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DEVELOPMENT OF NOVEL AND ACCESSIBLE TREATMENTS FOR TRICHOTILLOMANIA AND SKIN-PICKING DISORDER

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Development of novel and accessible treatments for Trichotillomania and Skin-picking disorder
Thesis for Doctoral Degree (Ph.D.)

By

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To Maja and Ellen,

Beloved daughters, the motivation to spend as much time with you as possible supported me in approaching my PhD studies with the dedication of a regular job. Titles and accomplishments fade next to the profound honor of being your mother.

Popular science summary of the thesis

Trichotillomania (TTM) and Skin-picking Disorder (SPD) are psychiatric conditions affecting many, marked by recurring and excessive hair-pulling and skin-picking. These behaviors lead to significant hair loss, skin lesions, and often consume substantial amounts of time, causing significant distress and functional impairment.

The primary treatment for TTM and SPD is behavior therapy (BT). However, accessing such treatments is often limited, especially for those in remote areas where healthcare practitioners might lack sufficient knowledge. To bridge this gap, this thesis explored innovative solutions. We investigated the potential of group therapy, allowing caregivers to help more people simultaneously. Taking it a step further, we developed therapist-supported internet-delivered behavior therapy (iBT). While iBT has been extensively studied for related disorders, its evaluation specifically for TTM and SPD was a novel undertaking.

Study I was a clinical trial conducted in routine psychiatric care, where we developed group behavior therapy treating groups of TTM and SPD participants together. The goal was to assess the feasibility and efficacy of the treatment. In total, 40 adult participants with TTM and/or SPD received the treatment, which included 10 group sessions. The treatment was found feasible, with high group attendance and few participants ending treatment prematurely. Additionally, it was found to be preliminarily effective in reducing symptoms of hair-pulling and skin-picking. The utilization of a group format allowed therapists to efficiently treat 25% more patients in comparison to an individual treatment format.

In **Study II**, also conducted in routine psychiatric care, we developed iBT and conducted an open pilot study with 25 adult participants with TTM and/or SPD to test the feasibility and preliminary efficacy of the treatment. The treatment comprised 10 modules delivered over 10 weeks, including text to read and exercises to perform. Each participant had their own therapist, providing feedback on assignments and who was available to answer questions. iBT was found feasible, with high levels of participant satisfaction and credibility of the treatment. The average module completion was high, and only a small number of participants discontinued treatment prematurely. iBT resulted in significant reductions in hair-pulling and skin-picking symptoms.

In **Study III**, we explored participants' experiences of undergoing iBT in a qualitative study. Ten participants who had undergone iBT in Study II were randomly selected for interviews about their perceptions of challenges and advantages with the treatment. Interviews revealed that participants perceived iBT as beneficial and efficacious, albeit time-consuming, leading to stress in some. The treatment's flexibility was appreciated by some participants, while others expressed a need for increased support, including phone calls or face-to-face sessions.

Study IV was a clinical trial conducted in an academic setting, where 70 participants with SPD were randomly assigned to either iBT or a waitlist of equal duration. The results demonstrated significantly greater improvement in skin-picking symptoms in participants receiving iBT compared to those in the waitlist group. The improvement compared to symptoms before the start of treatment was sustained at the 6-month follow-up.

In conclusion, both group therapy and iBT proved to be preliminarily effective, feasible, and safe treatment approaches for TTM and SPD. iBT, while advantageous, presented challenges for participants. Tailoring the treatment to individual needs or blending iBT with face-to-face treatment could enhance efficacy and applicability.

Future research includes evaluations of these treatments in larger studies with active control conditions. Additionally, analyses comparing these novel approaches to traditional face-to-face therapy in terms of cost savings are essential to make good use of healthcare resources. Furthermore, in order to enable nationwide access to BT for individuals with TTM and SPD, evaluations of the implementation of these approaches in regular healthcare is needed.

Abstract

Background: Trichotillomania (TTM) and Skin-picking disorder (SPD) are psychiatric conditions characterized by recurrent and excessive hair-pulling and skin-picking, respectively. These behaviors result in significant hair loss or skin lesions and often consume substantial amounts of time, leading to significant distress and functional impairment. Prevalence rates vary across studies but have been demonstrated to be as high as 3.5% for TTM and 5% for SPD.

The recommended first-line treatment for TTM and SPD is behavior therapy (BT). Unfortunately, healthcare practitioners often lack sufficient knowledge about these disorders, limiting the availability of treatments, particularly for individuals in geographically distant areas. Group therapy offers a potential solution, allowing caregivers to treat more people in the same timeframe. Further enhancement of availability can be achieved through online delivery. While therapist-supported internet-delivered behavior therapy (iBT) has been extensively studied for related disorders, treatments specifically for TTM and SPD have only been explored through unguided or minimally supported online interventions, yielding modest effect-sizes.

Objective: The thesis aimed to develop and evaluate formats for delivering BT to increase availability and accessibility for these disorders. Specifically, we aimed to:

1) test the feasibility and preliminary efficacy of ACT-enhanced group behavior therapy (AEGBT) for TTM and SPD in an open pilot study,

2) test the feasibility and preliminary efficacy iBT for TTM and SPD in an open pilot study,

3) explore the participants experiences of iBT for TTM and SPD in a qualitative study, and

4) test the feasibility and efficacy of iBT for adult patients with SPD compared to a wait-list condition in a randomized trial.

Methods: In **Study I**, based on the original protocol for individual face-to-face therapy we developed AEGBT and conducted an open pilot study with 40 adult participants with TTM and/or SPD in mixed diagnosis groups to test the feasibility and preliminary efficacy of the treatment. In **Study II**, we developed iBT and conducted an open pilot study with 25 adult participants with TTM

and/or SPD to test the feasibility and preliminary efficacy of the treatment. Both Study I and II were conducted in routine psychiatric care. In **Study III**, we explored the participants' experiences of undergoing iBT in a qualitative study. In **Study IV**, conducted in an academic setting, we randomized 70 participants with SPD to either iBT or a waitlist of equal duration.

Results: Study I demonstrated high group attendance and minimal treatment drop-out. AEGBT produced significant decreases in hair-pulling and skin-picking severity from pre- to post-treatment, with moderate to large within-group effects from *d* = 0.77 to 1.24. Symptom reduction was sustained for SPD participants, but not for those with TTM at the 12-month follow-up. The utilization of a group format allowed therapists to efficiently manage 25% more patients in comparison to an individual treatment format. **Study II** reported high levels of participant satisfaction and iBT credibility, reflected in high average module completion and few participants ending treatment prematurely. iBT resulted in significant decreases in hair-pulling and skin-picking severity with effect sizes ranging from *d* = 0.89 to 1.75. Similar to Study I, long-term efficacy favored SPD participants. **Study III,** identified five over-arching themes, unveiling that participants perceived iBT as beneficial and efficacious, albeit time-consuming, leading to stress in some. The treatment's flexibility was appreciated by some participants, while others expressed a need for increased support. **Study IV** demonstrated a significantly greater improvement in SPD symptoms in the iBT group compared to the control group at post-treatment, with a between-group effect-size in the large range (bootstrapped *d* = 1.3). The improvement compared to pre-treatment remained significant at the 6-month follow-up.

Conclusions: In conclusion, both AEGBT and iBT proved to be effective, feasible, and safe treatment approaches for TTM and SPD in routine psychiatric care. iBT, while advantageous, presented challenges for participants. Tailoring the treatment to individual needs or blending iBT with face-to-face treatment could enhance efficacy and applicability. Additionally, iBT demonstrated preliminary efficacy and sustained long-term benefits for SPD compared to a passive control condition. Directions for future research includes evaluating AEGBT and iBT in studies with larger sample sizes and active control conditions alongside cost-effectiveness analyses comparing face-to-face behavior therapy versus these novel treatment approaches. Furthermore, in order to enable nationwide access to BT for individuals with TTM and SPD, evaluations of the implementation of these approaches in regular healthcare is needed.

