse control disorder in the current DSM-5, similar to obsessive compulsive disorder. However, this classification has been questioned given the differences between the two conditions and the lack of treatment response in trichotillomania patients when managed with OCD first-line therapies (i.e., SSRIs) (Chamberlain et al., 2007; Lochner et al., 2005). In a study comparing 278 OCD patients and 54 TTM patients, it was found that OCD patients reported higher rates of comorbidities, more harm avoidance and more maladaptive beliefs compared to patients with TTM (Lochner et al., 2005). These differences emphasize the need to contrast different therapeutic approaches (Lochner et al., 2005). Condition-specific factors that may affect the conditions' characteristics also include several genes that were identified to characterize specific primary psychodermatologic conditions such as the SAP90/PSD9-associated protein (SAPAP3) gene for SPD and TTM (Bienvenu et al., 2009; Chattopadhyay, 2012), the Slit and Trk-like 1 (SLITRK1) for TTM (Zuchner et al., 2006), and the genes encoding Dopamine Receptor 1 (DRD1) and Serotonin Receptors (5-HTTLPR and 5-HT2A) for body-focused repetitive behaviors (BFRBs) (Chattopadhyay, 2012). Whether these genes affect treatment response or not is yet to be explored. Therefore, the gap of knowledge related to PPD's underlying etiologies and

factors that affect disease development, severity and progression might be contributing to the fact that we still have no standardized recommendations on pharmacological therapy.

Psychiatric conditions are not always managed pharmacologically. In fact, some argue that pharmacological interventions have failed to show long-term clinical benefits (e.g., relapse prevention, quality of life improvement, suicide prevention) that outweigh harms (e.g., side effects) (Cooper, 2014; Davidson, 2018). A Cochrane meta-analysis on compared tricyclic antidepressants and active placebos (placebos containing substances that mimic the side effects of TCAs) in depression and reported that the difference is small as well as that TCAs' effect on mood improvement might be overestimated (Moncrieff, Wessely, & Hardy, 2004). In addition, longer-term outcomes for schizophrenia patients were found to be better in developing countries compared to the United States (Padma, 2014). This unexpected finding implied a possible difference in use of antipsychotics in more acute stages of schizophrenia in developing countries compared to additional long-term antipsychotic treatment in developed countries and raised an argument on potential harm caused by maintenance use (e.g., metabolic complications) (Correll, Rubio, & Kane, 2018; Correll et al., 2017; Stubbs et al., 2016). Therefore, for PPDs, adjunctive or alternate therapies such as psychotherapy are important to consider when establishing treatment guidelines. For example, TTM patients on sertraline showed improvement in symptoms severity, but dual therapy with sertraline and habit reversal therapy (HRT) was significantly superior to mono-therapy (Dougherty et al., 2006). Pharmacological interventions should therefore be investigated in the short- and long-term, with a meticulous weighing of benefits against harms, and consideration of other treatment modalities that can substitute or support them.

There are several PPDs for which our search found no RCTs, including psychogenic pruritus, tanning dependence and dermatitis artefacta. Diagnosing and treating these conditions is challenging, especially with the lack of controlled trials which contributes to inadequate evidence and lack of guidance for approaching these conditions. As an example of inadequate evidence, several reports suggest TCAs, particularly doxepin and amitriptyline, for treatment of psychogenic pruritus (Kakunje, 2021; Kouwenhoven, van de Kerkhof, & Kamsteeg, 2017). However, this seems to be mainly based on case reports, expert opinions and reviews, with no controlled trials or meta-analyses to validate the use of these medications for psychogenic pruritus (Buteau & Reichenberg, 2018). As PPD patients tend to present to dermatologists first, interpreting their symptoms as skin-related, capturing these conditions in general dermatology clinics is important. However, it is challenging given patients' limited insight into their conditions (Thompson, 2014). Therefore, in order to better approach, capture and investigate more PPDs, especially the rarer ones that seem to be missing in the pool of studies we identified, multidisciplinary psychodermatology clinics are crucial. They were recently reported to be an optimal model for enhancing psychodermatologic care and research (Patel & Jafferany, 2020).

This review is focused on pharmacological interventions, which limits the ability to compare and contrast non-pharmacological approaches to PPDs such as cognitive behavioral therapy and stress reduction techniques (e.g., meditation). More research is warranted to bridge the gaps in knowledge highlighted in this review. In the meantime, this evidence mapping paper can serve as a roadmap for clinicians to assess available trials and choose evidence-based interventions when they include pharmacotherapy in their management plans. This review can also guide researchers to fill in the identified gaps and choose future interventions to investigate based on previous outcomes.

4.6. Conclusion

Limited RCT-derived evidence supports the use of antidepressants in TTM, PSP, pathologic nail biting and dermatitis from compulsive hand washing; antipsychotics in trichotillomania and delusional parasitosis; and N-acetyl cysteine in TTM and PSP. The evidence was inadequate to establish informed guidelines on the use of pharmacological interventions for the treatment of PPDs, especially considering the lack of controlled trials for several PPDs.

V. CHAPTER 5: Psychodermatology in Canada: a National Survey Assessment of Dermatologists' Perception, Practice Patterns and Challenges

Turk, T., Fujiwara, E., Abba-Aji, A., Mathura, P., & Dytoc, M. (2021).

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5.1. Abstract

Lack of knowledge of the challenges, current practices and best clinical approaches to psychodermatology may hinder improving the quality of care in this field. We aimed to assess the perception of psychodermatology, practice patterns and challenges reported by Canadian dermatologists. We designed an online questionnaire based on previous literature, including questions about practitioners' perceptions, practice patterns, training and challenges in psychodermatology. We solicited their opinions on desired training, research needs, and clinical approach recommendations. Our survey was distributed nationally by the Canadian Dermatology Association (CDA). Of the total of 78 participating dermatologists, >75% reported treating patients with psychodermatological conditions, with higher frequencies of secondary than primary psychodermatological conditions. While practitioners had some confidence in their understanding of psychodermatology (median = 4 on a 5-point scale), their comfort-levels to approach these patients were lower (median=3) and their confidence in prescribing psychotropic medication was markedly low (median=2). A total of 50% reported that a "multidisciplinary approach" would be best for these patients. Poor access to psychiatry was the most reported (26.9%) challenge, together with time constraints, lack of training, poor communication with patients, lack of patient insight and resources. While 46.2% reported having never participated in psychodermatology training, 55.1% expressed interest in doing so. We identified several challenges with knowledge, awareness and healthcare delivery in psychodermatological practice in Canada. A multidisciplinary approach and more specialized training are recommended to narrow the identified gaps.

5.2. Introduction

Psychodermatology focuses on mind-skin interactions and the disorders that result from their disturbance. These conditions are common in dermatological practice. It is estimated that every third patient in a dermatology clinic needs assessment for mental health symptoms (Bolognia et al., 2014; Gupta & Voorhees, 1990; Korabel et al., 2008). In addition, compared to the general population, patients with skin diseases have a higher prevalence of comorbid psychiatric disorders (Gupta & Gupta, 2003). Patients with psychiatric diagnoses are also more likely to be affected by skin conditions. Currently, there is no universal consensus on clinical categorization of these conditions, but they are often grouped into four broader categories: 1) primary psychodermatological disorders, 2) secondary psychodermatological disorders, 3) psychophysiologic disorders, and 4) psychogenic pruritus (Koo & Lee, 2003). Alternative classifications categorize conditions based on their assumed psychiatric aetiology and pathophysiology (i.e., psychocutaneous conditions due to psychotic, depressive, anxiety-related, or obsessive-compulsive symptoms) (Koo & Lee, 2003). The estimated high frequency of these diseases, combined with a lack of consensus on classification and clinical approach, highlights the clinical reality of concurrent mental health and dermatological conditions. This suggests the importance of establishing well-informed psychodermatology practice in medicine.

Healthcare delivery in psychodermatology can be difficult and unsatisfying for practitioners, as well as patients and their families. Several studies reported challenges that limit providing optimal care to patients with psychodermatological conditions. These include physicians' under-recognition of psychodermatological disorders, patients' poor insight into these conditions, and lack of specialized clinics to treat these disorders (Jafferany, Vander Stoep, Dumitrescu, & Hornung, 2010; R. B. Shah, 2018). In addition, dermatologists' lack of

confidence to initiate psychotropic therapy can be a barrier to successfully treating psychodermatology patients. A US-based survey of dermatologists found that only 3% of respondents reported they had confidence in prescribing these medications (Gee et al., 2013). Understanding pharmacological prescription practice in dermatology will help identify and address potential gaps and, consequently, improve quality of care for patients with psychodermatological conditions. In Canada, psychodermatology services are limited. Furthermore, the epidemiological characteristics, clinical experiences and challenges in psychodermatology in Canada have not been systematically reviewed (Kasar & Yurteri, 2020). In addition, no previous relevant study from other geographical locations (Jafferany et al., 2010; Ocek et al., 2015; Osman, Souid, Al-Mugaddam, Eapen, & Jafferany, 2017) differentiated between primary and secondary psychodermatological conditions. However, the latter have significantly different clinical implications and should be separated, as the course of treatment of these conditions differs as well. Hence, the overall lack of knowledge of the challenges and the current status of psychodermatology treatment in Canada may hinder improving the quality of care. In the current study, we aimed to assess the perception of psychodermatology, practice patterns and challenges reported by Canadian dermatologists in an attempt to highlight important aspects, bridge gaps in knowledge and detect potential shortfalls that should be addressed.