List of scientific papers

I. **Asplund, M.,** Rück, C., Lenhard, F., Gunnarsson, T., Bellander, M., Delby, H., & Ivanov, V. Z. (2021). ACT-enhanced group behavior therapy for trichotillomania and skin-picking disorder: A feasibility study. *J Clin Psychol*. doi:10.1002/jclp.23147

II. **Asplund, M.,** Lenhard, F., Andersson, E., & Ivanov, V. Z. (2022). Internet-delivered acceptance-based behavior therapy for trichotillomania and skin-picking disorder in a psychiatric setting: A feasibility trial. *Internet interventions: the application of information technology in mental and behavioural health, 30*, 100573-100573. doi:10.1016/j.invent.2022.100573

III. **Asplund, M.,** Lenhard, F., Rück, C., Forsberg, L., & Ivanov, V. Z. (2024) Experiences of internet-delivered acceptance-enhanced behavior therapy for trichotillomania and skin-picking disorder in a psychiatric setting: a qualitative study. *Unpublished manuscript*.

IV. **Asplund, M.,** Lenhard, F., Rück, C., Andersson, Erik., Grimlund, T., Nilsson, M., Sarachu Nilsson, M., Sundh, L., & Ivanov, V. Z. (2024) Internet-delivered acceptance-enhanced behavior therapy for skin-picking disorder: A randomized controlled trial. *Unpublished manuscript*.

Contents

List of abbreviations

ACT	Acceptance and commitment therapy
AEBT	Acceptance-enhanced behavior therapy
AEGBT	Acceptance-enhanced group behavior therapy
CGI-I	The clinical global impression - improvement scale
CGI-S	The clinical global impression - severity scale
BDD	Body dysmorphic disorder
BFRB	Body-focused repetitive behavior
BT	Behavior therapy
CBT	Cognitive behavior theapy
DBT	Dialectical behavior therapy
HRT	Habit reversal training
iBT	Internet-delivered behavior therapy
iCBT	Internet-delivered cognitive behavior therapy
MGH-HPS	The Massachusetts General Hospital hair-pulling scale
MIDAS	The Milwaukee inventory for the dimensions of adult skin-picking
MIST-A	The Milwaukee inventory for styles of trichotillomania – adult report
NE-Y-BOCS	The Yale-Brown obsessive compulsive scale modified for neurotic excoriation
NIHM-TSS/TIS	The National Institute of Mental Health trichotillomania severity scale and trichotillomania impairment scale
OCD	Obsessive compulsive disorder
OCDRD	Obsessive-compulsive disorder and related disorders
RCT	Randomized controlled trial

SAM2 TAI	The SAM2 trichotillomania assessment instrument
SPIS	Skin-picking impact scale
SPD	Skin-picking disorder
SPS-R	Skin-picking severity scale revised
TTM	Trichotillomania

1 Introduction

After dedicating the majority of my nearly 20 years as a clinical psychologist to working with individuals suffering from OCD and related disorders (OCDRD), I have a deep understanding of the suffering these individuals experience. Research on OCD is now extensive, and it is satisfying to be able to offer my OCD patients effective and evidence-based care. However, when I began working at a specialized unit for OCDRD almost 15 years ago, I soon realized that research on trichotillomania (TTM) and skin-picking disorder (SPD) was still in its infancy. The consensus in the existing research indicated that a specific form of behavioral therapy was the first-line treatment for these conditions. Still, treatment effectiveness, both short- and long-term, left much to be desired.

What troubled me even more was that so few people suffering from TTM or SPD had access to adequate treatment. The reasons seemed to revolve around the fact that many in society were unaware of these conditions, and knowledge within the healthcare system about how to treat these conditions was severely limited. I found it incredibly frustrating to see a large group of patients, who experienced significant suffering and impairment, without access to care.

Out of this frustration, my doctoral project took its first steps. Ten years have passed since I initially embarked on this project with the aim of increasing knowledge about these conditions and improving access to care for affected individuals. Since then, I have had the honor of developing both group and internet-based treatments for TTM and SPD. The group treatment has been implemented in several clinics in metropolitan areas in Sweden, and within a couple of years, I hope that patients across the country will be able to access internet-based treatment through regional healthcare services. Knowledge within the healthcare system about these conditions has increased to some extent, and the media has brought at least a little more attention to these disorders.

I am proud of these significant advancements, but I am not satisfied. More research is highly warranted and knowledge dissemination must continue. Ultimately, in my view, it's about achieving equitable healthcare – all psychiatric conditions must have a rightful place in both healthcare and academia.

Stockholm, January 2024

2 Background

2.1 Characteristics of trichotillomania and skin-picking disorder

2.1.1 Definition and description

Trichotillomania (TTM) and skin-picking disorder (SPD) are psychiatric conditions characterized by recurrent and excessive behaviors involving hair-pulling and skin-picking, respectively, resulting in hair loss or skin lesions (American Psychiatric Association, 2013). Individuals affected by TTM and SPD often dedicate significant amounts of time to these behaviors, spending several hours each day pulling or picking (Arnold et al., 1998; Odlaug & Grant, 2008a; Tucker et al., 2011; Woods, Flessner, et al., 2006). Furthermore, individuals with these disorders frequently try to hide the resulting hair loss or skin lesions (Arnold et al., 1998; Diefenbach et al., 2005). Despite numerous attempts, individuals often struggle to cease or limit these behaviors (American Psychiatric Association, 2013).

For those with TTM, the most common sites for pulling are the scalp (> 70%), eyebrows, eyelashes, and pubic area (> 50%) (Woods, Flessner, et al., 2006). On the other hand, SPD sufferers most frequently pick from the face (> 70%), followed by the scalp, arms, legs and chest (40 to 50%) (Tucker et al., 2011). Additionally, both hair-pullers and skin-pickers often engage in these behaviors across multiple body sites (Tucker et al., 2011; Woods, Flessner, et al., 2006). Notably, among women with TTM, the number of pulling sites appears to increase from approximately one site during childhood to three sites in early adulthood, stabilizing at two to three sites throughout adulthood (Flessner et al., 2009). The behavior of pulling hair or picking skin on others is observed in a minority of individuals within both TTM and SPD (Wilhelm et al., 1999; Woods, Flessner, et al., 2006). However, this behavior may be more prevalent among individuals with SPD (Odlaug & Grant, 2008b).

Both individuals with TTM and SPD often target hairs or skin irregularities that differ from the rest (e.g., coarse, curly or gray hairs; hairs perceived shorter than the rest or 'just doesn't feel right') or skin (imperfections such as pimples, enlarged pores or scabs etc.) (Arnold et al., 1998; Bottesi et al., 2016; Duke et al., 2009; Tucker et al., 2011). Sensory perceptions arising at the hair growth site may serve as triggers for the urge to engage in pulling. These sensations encompass tingling, burning, warmth, itching, irritation, pressure, or generalized discomfort.

Notably, these sensations may originate as a consequence of previous pulling episodes and simultaneously act as precursors for subsequent urges, underscoring the cyclical pattern characterizing pulling episodes (Mansueto et al., 1997). Typically, fingers or fingernails are used for pulling or picking, but individuals with SPD, frequently utilize sharp objects such as tweezers and pins to facilitate the picking (Tucker et al., 2011; Woods, Flessner, et al., 2006).

For individuals affected by TTM or SPD sufferers, the sight or feel of the aforementioned imperfections or irregularities often triggers episodes of urges or a sense of tension, which are subsequently relieved through the act of pulling or picking (Tucker et al., 2011; Woods, Flessner, et al., 2006). Additionally, it is common for individuals with TTM or SPD to exhibit post-pulling or post-picking behaviors. For TTM, these actions may include playing with pulled hair between the fingers, examining the hair, licking, or even ingesting it (Christenson, Mackenzie, et al., 1991). Studies have indicated that trichophagia, the act of eating pulled hair, occurs in approximately 20 to 25% of individuals with TTM (Bottesi et al., 2016; Grant & Odlaug, 2008). In the case of SPD, post-picking behavior might involve rolling the skin between fingers (45%), wiping the picked skin in a towel (52%), discarding the skin in the trash (42%), or even consuming the skin (35%) (Wilhelm et al., 1999).

There are two distinct styles of pulling and picking behavior: *focused* and *automatic/unfocused* pulling or picking (Arnold et al., 1998; Christenson & Mackenzie, 1994). *Focused* pulling or picking refers to a deliberate behavior aimed at regulating uncomfortable physical sensations or emotions preceding the action. In contrast, *automatic* pulling or picking involves a more automatic, habit-like behavior occurring without the individual's conscious awareness. This less conscious behavior often manifests when the individual is engaged in sedentary or passive activities like reading, studying, driving, watching television, or lying in bed (Arnold et al., 1998; Bottesi et al., 2016). Most individuals with TTM and SPD exhibit both focused and unfocused pulling or picking to some extent (Arnold et al., 1998; Christenson, Mackenzie, et al., 1991). Previous investigations have suggested that a minority, fewer than 0.01% of individuals, engage exclusively in either focused or unfocused pulling (C. A. Flessner et al., 2008).

Regarding the context of pulling or picking, most sufferers tend to engage in these behaviors when they are alone (Christenson, Mackenzie, et al., 1991; Wilhelm et al., 1999). Many sufferers describe entering a trance-like state,

experiencing a loss of control during the pulling or picking episodes (Bottesi et al., 2016; Wilhelm et al., 1999). Moreover, it is common to experience an increase in pulling or picking behaviors during the evenings (Arnold et al., 1999; Christenson, Mackenzie, et al., 1991), potentially related to increased fatigue that makes it more challenging to resist these urges.

2.1.2 Diagnostic criteria

TTM has traversed a notable journey within the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013). Initially introduced in the DSM-III-R in 1987, TTM was classified as an *impulse control disorder not otherwise specified*. Subsequent DSM versions (DSM-IV and DSM-IV-TR) retained TTM within this category, introducing a revised version of the diagnostic criteria, notably involving the necessity of reporting rising tension, or an "urge", before pulling or when attempting to resist pulling (criterion B), and experiencing subsequent pleasure, gratification, or relief during or post-pulling (criterion C) (Lochner et al., 2011).

However, over subsequent decades, a growing body of research raised doubts regarding the universal applicability of these criteria across all cases of TTM or their presence in every episode of hair-pulling (Duke et al., 2009; Lochner et al., 2011; Woods, Flessner, et al., 2006). Studies comparing individuals experiencing tension before pulling with those who did not, found no differences in severity, comorbidity, or impairment related to hair-pulling (du Toit et al., 2001; Lochner et al., 2011). Consequently, the current DSM-5 version eliminated criteria B and C for TTM and relocated it to the Obsessive-Compulsive and Related Disorders chapter (American Psychiatric Association, 2013).

While the updated criteria of DSM-5 are more including, Lochner et al. (2011) intriguingly posit that criterion B and C highlight "the characteristic driven nature of pulling" which could be valuable in differential diagnosis. They propose that to underscore the typical features of TTM, and refrain from perceiving it as a solitary symptom, descriptors such as "urge" or "seemingly driven" might be beneficial additions to the criteria in future iterations of the DSM (Lochner et al., 2011).

In contrast, despite documentation in medical literature dating back to the 19th century, SPD gained recognition as a distinct psychiatric disorder only in the

latest DSM-5 edition, where it finds its place in the Obsessive-Compulsive and Related Disorders category (American Psychiatric Association, 2013; Grant & Chamberlain, 2022).

2.1.3 Comorbidity

Psychiatric comorbidities are prevalent in both TTM and SPD, potentially exacerbating hair-pulling or skin-picking behaviors and impeding treatment efficacy, highlighting the necessity for their early identification during initial assessments (Jones et al., 2018).

A comprehensive survey conducted by Grant et al. (2020) revealed that a majority of individuals with TTM also presented with at least one concurrent psychiatric condition, consistent with previous studies indicating comorbidity rates ranging from 39% to 50% (Christenson, Mackenzie, et al., 1991; Houghton et al., 2016). Moreover, in TTM cases, comorbidity correlates with more severe TTM symptoms (Lochner et al., 2019). Common comorbidities in TTM encompass anxiety disorders, depression, OCD, SPD and attention deficit hyperactivity disorder (ADHD) (Grant et al., 2020; Lochner et al., 2019). Additionally, a substantial majority of TTM sufferers report a direct association between their TTM symptoms and the development of comorbidities (Woods, Flessner, et al., 2006).

Similarly, psychiatric comorbidities are highly prevalent among individuals with SPD. Studies suggest that approximately 50-65% of individuals with SPD concurrently manifest other psychiatric disorders (Arnold et al., 1998; Grant, Redden, Leppink, Odlaug, et al., 2016; Odlaug & Grant, 2008a). Consistent with TTM, the most frequently endorsed comorbidities in SPD include depression, anxiety disorders, OCD, TTM, ADHD and nicotine dependence, and alcohol dependence (Grant & Chamberlain, 2020; Machado et al., 2018; Odlaug & Grant, 2008a). Notably, a recent in-depth study by Grant et al. (2022) comprising in-person assessments of 260 individuals with SPD, identified TTM as the most prevalent comorbidity (24%), followed by generalized anxiety disorder and major depressive disorder (22% each). In contrast, comorbidity rates with other OCDRDs such as OCD (7%) and Body Dysmorphic Disorder (BDD) (2%) were notably lower compared to previous epidemiological studies on SPD comorbidity (Grant & Chamberlain, 2022). As postulated in another clinical study by Odlaug et al. (2008b), these elevated rates in prior epidemiological studies

might stem from the inclusion of individuals exhibiting skin-picking secondary to OCD and BDD, and thereby receiving dual diagnoses.

Moreover, recent research suggests that when TTM and SPD co-occur, there is a tendency for the severity of pulling and picking behaviors to be comparable, with more severe pulling correlating with more pronounced picking. In addition, in individuals exhibiting both TTM and SPD, the pulling/picking subtypes (automatic vs focused pulling/picking) were found to be correlated (Lin et al., 2023).

2.2 Epidemiology

2.2.1 Prevalence

TTM prevalence rates vary across studies, ranging from 0.6 % to 3.5 %. An earlier study reported that 0.6% of the surveyed US college or university students met the DSM-III-R criteria for lifetime TTM. However, when the tension criterion (Criterion B) was omitted, aligning with DSM-5 criteria, the lifetime prevalence rate for TTM increased to 2.5% (Christenson, Pyle, et al., 1991). Recent online survey-based studies revealed lifetime prevalence rates ranging from 0.7% to 3.5% (Grzesiak et al., 2017; Houghton et al., 2018; Solley & Turner, 2018). The first extensive epidemiological study assessing TTM prevalence in the US general population found a prevalence rate of 1.7% (Grant et al., 2020).

Historically, TTM has been associated with a pronounced female preponderance, with clinical samples being predominantly composed of females (Grant, Redden, Leppink, Chamberlain, et al., 2016). However, recent studies have questioned this gender disparity. In the comprehensive community study by Grant et al. (2020), TTM rates did not significantly differ by gender. This trend was also observed in some previous, albeit smaller, studies (Duke et al., 2009; Odlaug & Grant, 2010; Siddiqui et al., 2012). Additionally, among children, the gender distribution of TTM appears to be equal (Chang et al., 1991). Although the gender gap in TTM prevalence is less pronounced, females with TTM report significantly greater levels of distress and perceived impact on their lives due to hair-pulling compared to males with TTM (Grant et al., 2020).

SPD also exhibits varying prevalence rates across studies, ranging approximately from 1% to 5% (Grant & Chamberlain, 2020; Hayes et al., 2009; Keuthen et al.,

2010; Monzani et al., 2012). The most recent large-scale epidemiological study by Grant & Chamberlain (2020), the first of its kind in the US general population, reported a lifetime prevalence of SPD at 3.1%. Consistent with prior research, Grant et al. found SPD to be more common in females than males; however, the difference, a ratio of 1.2 females to males, was notably smaller than the previously reported female preponderance of approximately 75% (Arnold et al., 1998; Hayes et al., 2009; Keuthen et al., 2010; Machado et al., 2018).