5.3. Methods

5.3.1. Survey

We developed a questionnaire based on a literature review of articles addressing psychodermatology (Gee et al., 2013; Jafferany et al., 2010; Munoz, Calderon, Castro, & Zemelman, 2014; Ocek et al., 2015; Osman et al., 2017). We included questions to assess practitioners' subjective knowledge of psychodermatology, relevant practice patterns, and

perceived challenges, as well as past and desired training and education, attitudes towards research and future recommendations. In addition to previous studies in this area, we asked questions about psychotropic medication prescription pattern and differentiated primary from secondary psychodermatological conditions. Questions on demographic and other background characteristics of the participants were also included.

In order to explain primary and secondary psychodermatological conditions, at the beginning of the survey, we introduced primary psychodermatological conditions as "conditions in which the patient has no primary skin disease and all of the cutaneous findings are self-induced (e.g., delusions of parasitosis, excoriation disorder, trichotillomania)". Secondary psychodermatological conditions were described as “conditions that involve the development of psychological problems as the results of a skin disease, or the exacerbation of a skin disease due to psychological factors (e.g., anxiety and depression in patients with psoriasis or atopic dermatitis)” .

Answer formats included yes/no, 5-point Likert-scales, multiple choice, and free text, for a total of 29 questions. The survey was administered through Google Forms, and participants could choose to fill out an English or a French version.

5.3.2. Data Collection

Our online survey was distributed nationally by the Canadian Dermatology Association (CDA) in October, 2019. All CDA members (approximately 700 dermatologists and dermatology residents in Canada) were contacted through email with one reminder sent 4 weeks after initial contact. A consent form was included in the information sheet at the beginning of the survey. The study was approved by the University of Alberta Research Ethics Board (Pro00092486).

5.3.3. Statistical Analysis

Survey data were saved automatically in Google sheets. After cleaning typographical errors, repeated entries, and partial survey responses, all data were imported into the Statistical Package for the Social Sciences version 26.0 (IBM SPSS Statistics for Windows, version 26.0; IBM Corp., Armonk, N.Y., USA) for further analysis. Descriptive statistics included frequency counts and percentages out of the total number of participants who answered the corresponding question, as well as medians and ranges for the Likert scales.

5.4. Results

5.4.1. Participants

Overall, a total of 78 dermatologists and dermatology residents filled-out our survey, amounting to an approximate response rate of 11.1% (out of 700). As detailed in Table V.1, the majority of participants were female, practicing in private-solo practice in urban areas.

Table V.1 *Participants' Characteristics and Frequency of Psychodermatology (PD) Cases*

Characteristic	**n (%)**
Demographics	
Age in years (M= 50.5, SD=14.9)*	
26-47	32 (43.3)
48-69	36 (48.6)
70-91	6 (8.2)
Years of Practice (M= 19.3, SD=14.1)*	
0-4	16 (21.3)
5-25	30 (40)
>25	29 (38.6)
Gender	
Female	52 (67.5)
Male	23 (29.9)

Characteristic	n (%)
Prefer not to say	2 (2.6)
Language	
English	66 (84.6)
French	12 (15.4)
Type of Practice	
Private - solo	26 (33.3)
Private – group	18 (23.1)
University-based	22 (28.2)
Hospital-based	12 (15.4)
Area of Practice	
Urban	60 (76.9)
Suburban	5 (6.4)
Rural	13 (16.7)
Frequency of PD conditions	
Overall percentage of PD patients in responders' practice	
<10%	37 (47.4)
10-25%	25 (32.1)
26-50%	13 (16.7)
>50%	3 (3.8)
Frequency of primary PD conditions	
Never	1 (1.3)
Rarely (1 pat./6 months)	12 (15.4)
Occasionally (1 pat./1 months)	31(39.7)
Frequently (1 pat./week)	28 (35.9)
Very frequently (1 pat./day)	6 (7.7)
Frequency of secondary PD conditions	
Never	0
Rarely (1 pat./6 months)	4 (5.1)

Characteristic	n (%)
Occasionally (1 pat./1 months)	9 (11.5)
Frequently (1 pat./week)	22 (28.2)
Very frequently (1 pat./day)	43 (55.1)

*M: mean; SD: standard deviation

5.4.2. Psychodermatology-Perceived Frequencies

Table V.1 details the perceived frequencies of psychodermatological conditions in the practices of our responders. The largest proportion of participants (47.4%) reported that psychodermatological conditions consist of less than 10% of their practice; but almost one-third (32.1%) reported psychodermatological conditions to make up between 10% and 25% of their patients. Of the total of 78 participating dermatologists, >75% reported treating patients with psychodermatological conditions, with higher frequencies of secondary than primary psychodermatological conditions. For primary psychodermatological conditions, we had similar percentages of physicians who see one patient/month and one patient/week (39.7% and 35.9%, respectively), while for secondary psychodermatological conditions 83.3% of physicians reported seeing a minimum of one patient per week (55.1% one patient/day and 28.2% one patient/week).

5.4.3. Psychodermatology Practice

Figure IV.1 summarizes responses related to practitioners' perceived understanding of psychodermatology and comfort levels with psychodermatological patients. The respondents had some confidence in their understanding of psychodermatology (median = 4 on a 5-point scale). However, their comfort-levels to approach these patients were lower (median=3, range =4). Less than half of the participants (44.9%) reported having a comfort level >3 on a 1-5 Likert scale.

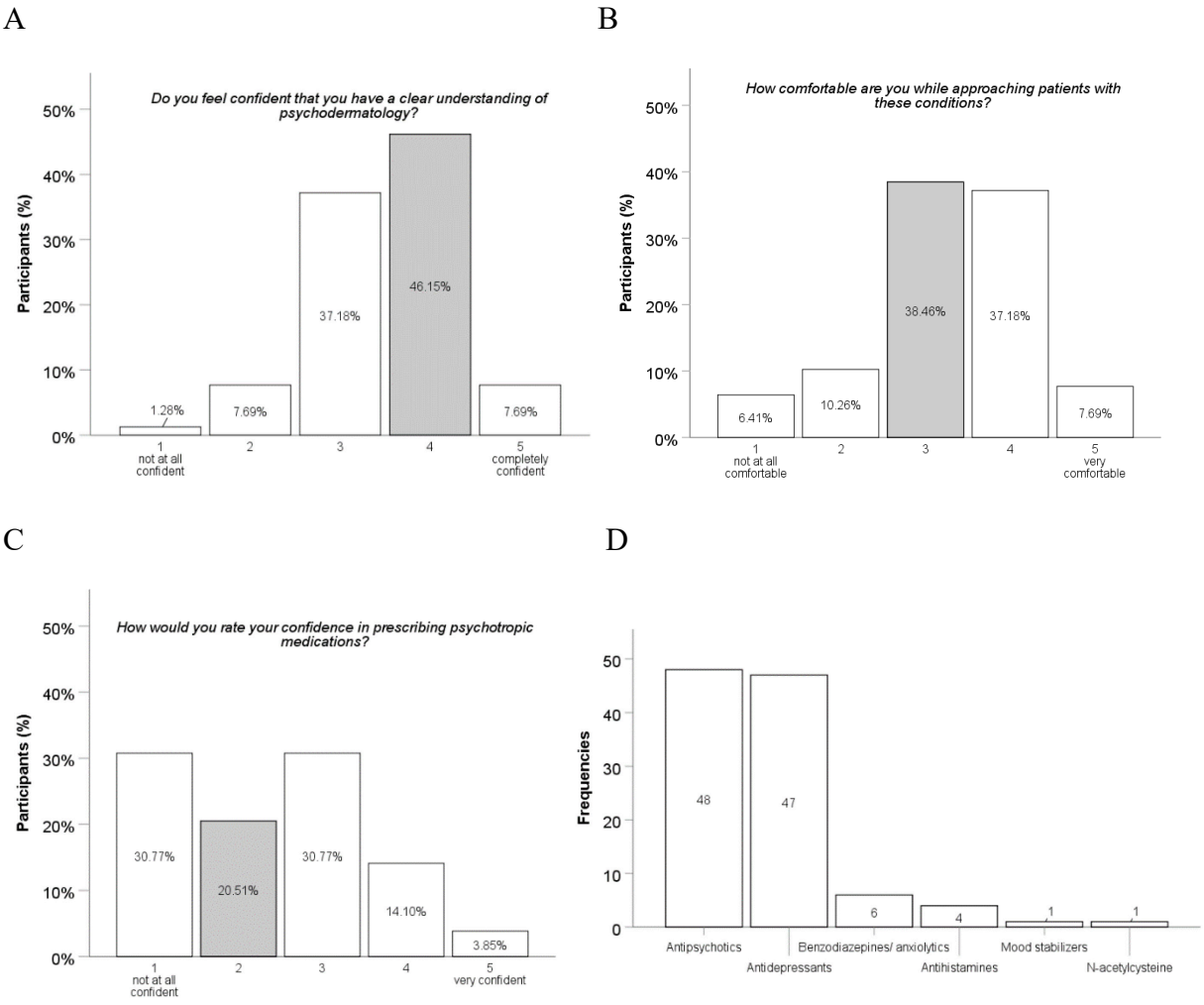

Figure V.1 *Participants' responses. A) Confidence in understanding of psychodermatology. B) Comfort level approaching psychodermatology patients. C) Confidence in prescribing psychotropic medications in the treatment of psychodermatological conditions. Panels A-C: Answers were given on 5-point Likert scales. Grey bars indicate group medians. D) Most commonly prescribed psychotropic medications in the treatment of psychodermatological conditions (N= 60); more than one answer was possible.*

Regarding practice patterns (Table V.2), a minority of participants (6.4%) reported managing primary psychodermatological conditions themselves, while 23.1% reported doing so for secondary psychodermatological conditions. About one-third (32.1%) of dermatologists who manage patients themselves have never prescribed a psychotropic medication. Of the

practitioners who reported having prescribed psychotropic medications, 45% reported prescribing psychotropic medications on an "occasional basis", while 35% reported using them only for severe cases (Table V.2). The vast majority of the participants (82.1%) reported their confidence in prescribing psychiatric drugs to be ≤3 on a 1-5 Likert scale (median =2; range =4). Most commonly prescribed psychotropic medication classes included antipsychotics, antidepressants, and benzodiazepines (Figure V.1 D) with risperidone as the most frequently reported drug, followed by the antidepressants doxepin and amitriptyline, as well as the antipsychotic pimozide. When asked about the best approach to psychodermatology, a "multidisciplinary approach" was endorsed by the largest proportion of responders (50%).