2.2.2 Course

TTM and SPD can manifest across all age groups, yet both disorders consistently exhibit an average onset in early adolescence (Bottesi et al., 2016; Christenson, Mackenzie, et al., 1991; Grant & Chamberlain, 2022; Jones et al., 2018), with the severity of pulling and picking peaking at the transition from adolescence to adulthood (Lin et al., 2023). Notably, the average age of onset for TTM tends to be significantly later for males (19.0 years) compared to females (14.8 years) (Grant et al., 2020). This difference, particularly with females experiencing onset closer to puberty, suggests hormonal implications in TTM (Christenson, Pyle, et al., 1991; Everett et al., 2020; Grant, 2019). Moreover, older onset in TTM has been linked to more severe hair-pulling symptoms (Odlaug et al., 2012) and greater impairment (Grant et al., 2020). Individuals with SPD often associate the onset of skin-picking with pre-existing dermatologic conditions, such as acne (Wilhelm et al., 1999). Unfortunately, recent research reports that dermatologists rarely consider the psychological dimension in acne treatment, with fewer than 5% of SPD patients referred to psychiatric care despite 90% undergoing topical acne treatments and 40% receiving systemic acne therapy (Anzengruber et al., 2018). This is concerning, as the lack of appropriate psychiatric support has the potential to trigger a resurgence of skin-picking, even in response to a minor reappearance of acne (Gupta & Gupta, 1996).

The chronic nature of both TTM and SPD typically involves fluctuating symptom severity (Snorrason et al., 2012). For some, the pulling- or picking severity increases premenstrually or during menstruation (Keuthen et al., 1997; Wilhelm et al., 1999). While automatic pulling seems to remain stable across the lifespan among women with TTM, focused pulling has exhibited fluctuations, in particular increasing during puberty and showing mild increments during perimenopause—

periods characterized by hormonal changes. However, this potential correlation necessitates further investigation (Flessner et al., 2009).

2.3 Etiology and maintenance

2.3.1 Etiology

The etiology of TTM and SPD is not well understood yet. However, an interaction of genetic, psychological, social and neurobiological factors is believed to explain the emergence and the maintenance of the disorders (Duke et al., 2010; Monzani et al., 2012; Woods & Houghton, 2014). It has been proposed that the etiological mechanisms of TTM and SPD are shared and are likely affecting both disorders (Monzani et al., 2014).

2.3.2 Genetic contribution

Both TTM and SPD run in families (Snorrason et al., 2012). Several studies report increased incidence of hair-pulling and skin-picking behaviors among relatives of individuals affected by TTM or SPD (Bienvenu et al., 2012; Christenson et al., 1992; Keuthen et al., 2014; Schlosser et al., 1994; Swedo & Rapoport, 1991). Moreover, higher-than-expected rates of hair-pulling (5%) and skin-picking (45%) have been noted among first-degree relatives of affected individuals (Schlosser et al., 1994; Wilhelm et al., 1999).

Twin studies have yielded varied outcomes regarding the genetic contribution to TTM. Monzani et al. (2014) reported that 32% of the variance in symptoms of TTM was attributed to genetic factors, whereas another study by Novak et al. (2009) indicated that as much as 76% of the variance could be accounted for by genetic influences. Research on genetic factors associated with SPD also vary. Earlier studies reported rates between 40% and 47% (Monzani et al., 2012; Monzani et al., 2014), whereas recent findings suggest that genetic factors contribute to approximately 80% of the variance in SPD (Khorramdel et al., 2022).

To date, no published genome-wide association studies (GWAS), copy number variant (CNV) analyses, or whole exome sequencing (WES) have been conducted

specifically on TTM) and SPD (Crowley, 2023). Nonetheless, animal research has identified several genes associated with these conditions, notably Hoxb8, Sapap3, and Slitrk5 (Everett et al., 2020; Grant, 2019). Mutations in Hoxb8 or Slitrk5 genes in mice have resulted in excessive grooming behavior (Nagarajan et al., 2018; Shmelkov et al., 2010). Similarly, mice with a deletion of the Sapap3 gene exhibited comparable excessive grooming behaviors (Welch et al., 2007). The potential involvement of the Sapap3 gene in TTM is further supported by human studies (Züchner et al., 2009), where rare heterozygous variants of Sapap3 were more prevalent in individuals with TTM compared to healthy controls. However, a comprehensive understanding of the genetic underpinnings of TTM and SPD requires genome-wide association studies for conclusive insights.

2.3.3 Environmental risk factors

Snorrasson et al. (2012), in their review of TTM and SPD, highlight evidence from experimental studies and self-report surveys indicating that an understimulated environment may pose a risk factor for these disorders. The lack of stimulation often leads to boredom, a known trigger for hair-pulling and skin-picking. Moreover, Snorrasson references case reports suggesting that prolonged periods of low stimulation may precede the onset of TTM and SPD. However, further studies are necessary to thoroughly investigate this hypothesis.

In Özten et al.'s study (2015), individuals diagnosed with TTM and SPD reported a significantly higher frequency of traumatic and negative events during childhood compared to healthy controls. This suggests a potential association between trauma, post-traumatic stress, and the development of TTM and SPD. Nevertheless, further longitudinal research is crucial to determine whether trauma and post-traumatic stress precede the onset of TTM and SPD.

2.3.4 Neurobiological underpinnings of hair-pulling and skin-picking

Significant gaps persist in understanding the neuroanatomical structures and functions associated with TTM and SPD. Specific studies have revealed functional abnormalities in the brains of individuals with TTM, involving affect regulation, habit learning, and top-down cognition (Chamberlain et al., 2018; Chamberlain et al., 2008). Furthermore, longer TTM duration and increased severity have shown associations with elevated mean diffusivity in white matter

tracts within the fronto-striatal-thalamic pathway (Roos et al., 2013). Roos et al. (2015) observed notable disparities in the neurobiological profiles of TTM and SPD, particularly in brain structure volumes, cortical thickness, and engagement of fronto-striatal pathways. Increased involvement of the ventral striatum, prevalent in individuals with SPD, implies heightened engagement of the reward system. Conversely, extensive engagement of the parahippocampal gyrus, observed in individuals with TTM, suggests a plausible explanation for the dissociative symptoms frequently experienced during hair-pulling in a 'trancelike' state (Roos et al., 2015).

A recent neuroimaging study by Grant et al., encompassing both TTM and SPD (2022), indicates abnormalities of the inferior frontal gyrus and suggests that these constitute a core feature of these disorders. Specifically, Grant et al.'s study explores reward-related task activation and reports significant hyperactivation of the bilateral inferior frontal gyrus in individuals with TTM and SPD compared to healthy controls when anticipating reward or punishment. These findings correspond with the diagnostic criteria for TTM and SPD, underscoring the failed attempts to reduce pulling or picking, indicating a dysregulated reward circuitry in these disorders. Grant et al. (2022) argue that these findings, combined with preceding neurocognitive studies, could imply an overactivation of the inferior frontal gyrus in response to reward or punishment anticipation in patients with TTM and SPD, impeding this region's capacity to effectively execute additional cognitive functions, such as the top-down regulation of automated behavior. If substantiated, therapeutic approaches targeting TTM and SPD through medications or psychotherapies mitigating sub-cortical reward pathways might aid the inferior frontal gyrus in enhancing top-down control. This could occur by liberating the processing capacity of this region.

Regarding medication responses, various neurotransmitter and neuropeptide systems have been implicated in TTM and SPD. Swedo et al. support the involvement of the serotonergic system in TTM, citing clomipramine's significant reduction of TTM symptoms (Swedo et al., 1989). Woods et al. (2014) note several studies supporting the role of the dopamine system in stereotypic and grooming behaviors in animals. Human studies have demonstrated increased stereotypic hair-pulling in response to dopaminergic agents (Martin et al., 1998) and decreased pulling with dopamine blockers (Van Ameringen et al., 2010). Additionally, the involvement of the glutamate system in TTM and SPD is

suggested by positive responses to N-acetylcysteine, with notable reductions in hair-pulling and skin-picking (Grant, Chamberlain, et al., 2016; Grant et al., 2009).

2.3.5 Psychological models

The emergence and maintenance of TTM and SPD can, to a certain extent, be explained by psychological factors. The actions of hair-pulling and skin-picking can be comprehended through a blend of classical and operant conditioning (Mansueto et al., 1997). The pulling and picking are typically triggered by a rising physical impulse or urge (Mansueto et al., 1997; Wilhelm et al., 1999). What stimuli that come to cue these triggers is developed by classical conditioning. These cues can be both external and internal (Mansueto et al., 1997).

External cues encompass settings such as bedrooms, bathrooms, cars, work desks, and implements like tweezers and mirrors. Activities, emotions, and thoughts contribute significantly to shaping the associations formed between these external cues and the urge to pull or pick. For instance, bedrooms often evoke grooming rituals, relaxation, or contemplation of emotionally impactful events from the day. Frequent co-occurrence of these conditions alongside pulling behaviors in the bedroom fosters secondary associations between the urge to pull and this specific setting, forged through classical conditioning. Over time, the bedroom evolves into a trigger for the urge to pull, even in the absence of the initial conditions. Similarly, implements like tweezers may, through classical conditioning, become associated cues that trigger the urge to pull or pick (Mansueto et al., 1997).

Internal cues, on the other hand, pertain to emotional triggers for pulling or picking, involving the physiological state of tension as well as a spectrum of feelings such as anxiety, boredom, anger, fatigue, guilt, and even positive emotions of happiness and excitement (Mansueto et al., 1997; Wilhelm et al., 1999). It is worth noting that, within a classical conditioning framework, both positive and negative emotions can act as cues for the behavior (Mansueto, 1997). Internal cues also encompass sensations—visual, tactile, and physical sensations associated with the hair or skin—that might serve as potential triggers for the impulse to pull or pick (Mansueto et al., 1997; Wilhelm et al., 1999).

Operant conditioning comes into play as the pulling or picking serves a function for the individual. The pulling or picking frequently function to down-regulate

negative emotionality, such as distressing thoughts, feelings and urges (Lochner et al., 2021; Roberts et al., 2013) and when this occurs the behavior is negatively reinforced. On the other hand, when the pulling/picking leads to pleasure or gratification, the behavior is positively reinforced. Subsequently, the urge experienced by the individual is likely to be followed by the behavior reinforced previously, perpetuating a cycle of pulling or picking (Mansueto et al., 1997; Odlaug & Grant, 2008a; Tucker et al., 2011).

Several studies have highlighted the counterproductive nature of pulling and picking, as a significant percentage of individuals report experiencing anxiety not only as a precipitator but also as a consequence of the behavior itself. Consequently, this reinforces the vicious cycle even further (Diefenbach et al., 2002; Mansueto et al., 1997; Woods, Flessner, et al., 2006).

The phenomena of escaping negative emotionality through maladaptive behaviors, like pulling/picking, is also known as *experiential avoidance*, a term coined within the framework of Acceptance and Commitment Therapy, which constitutes a part of the third wave of cognitive behavior therapy. As described above, a vicious circle of pulling/picking is created when the individual finds the avoidance behaviors initially effective in reducing the unwanted negative emotionality, but over time, the avoidance of negative emotionality paradoxically increases its frequency and exacerbates the struggles with it. This leads to a rigid and ineffective response to these private experiences, known as *psychological inflexibility*. This inflexibility limits adaptation in the face of uncomfortable experiences, hindering engagement in meaningful life activities based on personal values (Hayes et al., 1996).

Psychological inflexibility has been associated with TTM severity, urges to pull, increased distress related to pulling, and higher impairment levels (Alexander et al., 2017; Begotka et al., 2004; Houghton et al., 2014; Lee et al., 2020). It also mediates TTM severity and treatment outcomes (Houghton et al., 2014). These findings suggest that targeting psychological inflexibility in the treatment of TTM and SPD may be beneficial in reducing symptom severity associated with these disorders.

2.4 Impact

The impact of TTM and SPD on individuals is characterized by significant distress and functional impairment (Diefenbach et al., 2005; Tucker et al., 2011; Wilhelm et al., 1999; Woods, Flessner, et al., 2006). These disorders often disrupt various aspects of daily life, affecting social interactions and occupational activities. For instance, almost all TTM participants and nearly half of the SPD participants reported interference in social interactions. Additionally, around 80% of TTM participants and 35% of SPD participants reported disruptions in occupational activities (Diefenbach et al., 2005; Flessner & Woods, 2006). These disruptions are unsurprising given the time-consuming nature of hair-pulling and skin-picking behaviors. Besides the time spent engaging in these behaviors, individuals invest significant time concealing their effects due to social embarrassment (Arnold et al., 1998; Tucker et al., 2011; Woods, Flessner, et al., 2006). Feelings of social embarrassment are common among affected individuals and often hinder them from seeking treatment (Diefenbach et al., 2005; Wilhelm et al., 1999) .

The social impact of TTM and SPD extends to avoidance of social events, public spaces, vacations, and difficulties in maintaining close relationships (Flessner & Woods, 2006; Tucker et al., 2011; Woods, Flessner, et al., 2006). Studies suggest that social and interpersonal impairment tends to escalate with age, ranging from mild in childhood to moderate or severe during middle to late adulthood (Flessner et al., 2009).

Occupationally, these behaviors frequently interfere with job duties and pose challenges for students in academic settings. For some individuals, these challenges result in job loss or hindered career advancement (Flessner & Woods, 2006; Tucker et al., 2011; Woods, Flessner, et al., 2006).

Anxiety serves as both a trigger and a consequence of these behaviors. To cope with the distress, some individuals turn to substances like alcohol or tobacco to alleviate the negative feelings associated with pulling or picking (Woods, Flessner, et al., 2006). Recent studies indicate that nearly 20% of individuals with TTM and SPD also meet criteria for alcohol or drug abuse, suggesting this as a comorbidity further exacerbating the impact of these disorders (Grant & Chamberlain, 2020; Grant et al., 2020).

Beyond distress and functional impairments, medical complications arise from pulling and picking behaviors. TTM, for instance, may lead to the ingestion of

pulled hair, in rare cases forming trichobezoars (i.e., accumulations of hair masses) within the lower gastrointestinal tract. These masses vary in size and can result in abdominal pain, nausea, vomiting, and weight loss. In some cases, trichobezoars can obstruct the digestive system, necessitating surgical intervention (Snorrason et al., 2021). Other complications include infections, carpal tunnel syndrome, muscle fatigue, and atypical hair regrowth (regarding color or texture) or permanent hair loss (O'Sullivan et al., 1996).

Similarly, SPD often causes tissue damage and minor sores in the majority of individuals (90%) (Wilhelm et al., 1999). For many, these medical complications involve more severe tissue damage, including lesions (68%) or deep craters (45%) (Arnold et al., 1998; Wilhelm et al., 1999). In severe cases, individuals may appear slightly disfigured due to persistent picking. (Wilhelm et al., 1999). Additionally, a significant number of individuals (32 – 61%) report infections as a consequence of picking behaviors (Arnold et al., 1998; Wilhelm et al., 1999).

2.5 Assessment of trichotillomania and skin-picking disorder

Individuals suspected of having TTM or SPD, should undergo a comprehensive differential diagnosis evaluation (Jones et al., 2018). In cases where an underlying cutaneous complication is suspected, a thorough dermatologic assessment is advised. Instances exist where these disorders coincide with primary dermatological conditions like acne excoriée, or where hair-pulling or skin-picking cause medical complications necessitating prioritized medical intervention alongside or before psychiatric treatment (Jafferany & Patel, 2019; Jones et al., 2018).