Most participants reported referring psychodermatology patients to a psychiatrist, depending on the severity of the symptoms (Table V.2). The majority answered that they refer severe cases, 47.4% and 43.6% for primary and secondary psychodermatological conditions respectively. Four out of 78 dermatologists reported referring to general practitioners (GP) instead of referring patients to Psychiatry, with equal rates for primary and secondary psychodermatological conditions. A total of 61 participants provided responses to the open-ended question asking them to describe the referral process. Twenty-one of them (34.4%) reported accessibility issues to psychiatrists and/or psychologists. Eleven (18%) used negative expressions such as "poor", "slow", "difficult", "dreadful" and "horrible" to describe the referral process. Three (4.9%) reported frustration with a vague or malfunctioning process (e.g., "I cannot think of one example of a successful referral", "No one wants to see these patients", "There is no specific process to do it"). Most practitioners (62.8%) reported that they "sometimes" offer referral to Psychiatry. Almost half (44.9%) responded that patients decline referral in most cases. In addition, 36.4% of

dermatologists reported that >75% patients with primary psychodermatological conditions and 21.6% of patients with secondary conditions decline treatment.

Table V.2 *Practice Patterns in Psychodermatology (PD)*

Survey Areas *Questions*	**Frequencies (%)**
PD-management by self	
Have you ever prescribed a psychotropic medication?	
No	25 (32.1)
Yes	53 (67.9)
If yes, how frequently? (n = 60)	
Rarely, only severe cases	21 (35)
Occasionally, few cases	27 (45)
Frequently, most cases	10 (16.7)
Very frequently, all cases	2 (3.3)
How often do patients with primary PD conditions decline psychotropic medications?	
Never	3 (3.9)
Rarely (<10%)	1 (1.3)
Sometimes (10-25%)	8 (10.4)
Often (26-50%)	17 (22.1)
Very often (51-75%)	20 (26)
Most cases (>75%)	28 (36.4)
How often do patients with secondary PD conditions decline psychotropic medications?	
Never	3 (4.1)
Rarely (<10%)	5 (6.8)
Sometimes (10-25%)	16 (21.6)
Often (26-50%)	24 (32.4)
Very often (51-75%)	10 (13.5)

Survey Areas *Questions*	**Frequencies (%)**
Most cases (>75%)	16 (21.6)
PD-management by referral	
Have you ever offered a patient a psychiatric consultation?	
No	4 (5.1)
Sometimes	49 (62.8)
Often	15 (19.2)
Most cases	6 (7.7)
Other*	4 (5.1)
How often do you refer patients with primary PD conditions to a psychiatrist for further assessment?	
Never, I self-manage cases	5 (6.4)
Rarely, only severe cases	37 (47.4)
Occasionally	23 (29.5)
Frequently - most cases	4 (5.1)
Very frequently, all cases	1 (1.3)
Other*	8 (10.3)
How often do you refer patients with secondary psychodermatological conditions to a psychiatrist for further assessment?	
Never, I self-manage cases	18 (23.1)
Rarely, only severe cases	34 (43.6)
Occasionally	19 (24.4)
Frequently - Most cases	0 (0)
Very frequently, all cases	0 (0)
Other*	7 (9)

Survey Areas *Questions*	**Frequencies (%)**
Have you ever experienced that a patient declined psychiatric consultation?	
Never	6 (7.7)
Sometimes	12 (15.4)
Often	25 (32.1)
Most cases	35 (44.9)
Best practice approach to PD	
Which of the following describes the best approach to PD in your region?	
Dermatologists should manage these cases with psychiatry referral if necessary	11 (14.1)
Psychiatrists should manage these cases with dermatology referral if necessary	11 (14.1)
A multidisciplinary approach	39 (50)
Manage in a case-specific manner	11 (14.1)
Further research is needed to know	1 (1.3)
Other**	5 (6.4)

*Witten responses included: “Absolutely zero access, would love to refer lots/all”, “As a private billing specialist, I am not allowed to refer”, “Patients always reject/do not want to be referred”, “Ask GP to manage or refer to psychiatry”, “n/a”. **Written responses included: “Having a specialized clinic”, “PD patients are not dermatologists’ problem”, “Not sure

5.4.4. Challenges in psychodermatological practice

A total of 67 dermatologists responded to an open-ended question asking about the challenges in psychodermatology. In our survey, 26.9% of participants reported poor accessibility to psychiatrists and psychologists; 13.4% stated patients’ poor insight into their condition, with 32.8% reporting patients’ rejection of their diagnosis and treatment as the primary challenge. Other reported challenges included time constraints (16.4%), lack of training (16.4%), and poor

communication with the patients (4.5%). In addition, 87.2% reported a lack of awareness of patient and family resources for these conditions.

5.4.5. Education and Training

Of all participants, 46.2% reported having never participated in a psychodermatology training (Table V.3). Of the 42 physicians who reported some form of training in psychodermatology, 33.3% reported they received their training during residency, and 31% reported training through conferences. However, 68.9% reported that training in psychodermatology during residency was "poor" or "inadequate". Of our participants, 55.1% expressed an interest in some psychodermatology training, with preferred formats being workshops and seminars.

Table V.3 *Training in Psychodermatology*

Category	n (%)
Participation in a PD training	
Never	36 (46.2)
Once	20 (25.6)
Several times	22 (28.2)
Type of PD training*	
Lecture	4 (9.5)
Continued Medical Education (CME)	11 (26.2)
Residency	14 (33.3)
Conference	13 (31.0)
Workshop	2 (4.8)
Formal	6 (14.3)
Sessions at meetings	1 (2.4)
Informal	2 (4.8)
Seminar	2 (4.8)
Interest in and willingness to attend a CME training on PD	10 (12.8)

Category	n (%)
No	25 (32.1)
Maybe	43 (55.1)
Definitely	
Preferred training modality*	
Workshops	37 (47.4)
Seminars	29 (37.2)
Conferences	24 (30.8)

* multiple answers were permitted

5.4.6. Research & Future Development

Only 2 of the queried physicians (2.6%) reported that research is adequate in the field of psychodermatology. Table V.4 summarizes the responses we obtained on recommendations for future research. When asked about suggestions for future improvement in psychodermatology, 15 physicians (26.8%) emphasized the need for more collaboration with and accessibility to psychiatrists and psychologists. Fourteen physicians (25%) highlighted the importance of establishing specialized psychodermatology clinics. All other responses relating to recommendation for improving psychodermatology practice in the future are listed in Table V.5.

Table V.4 *Summary of Participants' Recommendations for Future Research in Psychodermatology (PD)*

Recommendations for future research
Aetiology of PD conditions • The role of inflammatory pathways in psychodermatological conditions
Clinical approach to PD • Best approach to initiate antipsychotic and anxiolytic therapy • The use of cognitive behavioural therapy in psychodermatology • Differences in treating secondary conditions (e.g., psoriasis- versus atopic dermatitis-induced anxiety) • Long term effectiveness of clinical management • Patterns of psychodermatological symptoms how to approach them • Challenges and education in psychodermatology • More evidence-based approaches
Condition-specific • Reactive anxiety in dermatological practice • Best approach to acne excoriee • Scalp Dysesthesia • Cutaneous Pain Syndrome
Miscellaneous • Risk and benefits of having a private psychodermatology billing in dermatology

Table V.5 *Reported Recommendations for Improving the Quality of Care in Psychodermatology (PD) (n= 56)*

Recommendations for better healthcare delivery in PD	**n (%)**
Better accessibility to mental health specialists including psychiatrists and psychologists.	15 (26.8)
Establishing Multidisciplinary PD Clinics	14 (25)
More training opportunities and better training during residency	8 (14.3)
Increase collaboration with psychiatrists including those interested in PD	7 (12.5)
Focusing training on initiating psychoactive medications	4 (7.1)
Circulating practical manuals for approaching PD patients	3 (5.4)
Better information to and inclusion of the patients and their families	3 (5.4)
Dedicate more time to PD patients and increase the duration of the consult	2 (3.6)

5.5. Discussion

Our results highlight several challenges with knowledge, awareness and healthcare delivery in psychodermatological practice in Canada. In line with several studies from locations outside Canada (Jafferany et al., 2010; Ocek et al., 2015; Osman et al., 2017), most of our participants' perceived understanding and knowledge of psychodermatology is not optimal. Clinically, in a survey to 102 dermatologists in Chile (Munoz et al., 2014), less than half the participants (41%)

reported being comfortable to manage patients with psychodermatological conditions, which was similar in Turkey (specialists 40.4%; n= 70; residents 18%; n= 45) (Ocek et al., 2015). Outcomes from a US-based survey study suggested that practitioners' comfort level in treating these disorders vary by condition. While 83% of the 40 responders reported being comfortable in the diagnosis of trichotillomania, fewer (57%) were comfortable to diagnose underlying major depression and only 10% reported being comfortable to diagnose psychotic disorders and borderline personality disorder (Gee et al., 2013).