During clinical interviews, evaluating the current hair-pulling or skin-picking manifestation, including specific pulling/picking behaviors, distress levels, and functional impairment, is crucial (Jafferany & Patel, 2019; Jones et al., 2018). Collecting information about pulling or picking styles (focused or automatic) is important as it may influence treatment focus (Christopher A. Flessner et al., 2008). Additionally, gathering details about past treatments - psychological and pharmacological - regarding duration, compliance, learned strategies, and perceived effectiveness is invaluable (Jones et al., 2018). Sensitivity and empathy in interviews are crucial due to the common feelings of shame and

embarrassment among individuals with these disorders (Jafferany & Patel, 2019; Jones et al., 2018). Furthermore, clinical interviews should also screen for comorbidities, which can complicate or hinder the TTM/SPD treatment (Jafferany & Patel, 2019; Jones et al., 2018).

The subsequent section presents commonly used assessment tools for TTM and SPD.

2.5.1 Instruments measuring trichotillomania

2.5.1.1 The National Institute of Mental Health Trichotillomania Severity Scale and Trichotillomania Impairment Scale (NIMH TSS/TIS)

The National Institute of Mental Health Trichotillomania Severity Scale and Trichotillomania Impairment Scale (NIMH-TSS/TIS) is a clinician-administered questionnaire rating TTM symptoms (Swedo et al., 1989). The questionnaire consists of two sub scales, NIMH-TSS and NIMH-TIS. The NIMH-TSS rates the severity according to various aspects of TTM such as time spent pulling, resistance to urges, overall distress, and interference on a 0-5 scale. The NIMH-TIS rates the impairment due to the pulling on a scale from 0 (indicating no impairment) to 10 (indicating severe impairment). The psychometric properties of NIMH-TSS and TIS are weak, with low internal consistency (α = 0.52) and low test-retest reliability (r =0.61) (Barber et al., 2023).

2.5.1.2 The Massachusetts General Hospital Hairpulling Scale (MGH-HPS)

The Massachusetts General Hospital Hairpulling Scale (MGH-HPS) (Keuthen et al., 1995) is a self-report questionnaire designed to assess the severity of hair-pulling behaviors. Comprising 7 items, the scale explores aspects such as urges to pull hair, actual pulling behavior, and the resulting consequences. The items are rated on a scale from 0 to 4 and subsequently summed to yield a total score ranging from 0 to 28, where higher scores indicate greater severity. The MGH-HPS has exhibited robust internal consistency ((α = .89) (Keuthen et al., 1995) and (α=0.83) (Barber et al., 2023)), favorable to moderate convergent validity (Barber et al., 2023; O'Sullivan et al., 1995) and favorable divergent (O'Sullivan et al., 1995) and discriminant validity (Barber et al., 2023). The level of the test-retest reliability varies considerably across studies ((r = .97) (O'Sullivan et al., 1995), and (r=0.55) (Barber et al., 2023)).

2.5.1.3 The Milwaukee Inventory for Styles of Trichotillomania – Adult Report (MIST-A)

As different styles of pulling can have implications for which treatments sufferers should receive, the assessment of these is important (Jones et al., 2018). The Milwaukee Inventory for Styles of Trichotillomania – Adult Report (MIST-A) is a self-report scale intended to assess the different subtypes or styles of pulling (C. Flessner et al., 2007). The scale measure two factors, focused pulling and unfocused (automatic) pulling and each factor consists of several items. Research suggest that the MIST-A demonstrates adequate psychometric properties (C. Flessner et al., 2007).

2.5.1.4 The SAM2 Trichotillomania Assessment Instrument (SAM2 TAI)

Most TTM-assessment tools lack contextuality, requiring individuals to evaluate their hair-pulling behavior based on generalizations across various life situations, fostering broad conclusions. In order to the decrease the risk of overlooking crucial situational differences, the SAM2 Trichotillomania Assessment Instrument (SAM2 TAI) was recently developed (Taylor Browne Lūka et al., 2023). The SAM2 TAI represents a "situated" tool designed to assess TTM, examining 52 specific situations to gauge the frequency of pulling and the intensity of urges. It also encompasses various factors known to impact pulling behavior, such as external triggers, emotion regulation, and situational control. The SAM2 TAI has demonstrated high levels of construct and content validity. In addition, it was shown to only moderately correlate with the MGH-HPS, which suggests that while both situated and "not-situated" measures evaluate TTM, they capture distinct information (Taylor Browne Lūka et al., 2023).

2.5.2 Instruments measuring skin-picking disorder

2.5.2.1 The Yale-Brown Obsessive Compulsive Scale Modified for Neurotic Excoriation (NE-Y-BOCS)

The Yale-Brown Obsessive Compulsive Scale Modified For Neurotic Excoriation (Arnold et al., 1999) is a semi-structured and clinician-administered adaptation of the standard Yale-Brown Obsessive Compulsive Scale (Y-BOCS) that measures skin-picking symptoms concerning preoccupation with skin as well as behaviors associated with skin-picking (i.e., time occupied, interference with functioning, distress, resistance and control). Comprising ten questions rated on a scale from 0 to 4, the NE-Y-BOCS yields a total score ranging from 0 to 40,

where elevated scores signify heightened severity of skin-picking symptoms. The NE-Y-BOCS has demonstrated favorable internal consistency (α = .95) (Aydin et al., 2021) and robust test-retest reliability (r = .83) (Grant et al., 2007).

2.5.2.2 The Skin Picking Scale - Revised (SPS-R)

The Skin Picking Scale - Revised (SPS-R) (Snorrason et al., 2013) serves as a self-administered tool to assess the severity and impairment associated with skin-picking behaviors. Comprising 8 items, the scale comprehensively addresses the three impairment domains outlined in the DSM-5 criteria for SPD, namely skin lesions, subjective distress, and functional impairment. Responses are rated on a 0-4 scale and then aggregated into a 32-point total score, where higher scores indicate more pronounced skin-picking severity. The SPS-R has demonstrated satisfactory psychometric properties, exhibiting high internal consistency (α = .83) and offering preliminary evidence of convergent and discriminant validity for its two subscales (severity and impairment) (Snorrason et al., 2013).

2.5.2.3 The Skin Picking Impact Scale (SPIS)

The Skin Picking Impact Scale (SPIS) (Keuthen et al., 2001) is a self-administered questionnaire designed to assess the social, behavioral, and emotional consequences associated with skin-picking. Comprising 10 items, the scale employs a rating system from 0 to 5, which are then aggregated into a 50-point total score. Elevated scores on the SPIS signify heightened severity of skin-picking. The SPIS has demonstrated satisfactory psychometric properties, including high internal consistency (α = 0.94), along with evidence of convergent and discriminant validity for its two subscales (severity and impairment) (Keuthen et al., 2001).

2.5.2.4 The Milwaukee Inventory for the Dimensions of Adult Skin Picking (MIDAS)

Similarly, to MIST-A for TTM, The Milwaukee Inventory for the Dimensions of Adult Skin Picking (MIDAS) (Walther et al., 2009), was developed in order to assess the different subtypes of picking. MIDAS is a self-rated assessment measuring two factors, focused picking and automatic picking, each factor consisting of several items. The MIDAS has demonstrated adequate internal consistency for the two subscales (“focused picking” (α = 0.81), “automatic picking” (α = 0.77)), favorable construct validity, and good discriminant validity (Walther et al., 2008).

2.5.3 Treatment response

Across the literature, TTM symptom severity is most commonly rated using the self-rated MGH-HPS and the clinician-rated NIMH-TSS. Optimal cut-points for treatment response have also been established in a recent meta-analysis. For the MGH-HPS the optimal definition of response was 35% or a 7-point reduction compared to base-line (Farhat et al., 2019). This is in line with the cut-off proposed by Houghton et al. (2015) (45% reduction or a 7-point raw score change on the MGH-HPS). According to Farhat et al. the optimal definition of response on the NIMH-TSS is 50% or a 6-point reduction (Farhat et al., 2019). This is again, more or less in keeping with the findings by Houghton et al. (30-40% reduction or 6-point raw score difference on the NIMH-TSS) (Houghton et al., 2015). A less conservative cut-off for treatment response has been suggested by Nelson et al. (2014), recommending that researchers report it as the proportion of participants achieving a symptom reduction of 25% or more on the MGH-HPS.