The frequency of psychodermatological conditions in dermatology practice is generally estimated to be 30-40% (Bolognia et al., 2014; Gupta & Gupta, 2003; Korabel et al., 2008). However, few studies have reviewed the epidemiological characteristics of these conditions and most survey-based studies estimate the frequency based on dermatologists' perception and practice patterns. Similar rates were observed in different studies where the majority of participants in all studies reported that psychodermatological conditions represent 10-25% of their practice (Jafferany et al., 2010; Ocek et al., 2015; Osman et al., 2017). However, it is noteworthy that in our Canadian population, 20.5% of the dermatologists reported that more than 25% of their cases might be psychodermatological in nature. In Turkey, 40.3% of specialists (n=70) and 46.5% of residents (n=45) reported similarly high rates above 25% (Ocek et al., 2015); in a Middle Eastern study, 18% (n= 57) of dermatologists reported a similar rate (Osman et al., 2017). The reported frequencies of encounters with these patients, especially considering the practitioners' relatively low comfort-levels approaching these conditions, were striking and emphasize the need for more efforts to enhance the training and quality of care in psychodermatology. Validating the numbers in survey studies with more objective, population-based measures will achieve a more accurate estimate of the frequency of psychodermatological

conditions in Canada. This remains crucial to understand and optimize current and future interventions. Therapeutic approaches to psychodermatological conditions include a wide spectrum of interventions that can be pharmacological, psychological or combined. Our results highlight the discrepancy between the high demand on psychodermatological services, difficulties in the referral process to psychiatry, the high rates of patients who will not accept referrals to psychiatry. There are also low rates of dermatologists who reported being confident in managing and initiating psychopharmacological therapy themselves. All of these factors are implicated in possible shortfalls in healthcare delivery for psychodermatology patients and highlight the need for a multidisciplinary approach, which was reported by the majority of our dermatologists as the best way to tackle psychodermatology. This is also emphasized in a recent review of 23 psychodermatology clinical models where the authors concluded that these clinics can improve the quality of care, reduce the costs and provide training opportunities (Magid & Reichenberg, 2020; Patel & Jafferany, 2020). In addition, in our survey, the top recommendation made by dermatologists to improve the quality of care to these patients was increasing access to mental health specialists. Furthermore, in terms of diagnosis and management of psychodermatology conditions, dermatologists missing psychiatric components of a condition, or vice versa, can impose medico-legal consequences, which, again, emphasize the importance of multidisciplinary approaches, as well as increasing dermatologists' access to psychiatric consultations. Regarding psychotropic prescription practices, antipsychotic and antidepressant medications were the most commonly reported drugs for the treatment of psychodermatological conditions. In dermatology, antipsychotics are mainly prescribed to treat patients with primary psychodermatological conditions such as delusions of parasitosis, or other conditions in which the skin symptoms are thought to be driven by psychosis (Gupta et al., 2018). In our survey, the

most commonly reported antipsychotic agent was risperidone, followed by pimozide. The latter is a high potency typical antipsychotic medication that traditionally was the drug of choice for treatment of delusions of parasitosis (Lorenzo & Koo, 2004). However, due to common and partly irreversible side-effects such as extrapyramidal symptoms (i.e., acute dyskinesias and dystonic reactions), atypical antipsychotic medications such as risperidone are generally preferred today as they are associated with fewer adverse effects (Campbell et al., 2019). The relatively high numbers of pimozide use in our cohort raises the opportunity to promote the use of newer antipsychotic medications in dermatological practice, including for the treatment of delusional parasitosis. The most commonly prescribed antidepressant was doxepin. There is no preferred class of antidepressants in psychodermatology according to a comprehensive review on the use of these drugs in dermatology (Gupta & Gupta, 2001). The first-line treatment of mood disorders in psychiatry would typically involve medications other than older tricyclic antidepressants like doxepin (e.g., selective serotonin/noradrenaline reuptake inhibitors). Doxepin is frequently used for the treatment of pruritus in dermatology. The use of antidepressants in psychodermatology need to be investigated further. To our knowledge, no previous study has queried dermatologists regarding their prescription patterns for psychoactive medications. More detailed investigations on the current use of specific psychotropic medications would be helpful to establish evidence-based guidelines of the use of these drugs in psychodermatology.

Several issues have been previously highlighted in dermatology training in Canada. An important example is the discrepancy in residents' exposure to different areas of dermatology (Freiman, Barzilai, Barankin, Natsheh, & Shear, 2005). Our results emphasize the need for more training in psychodermatology. 68% of our participants rated psychodermatology training during

residency as “poor” or “inadequate”. Similar to other studies (Jafferany et al., 2010; Ocek et al., 2015; Osman et al., 2017), we call for more training opportunities for residents and specialists, especially as 55.1% of the dermatologists in our survey indicate definite interest in such training.

This study has several strengths and limitations. To our knowledge, it is the first study to investigate psychotropic prescription rates of practicing dermatologists when they treat psychodermatological conditions. It is the first to investigate Canadian dermatologists’ perceived knowledge, awareness and practice patterns surrounding psychodermatological conditions. The online nature of the survey may have affected our response rate and likely limited our reach to some dermatologists (i.e., those who were unable or unwilling to provide information online as opposed to a paper format). As in any voluntary survey, we were only able to collect responses from interested participants. A less self-selected cohort would be more representative of all dermatologists. In addition, as our survey was an ad-hoc tool created by the authors, the wording of some questions might have been suboptimal. More efforts are recommended in future studies to validate and optimize the used surveys for more meaningful participation and, possibly, a better response rate.

5.6. Conclusion

We identified several challenges with knowledge, awareness and healthcare delivery in psychodermatological practice in Dermatology in Canada. Increasing dermatologists’ access to psychiatric consultations/services, a multidisciplinary approach with dermatologists and psychiatrists co-providing care, and more specialized training in this area are recommended to narrow the identified gaps.

Declaration of Conflict of Interest: There is no conflict of interest disclosed by the authors.

VI. CHAPTER 6: General Discussion and Conclusion

The work presented in this thesis explores the realm of psychodermatologic conditions and addresses several pivotal questions within this niche area of medicine. Aiming to optimize care, it becomes crucial to gain a comprehensive understanding of the prevalence, efficacy of existing treatment options, along with current treatment patterns and challenges in psychodermatology. This thesis undertook a comprehensive investigation through four distinct studies.

The first study aimed to estimate the frequency of psychodermatologic conditions in Alberta, Canada. It revealed that 28.6% of patients visiting dermatology clinics were concurrently dispensed psychotropic medications, indicating a potential presence of psychodermatologic conditions (Chapter II) (Turk, Dytoc, et al., 2021). To my knowledge, this is the first prevalence study of psychodermatology in Canada and my findings align with previous studies from other countries suggesting that one in three patients in dermatology clinics could have associated mental health issues. Moreover, my study highlighted the frequent use of psychotropic medications among dermatology patients, particularly antidepressants and anxiolytics (Turk, Fujiwara, et al., 2021). For instance, psoriasis patients had the highest rates of antidepressant dispensations, while atopic dermatitis had the highest rates of anxiolytic prescriptions (Turk, Dytoc, et al., 2021). This investigation provided valuable insights into the potential burden of these conditions on both the healthcare system and the population, offering an estimation of their previously unknown prevalence in the region. The global prevalence of primary psychodermatologic conditions was the subject of the second study, which employed systematic reviews to gather and analyze the currently scarce and scattered data (Chapter III) (Turk et al., 2022). The study highlighted that the pathologic and subclinical forms of PPDs had

a minimum prevalence of 0.3% (median=7.0%; mean=17.0%) (Turk et al., 2022). The most common condition in the general population was pathologic skin picking (prevalence, 1.2%–11.2%), while the rarest was delusional parasitosis (prevalence, 0.0002%-0.03%) (Turk et al., 2022). A comprehensive understanding of the prevalence of psychodermatologic conditions is crucial for informing effective interventions. The outcomes of my work emphasize that psychodermatologic conditions can be widely prevalent in the general population (Turk, Dytoc, et al., 2021; Turk et al., 2022). It also highlights how prevalence rates can vary across different populations and settings, determined by factors such as study designs, diagnostic criteria, and the specific demographic characteristics of the sample. However, inconsistencies in reporting and methodologies limited the generalizability of my findings in the systematic review and more extensive population-based studies following standardized diagnostic criteria are essential to accurately determine the true burden of PPDs to better inform healthcare policies and interventions.

The third study, detailed in Chapter IV, delved into the efficacy of pharmacologic interventions in managing primary psychodermatologic conditions (Turk et al., 2023). Through a comprehensive analysis of existing literature and clinical trials, this investigation aimed to discern the effectiveness of various therapeutic options available to healthcare practitioners, empowering them to make informed treatment decisions. The study mapped out seven distinct classes of pharmacologic interventions, scrutinizing their effectiveness from 21 controlled clinical trials across five psychodermatologic conditions (Turk et al., 2023). It provided valuable insights into which medications showed more promising effectiveness for specific conditions. Atypical antipsychotics, for example, has shown promising results in improving the outcomes of some psychodermatologic conditions such as risperidone in delusional parasitosis (Hamann &

Avnstorp, 1982) and olanzapine in trichotillomania (Van Ameringen et al., 2010). Moreover, the study brought attention to the existing gaps in evidence, notably the absence of controlled clinical trials for certain conditions like psychogenic pruritus, highlighting areas where further research is needed to advance our understanding and treatment options in psychodermatology.

Finally, to gain a deeper understanding of the challenges faced by dermatologists when treating psychodermatologic conditions, the fourth study involved surveying the perceptions, practice patterns, and difficulties encountered by Canadian dermatologists (Chapter V) (Turk, Fujiwara, et al., 2021). Of 78 participants, we found that over 75% reported treating patients with psychodermatological conditions (Turk, Fujiwara, et al., 2021). While practitioners reported moderate confidence in their understanding of psychodermatology (median = 4 on a 5-point scale), their comfort-levels in approaching these patients were lower (median = 3), particularly concerning prescribing psychotropic medication (median = 2). Approximately 50% of dermatologists advocated for a "multidisciplinary approach" for these patients. By combining these four studies, this thesis contributes significantly to the field of psychodermatology. It enhances our understanding of the prevalence of these conditions, the efficacy of various therapeutic interventions, and the hurdles faced by healthcare practitioners. Armed with this knowledge, healthcare professionals can develop more targeted and effective treatment strategies, ultimately improving the overall care and well-being of patients with psychodermatologic conditions. The findings presented here underscore the importance of considering psychological factors alongside dermatologic manifestations, thereby paving the way for more integrated and holistic care in this complex and fascinating area of medicine.

6.1. Multidisciplinary Psychodermatology Clinic in Alberta

One salient conclusion from my research work and other studies in the literature underscores the significant potential for integrating joint multidisciplinary approaches between psychiatry and dermatology into psychodermatology practice (Patel & Jafferany, 2020; Turk, Fujiwara, et al., 2021). This integration of mental health support alongside dermatological care facilitates a comprehensive understanding of patient needs and allows for tailored interventions (Patel & Jafferany, 2020; Turk, Fujiwara, et al., 2021). By offering a holistic approach, healthcare providers can effectively address both the visible physical manifestations and the underlying psychosocial factors that influence dermatological conditions. For that reason, and based on our findings from the survey to Canadian dermatologists, we established a psychodermatology multidisciplinary clinic at Kaye Edmonton Clinic in Alberta, Canada, the Skin Health Clinic (Psychodermatology). I would like to share some preliminary findings from this facility here (see Appendix S4). Upon retrospective assessment of the clinic's first year (2021-2022), 21 patients attended, including 16 females and 4 males. Their ages ranged from 23 to 69 years (mean [SD] age: 53.8 [±13.2] years). The wait time varied from 2 to 120 days (mean [SD]: 52 [±29] days). Referrals came from family physicians (43%), dermatologists (38%), and a psychiatrist (4.7%). Before referral, the most common diagnoses were delusional parasitosis (43%), GAD (33%), and MDD (28.6%), among others. The duration of symptoms ranged from 3 weeks to 10 years (mean [SD]: 3.2 [±2.4] years). Pre-referral prescriptions included topical corticosteroids (47.6%), antipsychotics (24%), and antidepressants (38%), among others. After comprehensive evaluation in our clinic, delusional parasitosis remained the most common diagnosis (66.6%), followed by PTSD and BPD (14.3% each). Antipsychotics (52.3%) and antidepressants (33%) were the primary treatment choices, alongside other modalities like betamethasone and petrolatum (33%

each) and menthol (24%). Notably, 38% of patients adhered to follow-up visits, with outcomes revealing complete recovery (14.3%), ongoing symptoms (14.3%), and non-compliance with medications (4.7%), while the remaining 66.6% did not attend follow-ups.

Delusional parasitosis emerged as the most common diagnosis in our cohort. This finding misaligns with our studies on the prevalence of these conditions were delusional parasitosis was relatively rarer compared to other psychodermatology conditions such as skin picking disorder and trichotillomania (Turk et al., 2022). It, however, aligns with previous assumptions that delusional parasitosis is the most prevalent amongst psychodermatologic conditions (Trabert, 1995). This discrepancy might be an artefact due to the dramatic symptoms of delusional parasitosis, i.e., general practitioners may feel least confident to manage these patients and definitively know they need to refer them to a specialized clinic. Inspection of the prescription patterns before referral to our clinic revealed that topical corticosteroids were the most frequently prescribed treatment, reflecting the primary focus on dermatologic symptoms and the attempt to alleviate skin manifestations. Following evaluation at the clinic, the treatment modalities employed included more prescriptions of antipsychotics and antidepressants. Preliminary treatment outcomes of patients treated in our clinic showed some patients achieving complete recovery with a comprehensive approach involving pharmacologic and non-pharmacologic interventions for psychodermatologic conditions. However, others experienced ongoing symptoms and non-compliance with medications, highlighting the challenges in managing these complex conditions. We also experienced a high rate of loss to follow-up, which emphasizes the need for improved patient engagement and compliance strategies in psychodermatologic care. It is noteworthy that the clinic was launched during the COVID-19 pandemic, which might have

increased the loss to follow up ratio due to limited access to healthcare facilities, fear of exposure to infection, and overall disruptions in routine healthcare services.

6.2. Limitations

The work presented in this thesis had some limitations to acknowledge and tackle in future studies. For instance, my study estimating the frequency of psychodermatologic conditions in Alberta, Canada, was a retrospective review that mainly relied on administrative health data from which we inferred potential psychodermatologic conditions. While this approach offered valuable data, it may not fully represent or estimate the true prevalence of psychodermatologic conditions. Additionally, the global prevalence study, while comprehensive and systematic, faced challenges due to inconsistencies in reporting and methodologies across different studies. Psychodermatologic conditions are still relatively underexplored in the literature, and the scarcity of standardized diagnostic criteria makes it challenging to compare prevalence rates accurately. The variations in study designs, patient populations, and diagnostic criteria across different regions may introduce heterogeneity into the results, making it difficult to establish a clear global prevalence estimate, even for the easier to diagnose primary psychodermatologic conditions. Moreover, the investigation into pharmacologic interventions, again while thorough in analyzing existing literature and clinical trials, revealed limitations in the evidence base for certain treatments. Although the study mapped out seven distinct classes of pharmacologic interventions and provided insights into their efficacy, the overall pool of controlled clinical trials was very limited. This limitation hinders the establishment of evidence-based recommendations for specific psychodermatologic conditions, leaving healthcare practitioners with a degree of uncertainty when choosing treatment approaches. Further well-designed and adequately powered clinical trials are needed to strengthen the evidence base and provide more robust guidance for

treatment decisions. Lastly, the online nature of our survey to Canadian dermatologists may have affected our response rate and likely limited our reach to some dermatologists (i.e., those who were unable or unwilling to provide information online as opposed to a paper format). As in any voluntary survey, we were only able to collect responses from interested participants. In addition, as our survey was an ad-hoc tool created by the authors, the wording of some questions might have been suboptimal. More efforts are recommended in future studies to address those limitations, validate the findings in this thesis and create the most effective interventions to improve care to psychodermatology patients.

6.3. Future Directions

The thesis presents findings that offer valuable insights and pave the way for advancements in the field of psychodermatology. One important area for future work is conducting larger-scale population-based research using standardized diagnostic criteria. This would help estimate the frequency of psychodermatologic conditions across diverse demographic groups and geographical regions, offering a more comprehensive understanding of their true burden and impact on public health. Another crucial aspect is the need for improved data collection methodologies to assess the prevalence of primary psychodermatologic conditions on a global scale. Collaborative efforts among researchers and institutions can establish a unified approach to gathering data, leading to more accurate estimations and enabling targeted public health interventions. Additionally, the findings in this thesis shed light on the importance of conducting larger and better quality controlled clinical trials to evaluate the efficacy and safety of various pharmacologic treatments for specific psychodermatologic conditions. Exploring innovative therapeutic options, like combination therapies and personalized medicine approaches, may further enhance treatment efficacy.

Furthermore, it is crucial to invest more efforts into integrating multidisciplinary approaches in psychodermatology practice to address the complex interplay between psychological and dermatologic factors. Collaborative efforts between psychiatrists, dermatologists, psychologists, and other healthcare professionals can lead to a more holistic and patient-centered approach to care. The findings from the survey of Canadian dermatologists highlight the importance of specialized training in psychodermatology, indicating a need for educational programs to enhance practitioners' skills in diagnosing and managing psychodermatologic conditions effectively. The establishment of the psychodermatology clinic in Alberta, Canada, offers a promising foundation for future research and clinical practice. Long-term follow-up studies with larger patient cohorts could provide deeper insights into treatment outcomes and the factors influencing treatment adherence. Understanding the psychosocial and environmental determinants of patient compliance can inform the development of tailored interventions to improve patient engagement and overall treatment success.

In summary, as the number of patients seeking help for psychodermatologic conditions increases, dermatologists play a crucial role in addressing both the dermatological and psychological aspects of these conditions. By expanding their therapeutic options and integrating psychological interventions into their practice, dermatologists can provide more comprehensive and personalized care to their psychodermatology patients. Standardizing these approaches through interdisciplinary collaboration and education ensures that patients receive consistent and evidence-based care, leading to better outcomes and improved quality of life. Continuing medical education programs and professional training should emphasize the importance of psychodermatology and equip dermatologists with the knowledge and skills necessary to address the psychological aspects of skin conditions, as well as psychotherapeutic options.