In my knowledge there is no empirically supported definition of treatment response in SPD. However, Grant et al. (2010) has proposed that a 35% or greater decrease in the total score of the clinician-rated NE-Y-BOCS, should define treatment response. This definition has been used in a few studies (Aydin et al., 2020; Grant et al., 2010).

Treatment response ratings for TTM and SPD can also be based on The Clinical global impression – improvement scale (CGI-I) (Guy, 1976). The CGI-I is a well-known scale, which provides a brief assessment of a clinician's overall view of a patient's global functioning. The scale has been widely used to determine treatment response in clinical trials across psychiatric conditions (Busner & Targum, 2007) and is part of the established expert consensus definitions for treatment response in the related disorder, OCD (Mataix-Cols et al., 2016). In CGI-I, improvement is rated by an independent clinician on a seven-point scale ranging from 1 (very much improved) to 7 (very much worse). Treatment response is typically defined by a score of either 2 ("much improved") or 1 ("very much improved").

2.5.3.1 Remission

In clinical trials of TTM, remission has been reported in different ways. Houghton et al. defines disorder remission in TTM as a 55-60% reduction or 7-point raw score change on the MGH-HPS and/or a 65% reduction or 6-point raw score on

the NIHM-TSS/TIS (Houghton et al., 2015). Diefenbach et al. define remission as a total score of 6 or below on the MGH-HPS (Diefenbach et al., 2006), whereas Nelson et al. set the cut-off for return to normal functioning to a total score of 9 or below.

The cut-off proposed by Nelson (1991), is derived from the definition provided by Jacobson and Truax (1991), which is widely employed as a criterion for *clinically significant change* in clinical trials involving psychiatric disorders. Following their definition, individuals whose scores fall at least two standard deviations below the mean of the dysfunctional population are deemed to have experienced clinically significant change. Although the term clinically significant change is closely associated with remission, it diverges in that it evaluates whether the improvements observed in an individual's condition are not only statistically reliable but also clinically or practically meaningful, regardless of whether they reach the threshold of diagnostic remission.

Moreover, Nelson et al. (2014) argue that because most people do not pull their hair at all for non-cosmetic reasons, complete abstinence from hair-pulling should be used as a more conservative supplement for measuring clinically significant change. Complete abstinence is reported based on the score on item 4 of the MGH-HPS, where 0 indicates complete abstinence from hair-pulling. Complete abstinence at post-treatment has predicted superior 2-year follow-up results after behavior therapy for TTM (Keijsers et al., 2006), which supports the use of this supplement according to Nelson et al (2014).

As for SPD, research by Snorrasson et. al. found that a cut-off score of 9 or higher on the SPS-R can differentiate between normal skin-picking behavior and compulsive skin-picking (Snorrason et al., 2022). In addition to this cut-off, Keuthen et.al., carried out sensitivity and specificity analyses on the SPIS. As per these criteria, a score of 7 or above serves to distinguish compulsive skin-picking from normal skin-picking (Keuthen et al., 2001).

Despite the above definitions, there is a lack of consistent definitions and operationalizations for treatment response and remission in TTM and SPD. This deficiency hinders the comparisons of results and communication within the field.

2.6 Treatment for trichotillomania and skin-picking disorder

The recommended first-line treatment for TTM and SPD is behavior therapy (Jones et al., 2018). Several controlled studies have evaluated the effect of behavior therapy for TTM (Azrin et al., 1980; Keijsers et al., 2016; Keijsers et al., 2006; Keuthen et al., 2011; Ninan et al., 2000; Shareh, 2018; van Minnen et al., 2003; Woods, Wetterneck, et al., 2006) and SPD (Mashayekhi Goyonlo et al., 2020; Moritz et al., 2012; Schuck et al., 2011; Teng et al., 2006; Xavier et al., 2020). While full abstinence from pulling/picking is rare in individuals who have received treatment, behavior therapy is generally considered effective, showing substantial effects for TTM (Farhat et al., 2020; McGuire et al., 2014; Slikboer et al., 2017) and moderate to large effects for SPD (Schumer et al., 2016; Selles et al., 2016) at post-treatment. However, when reported, data indicate high relapse rates following behavior therapy (Diefenbach et al., 2006; Keijsers et al., 2016; Keijsers et al., 2006; K. Rogers et al., 2014). For instance, according to Keijsers et al.'s follow-up,, 50% of participants had relapsed two years after treatment (Keijsers et al., 2006). In a trial by Rogers et al., (2014), the percentage meeting TTM criteria increased from 51% to 67% between post-treatment and 3-month follow-up. Regarding SPD, data from controlled trials have demonstrated sustained improvement until 3 months post-treatment (Schuck et al., 2011; Teng et al., 2006). Follow-up data longer than 3 months is lacking.

Unlike disorders such as OCD and BDD, where exposure and ritual prevention therapy (ERP) is the primary treatment, ERP for TTM has only been examined in case studies, showing some success (Brauer & Grant, 2017). To my knowledge, presently, there is no published study of ERP for SPD.

Behavioral treatments, with their strong evidence base and large effect sizes, appear more effective than most pharmacological treatments (Farhat et al., 2020; Ninan et al., 2000; Schumer et al., 2016; Selles et al., 2016; Slikboer et al., 2017; van Minnen et al., 2003). Selective serotonin reuptake inhibitors (SSRIs) have generally shown limited efficacy in treating TTM (Farhat et al., 2020) and have produced minor or inconclusive outcomes for SPD (Lochner et al., 2017). As of now, the American Food and Drug Administration (FDA) has not approved any medications for these disorders (Farhat et al., 2020; Jones et al., 2018). There are however single randomized trials suggesting that N-acetyl cysteine (NAC) for TTM and SPD (Grant, Chamberlain, et al., 2016; Grant et al., 2009), Memantine for TTM and SPD (Grant et al., 2023), Clomipramine (CMI) for TTM (Ninan et al., 2000; Swedo et al., 1989) and Olanzapine for TTM (Van Ameringen et al., 2010)

may be at least as effective as behavioral treatments (Farhat et al., 2020; Stein et al., 2021). Replication of these head-to-head trials would strengthen the evidence base.

2.6.1 Behavior therapy

2.6.1.1 Habit reversal training

The cornerstone of behavior therapy for TTM and SPD is Habit Reversal Training (HRT). Initially developed by Azrin et al. in the early 1970s to mitigate repetitive behaviors such as habits and tics (1973), HRT was subsequently tailored for treating TTM (Azrin et al., 1980). Its primary objective is to heighten awareness of pulling or picking behaviors and disrupt automatic behavioral patterns. Presently, HRT stands as the most widely utilized technique for both TTM and SPD, adaptable to varying levels of symptom severity (Jones et al., 2018).

HRT encompasses three fundamental components: *awareness training*, *competing response* and *social support*. Awareness training aims to augment patients' consciousness of their pulling or picking behaviors. Competing response training instructs patients to engage in incompatible actions (e.g., folding hands, clenching fists) upon experiencing urges or noticing the behavior. Social support involves enlisting a close friend or relative to observe and point out the occurrence of pulling/picking, providing friendly reminders to engage in the competing response. Several meta-analyses demonstrate the efficacy of HRT for both TTM and SPD (Farhat et al., 2020; Selles et al., 2016).

2.6.1.2 Stimulus control

Another frequently employed behavioral technique, often complementing HRT, is stimulus control, aimed at reducing the occurrence of pulling or picking behaviors. Initially, stimulus control entails a comprehensive assessment of the triggers and consequences associated with pulling/picking. The patient is encouraged to observe and note the specific circumstances, settings, activities, thoughts, and emotions before and after engaging in pulling/picking behavior. Additionally, the patient tracks subsequent actions with the pulled or picked hair or skin. Following this thorough assessment, the therapist collaborates with the patient to devise strategies that diminish triggers (e.g., hiding tweezers, covering mirrors, using gloves, engaging with a fidget toy), reduce reinforcing outcomes

(e.g., employing a numbing cream), or introduce alternative sources of reinforcement (e.g., interacting with a soft object) (Woods & Miltenberger, 2001).