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Appendix

Appendix S1 - Chapter 3

Outcome measures and definitions

The two primary outcomes were the prevalence and incidence of primary psychodermatologic disorders. The prevalence for each condition was calculated by dividing the number of cases (current and pre-existing) at a specific period by the size of the reference population for the same period of time. The incidence was calculated by dividing the number of new cases in a specific time interval by the size of the population at the start of the time interval.

Disease-specific secondary outcome measures included the location of skin injury, the frequency of injury and/or the frequency of repetitive behaviors leading to injury, frequency and type of comorbidities, and types of treatments used. The secondary outcomes were searched during the extraction phase and documented if reported in the included studies.

In addition to including studies on primary psychodermatologic disorders, we included studies reporting subclinical behavioral manifestations that are central to primary psychodermatologic disorders. The four target behaviors were skin picking, hair pulling, nail biting, and excessive tanning. We distinguished populations with clinical diagnoses (e.g., pathologic skin picking, trichotillomania) from populations with subclinical target behaviors (e.g., occasional skin picking and repetitive hair pulling) by following the narrative definitions provided in each study. We classified the conditions as clinically significant if:

a) Symptoms were explicitly described as pathologic
b) When psychiatric diagnostic criteria were used to determine the diagnosis, or

c) When target behaviors are reported to result in tissue damage accompanied by significant distress or functional impairment.

In all other cases, such as having a repetitive behavior with no distress or impact on daily life, we defined the relevant behaviors as subclinical.Quality assessment

To assess the quality of the identified studies, two reviewers working independently conducted a quality assessment using the rating scheme endorsed by the Oxford Center for Evidence-based Medicine. Table S1 shows the rating scheme as used in this manuscript.

Table S1. Quality Rating Scheme (adopted from the Oxford Center for Evidence-based Medicine Criteria)

Rate	Study Design/Evidence Type
1	Properly powered and conducted randomized clinical trial; systematic review with meta-analysis
2	Well-designed controlled trial without randomization; prospective comparative cohort trial
3	Case-control studies; retrospective cohort study
4	Case series with or without intervention; cross-sectional study
5	Opinion of respected authorities; case reports =

Appendix S2 – Chapter 3

Upon attempting a meta-analysis of the prevalence rates of identified primary psychodermatologic disorders, there were only a few studies for which one could reasonably assume that the study samples were randomly drawn from the respective populations, and the populations themselves differed, which made it impossible to draw pooled estimates. The determinants of heterogeneity based on which we judged our included studies against are as follows: I) participants' characteristics (e.g., different age groups, socio-economic status, geographic area); II) participants receiving care with different comorbidities (e.g., obsessive-compulsive disorder) and receiving care in different settings (psychiatric inpatient, psychiatric outpatient or dermatologic settings); III) different methods of diagnosis (e.g., clinicians assessment or self-reported surveys); and IV) various recruitment methodologies (e.g., identifying subjects in clinics, through online websites, or phone interviews). We tried grouping studies based on the general characteristics of the populations that appeared comparable. We sorted all studies into four categories.

Category A: General population – defined as a sample drawn randomly from the general population with no specific characteristics related to demographics or health status.

Category B: Psychiatric setting – studies here had a sample drawn from a population of people who are receiving or have received care for a psychiatric condition (e.g., body dysmorphic disorder) whether inpatients or outpatients.

Category C: Dermatologic setting – for studies with a population of people who are receiving or have received care for dermatologic conditions (e.g., acne).

Category D: Students – defined as population of university, college, and/or school students.

We found that the effects were too heterogeneous to retain at least three homogeneous studies. In fact, the p-values were extremely low for the relevant hypothesis tests. Conducting any meta-analysis was therefore deemed inappropriate, given the included studies. The following are the most relevant outcomes of the attempted meta-analysis. The outcomes were deemed inappropriate for drawing clinically or epidemiologically significant conclusions. However, these outcomes might inform future endeavors to investigate primary psychodermatologic disorders. Table S2 presents the heterogeneity of the identified studies.

Table S2. Heterogeneity of included studies

Table	Sub-group	Number of studies	Tau^2	I^2	p-value (H0: homogeneity)
1	Delusional Parasitosis	3	0.13	0.76	0.0008
2	Subclinical Skin Picking	8	1.67	0.99	<0.0001
2	Pathologic Skin Picking	12	0.87	0.96	< 0.0001
3	Hair Pulling	10	0.49	0.96	< 0.0001
3	Trichotillomania	23	0.89	0.93	< 0.0001
4	Subclinical Nail Biting	4	1.33	0.99	< 0.0001
4	Pathologic Nail Biting	3	0.26	0.87	< 0.0001

Delusional Parasitosis

The pooled estimate of the prevalence of delusional parasitosis in psychiatric settings was 0.0063 (95% CI = 0.0034–0.114). Heterogeneity, however, was found to be high in this population of

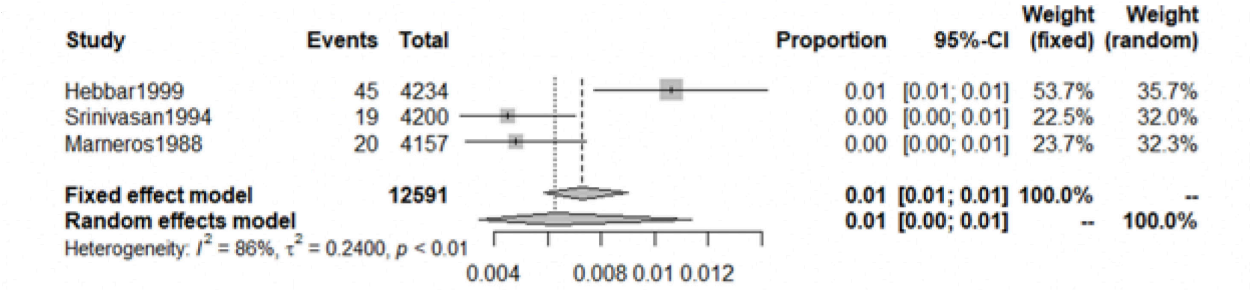
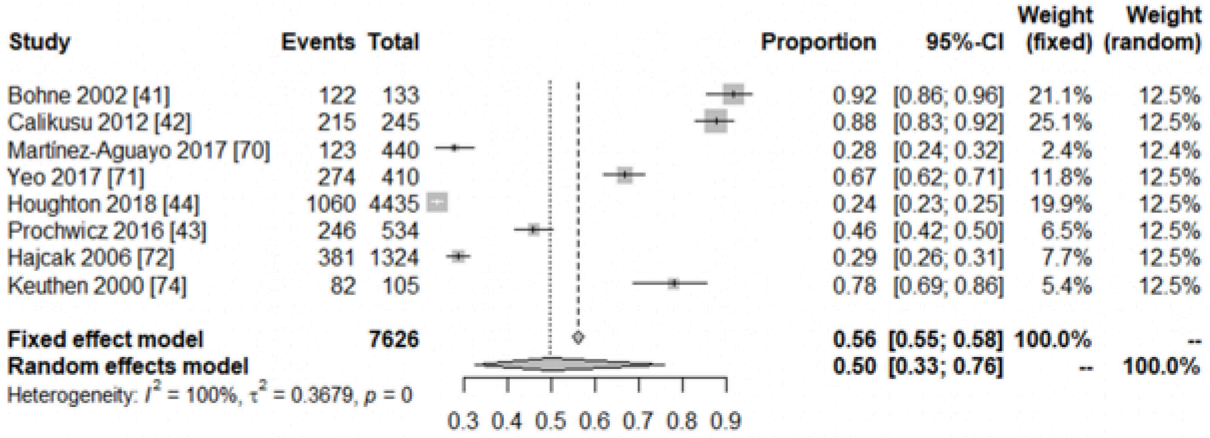


Figure S1. Forest plot of the pooled estimate of prevalence of delusional parasitosis in psychiatric settings.

Skin Picking and Dermatillomania

The pooled estimate of subclinical skin picking prevalence in students was found to be 0.50 (95% CI = 0.33–0.76). However, heterogeneity was estimated to be significant (tau^2 = 0.36; p = 0.00; I^2 = 100%). For pathologic skin picking, it was estimated to be 0.06 (95% CI = 0.04–0.08), with s

A)



B)

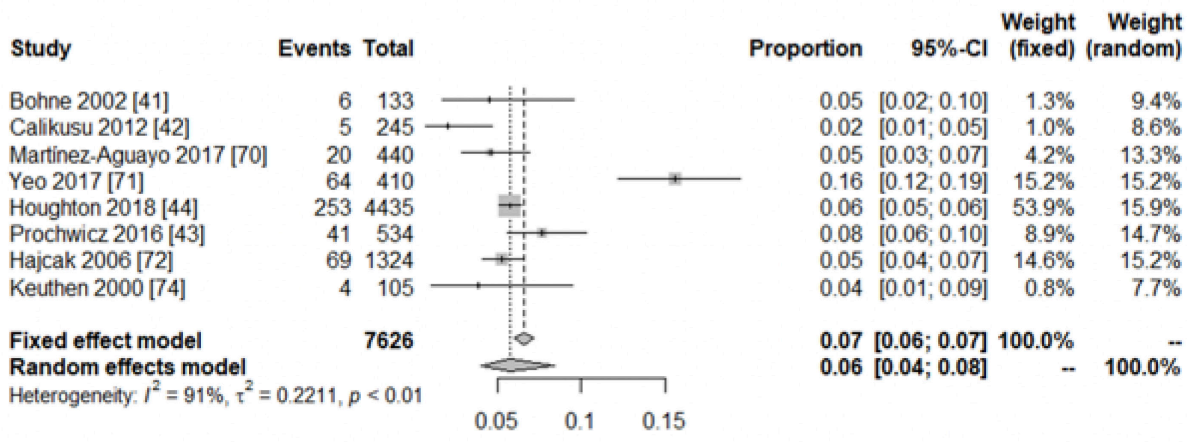


Figure S2. Forest plot of the pooled estimate of the prevalence of subclinical (a) and pathologic (b) skin picking in students.

Hair Pulling and Trichotillomania

The pooled estimate of the prevalence of subclinical hair pulling in students (population category D) was found to be 0.073 (95% CI = 0.047–0.112). However, heterogeneity was estimated to be significant (tau^2 = 0.45; p <0.01; I^2 = 97%). For pathologic hair pulling, the pooled estimate of the prevalence was estimated to be 0.02 (95% CI = 0.01–0.04), with significant heterogeneity (tau^2 = 1.3; p = <0.01; I^2 = 95%) (Figure S3).

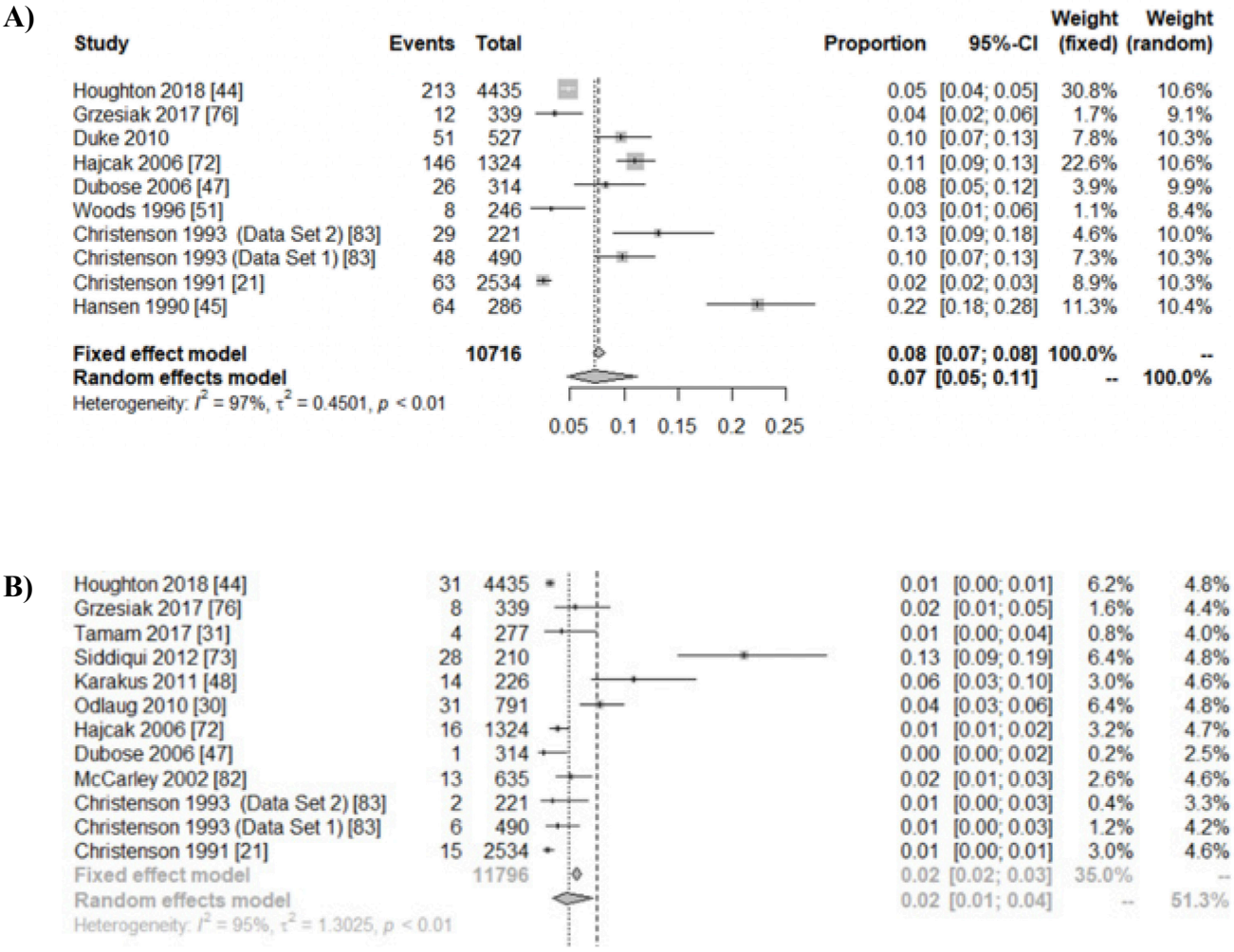


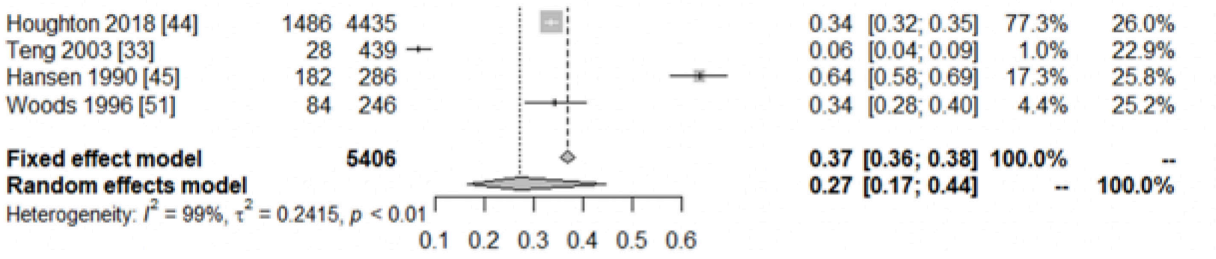
Figure S3. Forest plot of the pooled estimate of the prevalence of subclinical (a) and pathologic (b) hair pulling in students.

Nail Biting

The pooled estimate of the prevalence of subclinical nail biting in students (population category D) was found to be 0.27 (95% CI = 0.17–0.44). However, heterogeneity was found to be significant (tau^2 = 0.24; p <0.01; I^2 = 99%). For pathologic nail biting, the pooled estimate of the

prevalence was estimated to be 0.06 (95% CI = 0.02–0.13), with significant heterogeneity (tau^2 = 0.52; p = <0.01; I^2 = 95%) (Figure S4).

A)



B)

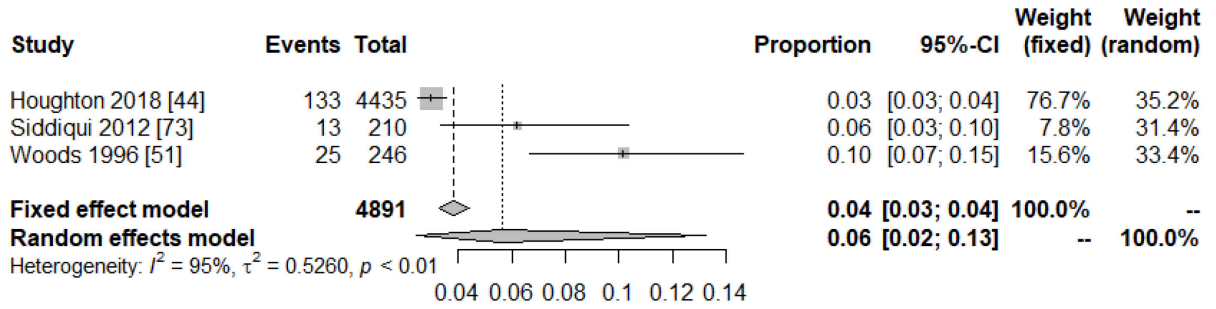


Figure S4. Forest plot of the pooled estimate of the prevalence of subclinical (a) and pathologic (b) nail biting in students.

Appendix S3 – Chapter 4

The following five search strings were used to retrieve articles from five engines: a) Ovid MEDLINE; b) EMBASE; c) APA Psycinfo; d) Cochrane Library; and e) Scopus.

a) Ovid MEDLINE(R)

1. Trichotillomania/

2. neurodermatitis/

3. (psychoderm* or psychocutaneous or neuroderm*).mp.

4. (skin-picking or dermatillomani* or trichotillomani* or Trichotemnomani* or hair-pulling or Factitious-dermatitis or dermatitis artefacta or psychogenic pruritus or psychogenic purpura or olfactory reference syndrome).mp.

5. (Delusion* adj3 parasitos*).mp.

6. ((neurotic or disorder*) adj4 excoriation*).mp.

7. body-focused repetitive behavio*.mp.

8. ((excessive* or frequent or addict*) adj7 (tanners or tanning or tanned)).mp.

9. Morgellon* disease.mp.

10. ((excessive* or repetitive or obsess* or psych*) adj7 (handwash* or (wash* adj2 hand*))).mp.

11. ((excessive* or repetitive or obsess* or psych*) adj7 ((lip or lips) adj3 (lick* or bite or biting or smack*))).mp.

12. ((body-dysmorphi* or obsessive-compulsive-disorder or ocd or phobia* or self-injur* or impulse-control) and (skin or dermatolog* or cutaneous or handwash* or (wash* adj3 hand) or ((lip or lips) adj3 (lick* or bite or biting or smack*)))).mp.

13. or/1-12

14. exp Clinical trial/ or placebo.tw. or dt.fs. or random*.mp. or trial.tw,kf. or groups.tw.

15. 13 and 14

16. 15 not (case reports/ or (case-stud* or case-report*).jw. or (case-study or case-report).mp.)

b) Embase

1. psychocutaneous disease/ or trichotillomania/

2. neurodermatitis/

3. (psychoderm* or psychocutaneous or neuroderm*).mp.

4. (skin-picking or dermatillomani* or trichotillomani* or Trichotemnomani* or hair-pulling or Factitious-dermatitis or dermatitis artefacta or psychogenic pruritus or psychogenic purpura or olfactory reference syndrome).mp.

5. (Delusion* adj3 parasitos*).mp.

6. ((neurotic or disorder*) adj4 excoriation*).mp.

7. body-focused repetitive behavio*.mp.

8. ((excessive* or frequent or addict*) adj7 (tanners or tanning or tanned)).mp.

9. Morgellon* disease.mp.

10. ((excessive* or repetitive or obsess* or psych*) adj7 (handwash* or (wash* adj2 hand*))).mp.

11. ((excessive* or repetitive or obsess* or psych*) adj7 ((lip or lips) adj3 (lick* or bite or biting or smack*))).mp.

12. ((body-dysmorphi* or obsessive-compulsive-disorder or ocd or phobia* or self-injur* or impulse-control) and (skin or dermatolog* or cutaneous or handwash* or (wash* adj3 hand) or ((lip or lips) adj3 (lick* or bite or biting or smack*)))).mp.

13. or/1-12

14. exp clinical trial/

15. placebo.tw. or random*.mp. or trial.tw,kw. or groups.tw.

16. 13 and (14 or 15)

c) APA Psycinfo

1. trichotillomania/

2. neurodermatitis/

3. (psychoderm* or psychocutaneous or neuroderm*).mp.

4. (skin-picking or dermatillomani* or trichotillomani* or Trichotemnomani* or hair-pulling or Factitious-dermatitis or dermatitis artefacta or psychogenic pruritus or psychogenic purpura or olfactory reference syndrome).mp.

5. (Delusion* adj3 parasitos*).mp.

6. ((neurotic or disorder*) adj4 excoriation*).mp.

7. body-focused repetitive behavio*.mp.

8. ((excessive* or frequent or addict*) adj7 (tanners or tanning or tanned)).mp.

9. Morgellon* disease.mp.

10. ((excessive* or repetitive or obsess* or psych*) adj7 (handwash* or (wash* adj2 hand*))).mp.

11. ((excessive* or repetitive or obsess* or psych*) adj7 ((lip or lips) adj3 (lick* or bite or biting or smack*))).mp.

12. ((body-dysmorphi* or obsessive-compulsive-disorder or ocd or phobia* or self-injur* or impulse-control) and (skin or dermatolog* or cutaneous or handwash* or (wash* adj3 hand) or ((lip or lips) adj3 (lick* or bite or biting or smack*)))).mp.

13. or/1-12

14. exp clinical trials/

15. placebo.tw. or random*.mp. or trial.tw. or groups.tw.

16. 14 or 15

17. 13 and 16

d) Cochrane Library Trials database (Wiley Interface)

#1 [mh ^"Trichotillomania"] or [mh ^"neurodermatitis"]

#2 (psychoderm* or psychocutaneous or neuroderm*):ti,ab,kw

#3 (skin-picking or dermatillomani* or trichotillomani* or Trichotemnomani* or hair-pulling or Factitious-dermatitis or dermatitis-artefacta or psychogenic-pruritus or psychogenic-purpura or olfactory-reference-syndrome):ti,ab,kw

#4 (Delusion* near/3 parasitos*):ti,ab,kw

#5 ((neurotic or disorder*) near/4 excoriation*):ti,ab,kw

#6 (body-focused-repetitive next behavio*):ti,ab,kw

#7 ((excessive* or frequent or addict*) near/7 (tanners or tanning or tanned)):ti,ab,kw

#8 (Morgellon-disease):ti,ab,kw

#9 ((excessive* or repetitive or obsess* or psych*) near/7 (handwash* or (wash* near/2 hand*))):ti,ab,kw

#10 ((excessive* or repetitive or obsess* or psych*) near/7 ((lip or lips) near/3 (lick* or bite or biting or smack*))):ti,ab,kw

#11 (((body next dysmorphi*) or obsessive-compulsive-disorder or ocd or phobia* or (self next injur*) or impulse-control) and (skin or dermatolog* or cutaneous or handwash* or (wash* near/3 hand) or ((lip or lips) near/3 (lick* or bite or biting or smack*)))):ti,ab,kw

#12 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)

e) Scopus

TITLE-ABS-KEY (
psychoderm* OR psychocutaneous OR neuroderm* OR skinpicking OR dermatillomani* OR trichotillomani* OR trichotemnomani* OR hair-pulling OR factitious-dermatitis OR dermatitis-artefacta OR psychogenic-pruritus OR psychogenic-purpura OR olfactory-reference-syndrome OR (delusion* W/3 parasitos*) OR ((neurotic OR disorder*) W/4 excoriation*) OR body-focused-repetitive-behavio* OR ((excessive* OR frequent OR addict*) W/7 (
tanners OR tanning OR tanned)) OR morgellon*-disease OR ((
excessive* OR repetitive OR obsess* OR psych*) W/7 (handwash* OR (
wash* W/2 hand*
))) OR ((excessive* OR repetitive OR obsess* OR psych*) W/7 ((lip OR lips) W/3 (lick * OR bite OR biting OR smack*))) OR ((body-dysmorphi* OR obsessive-compulsive-disorder OR ocd OR phobia* OR self-injur* OR impulse-control) AND (skin OR dermatolog* OR cutaneous OR handwash* OR (wash* W/3 hand) OR ((lip OR lips) W/3 (lick* OR bite OR biting OR smack*))))) AND TITLE-ABS-KEY ((Glanville et al.) OR placebo OR random* OR {groups}) AND NOT (INDEX (medline OR embase) OR PMID (
1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9* OR 0*))

Appendix S4 – Chapter 6

Table S3: Patient demographics and referral characteristics from the Skin Health Clinic (Psychodermatology). (April 2021-April-2022)

Patient Demographics	
Total number of patients	21
Average age in years (range)	53.8 (23 - 69) years
Residence	
Edmonton, n (%)	12 (57%)
Outside Edmonton, n (%)	9 (43%)
Referral Characteristics	
Average wait time in days (range)	52 (2 - 120) days
Family physician referrals, n (%)	9 (43%)
Dermatologist referrals, n (%)	8 (38%)
Psychiatrist referrals, n (%)	1 (4.7%)

Table S4: Diagnosis, prescription pattern, and duration of symptoms of patients before referral to the Skin Health Clinic (Psychodermatology).

Diagnosis before Referral	
Delusional parasitosis, n (%)	9 (43%)
GAD, n (%)	7 (33%)
MDD, n (%)	6 (28.6%)
PTSD, n (%)	3 (14.3%)
ADHD, n (%)	2 (9.5%)
Telogen effluvium, n (%)	2 (9.5%)
MDD with psychotic features, n (%)	1 (4.7%)

Diagnosis before Referral	
BPD, n (%)	1 (4.7%)
Prurigo nodularis, n (%)	1 (4.7%)
Androgenetic alopecia, n (%)	1 (4.7%)
Anorexia nervosa, n (%)	1 (4.7%)
Neurotic excoriations, n (%)	1 (4.7%)
OCD, n (%)	1 (4.7%)
Morgellons disease, n (%)	1 (4.7%)
Adjustment disorder, n (%)	1 (4.7%)
Prescription Pattern before Referral	
Topical corticosteroids, n (%)	10 (47.6%)
Antipsychotics, n (%)	5 (24%)
Antidepressants, n (%)	8 (38%)
Antibiotics, n (%)	7 (33%)
Average Duration of Symptoms in Years (range)	3.2 (0.06 - 10) years

Table S5: Definitive diagnosis, treatment, and outcome of patients seen at the Skin Health Clinic (Psychodermatology). (April 2021-April-2022)

Diagnosis at Clinic	
Delusional parasitosis, n (%)	14 (66.6%)
PTSD, n (%)	3 (14.3%)
BPD, n (%)	3 (14.3%)
MDD, n (%)	2 (9.5%)

Diagnosis at Clinic	
GAD, n (%)	2 (9.5%)
Prurigo nodularis, n (%)	1 (4.7%)
Neurotic excoriations, n (%)	1 (4.7%)
Generalized xerosis, n (%)	1 (4.7%)
Androgenetic alopecia, n (%)	1 (4.7%)
Morgellons disease, n (%)	1 (4.7%)
Atopic dermatitis, n (%)	1 (4.7%)
Psychogenic pruritus, n (%)	1 (4.7%)
Treatment	
Antipsychotics, n (%)	11 (52.3%)
Antidepressants, n (%)	7 (33%)
Betamethasone, n (%)	7 (33%)
Petrolatum, n (%)	7 (33%)
menthol, n (%)	5 (24%)
Outcome	
Patients with complete recovery, n (%)	3 (14.3%)
Patients with ongoing symptoms, n (%)	3 (14.3%)
Patients not compliant with medications	1 (4.7%)
Unknown	14 (66.6%)