2.6.1.3 Treatment tailored to the individual's pulling/picking style

The components of HRT and stimulus control predominantly address automatic pulling/picking behaviors. On the other hand, studies suggest that when emotional or physical distress drives these behaviors, these traditional behavioral components, may exhibit limited effectiveness, and high relapse rates in TTM and SPD (Snorrason et al., 2012; Walther et al., 2010).

To improve treatment outcomes, tailored approaches based on individual pulling or picking styles are advocated. Those engaging in focused pulling/picking may benefit from interventions targeting associated negative private experiences and teaching emotional regulation skills. Meanwhile, individuals with both automatic and focused pulling/picking might benefit from a combination of HRT and interventions aimed at addressing focused pulling (Flessner et al., 2009; Walther et al., 2010).

In line with the above, behavior therapy for TTM and SPD has been augmented with various enhancements, including cognitive therapy (Mashayekhi Goyonlo et al., 2020; Ninan et al., 2000), metacognitive therapy (Shareh, 2018), acceptance and commitment therapy (ACT) (Lee et al., 2018; Woods et al., 2022; Woods, Wetterneck, et al., 2006) and dialectical behavior therapy (DBT) (Keuthen et al., 2012). A meta-analysis by McGuire et al. (2014) suggests that behavior therapy with these enhancements yields larger effect sizes at post-treatment and subsequent 3- and 6-month follow-ups compared to stand-alone behavior therapy. However, interpreting these findings requires caution due to the increased therapeutic contact in the enhanced therapies compared to the standalone approaches. Although not specifically studied in controlled trials for SPD, evidence from the above TTM trials implies potential benefits of these enhancements for SPD patients due to the shared characteristics between the disorders (Selles et al., 2016).

2.6.1.4 ACT-enhanced behavior therapy

ACT-enhanced Behavior Therapy (AEBT) combines behavior therapy with ACT to target automatic pulling/picking while addressing focused pulling/picking through acceptance-based strategies (Woods, Wetterneck, et al., 2006).

More specifically, the ACT-components of AEBT are directed toward accomplishing four key goals: diminishing patients' dependence on ineffective emotional control strategies, nurturing patients' acceptance and willingness to engage with private experiences, training patients in recognizing how they ascribe meaning to words and thoughts and that these are not the same as reality, and encouraging patients to embrace their private experiences while actively engaging in behaviors aligning their core life values (Woods et al., 2022)

Several controlled studies have demonstrated the efficacy of AEBT for TTM in adults (Lee et al., 2018; Woods et al., 2022; Woods, Wetterneck, et al., 2006). In addition, AEBT have been found to be preliminary effective in reducing TTM-symptoms in adolescents (Twohig et al., 2021). Furthermore, apart from the studies included in this thesis, AEBT for SPD has only been evaluated in case studies (Capriotti et al., 2015).

2.6.1.5 ACT as a standalone approach

The treatment effects of ACT used as a standalone approach for TTM (Lee et al., 2020) and SPD (Twohig et al., 2006), appear to be similar to trials combining ACT and HRT. However, the small sample sizes and the uncontrolled study design in the SPD trial call for cautious interpretation of treatment effects.

2.6.2 Delivering behavior therapy in different treatment formats

Despite the existence of effective treatments, a considerable gap persists in healthcare practitioners' understanding of TTM and SPD (Capel, Petersen, Woods, et al., 2023). Consequently, individuals dealing with these conditions often report receiving uninformed care, with first-line treatments seldom being administered (Gallinat et al., 2019a; Tucker et al., 2011; Woods, Flessner, et al., 2006). For instance, Woods et al., (2006) noted that SSRIs were the most common TTM treatment, with only 15% receiving HRT. Similarly, in cases of SPD, only 26% received behavioral treatment, and less than half of these included HRT (Tucker et al., 2011).

Moreover, the lack of understanding and geographical and economic constraints significantly limit access to behavioral treatments for many affected individuals (Capel, Petersen, Woods, et al., 2023; Gallinat et al., 2019a). Additionally, shame and stigma surrounding these disorders deter individuals from seeking help (Gallinat et al., 2019a; Grant & Chamberlain, 2021). In response to these

challenges, various alternative treatment formats have been developed for TTM and SPD.

2.6.2.1 Group therapy

Group treatment is a potentially cost-effective solution, allowing specialized therapists to treat more patients in a shorter time, thereby enhancing treatment accessibility (Morrison, 2001). Studies examining behavior group therapy for TTM and SPD have demonstrated initial feasibility and efficacy (Diefenbach et al., 2006; Haaland et al., 2017; Mashayekhi Goyonlo et al., 2020; Toledo et al., 2015; Xavier et al., 2020).

2.6.2.2 Teletherapy

One drawback of group therapy is that it does not address the challenge of accessing treatment for individuals residing in geographically remote areas. For such cases, teletherapy may enhance access to treatment for TTM and SPD, via digital communication platforms. Teletherapy, explored in a controlled trial for adults with TTM, demonstrated preliminary efficacy in reducing TTM-symptoms, with nearly 60% of participants reporting clinically significant improvements (Lee et al., 2018). In addition, teletherapy has also demonstrated preliminary efficacy in reducing hair-pulling severity in adolescents with TTM (Twohig et al., 2021).

2.6.2.3 Online interventions

Online interventions offer another promising avenue for improving accessibility, particularly in regions lacking treatment providers. They possess the advantage of scaling treatment delivery, enabling fewer therapists to reach a larger patient base, thereby addressing the availability challenge. For instance, the recent implementation of iCBT for OCD and BDD in the Swedish public health system significantly reduced the average number of patients on waiting lists for face-to-face treatment by 60-70% from 2018 to 2020, while maintaining the same number of employed therapists (Lundström et al., 2023).

Controlled trials have provided some evidence supporting the use of digital behavioral treatments for TTM (Capel, Petersen, Becker, et al., 2023; Kate Rogers et al., 2014; Weidt et al., 2015) and SPD (Gallinat et al., 2019b; Moritz et al., 2012; Moritz & Rufer, 2011) reporting small to moderate effect-sizes when compared to either passive or active controls. However, interpreting these outcomes requires caution due to methodological limitations such as non-referred samples, self-reported online assessments, and high attrition rates in some studies. Notably,

the digital treatments in these trials were mostly unguided or minimally supported, lacking frequent therapist monitoring and guidance, which might account for the modest effect sizes observed.

In addition to the self-help format used in the above trials, a combination of web-based self-help and in-person HRT sessions in a stepped-care approach has been proposed for severe TTM-symptoms (K. Rogers et al., 2014). An alternative, less therapist-intensive approach to enhance online interventions' effectiveness for these disorders involves therapist-supported internet-delivered behavior therapy (iBT). iBT includes tailored, interactive email support, and close monitoring of homework assignments by a therapist in addition to written self-help materials.

Supported online interventions have shown greater efficacy compared to unsupported interventions for various psychiatric disorders (Andersson et al., 2005; Richards & Richardson, 2012). Notably, individuals with TTM have expressed a preference for therapist-supported interventions over non-supported versions (Arabatzoudis et al., 2021). Prior research has demonstrated the effectiveness of iBT for related disorders like obsessive-compulsive disorder and body dysmorphic disorder (Andersson et al., 2012; Enander et al., 2016) suggesting potential applicability for TTM and SPD.

2.7 Conclusions

TTM and SPD are two relatively common psychiatric conditions associated with high levels of distress and impairment in social, as well as in occupational domains. Behavior therapy (i.e., HRT) is the first-line treatment, but the majority of individuals suffering from TTM or SPD are unable to access to this treatment due to a shortage of competence amongst health care professionals and likely also due to geographic barriers. New treatment formats, such as internet-delivered therapy, if proven efficacious, have the potential to make evidence-based treatment for TTM and SPD more available nationwide.

3 Aims

The overall aim of this thesis was to develop and evaluate behavioral treatments for TTM and SPD in formats that were easy to disseminate in order to increase the availability and accessibility of evidence-based treatment for these disorders. More specifically the aims of this thesis were as follows below:

3.1 Study I: ACT-enhanced group behavior therapy for trichotillomania and skin-picking disorder: A feasibility study

To enhance the availability of treatment for TTM and SPD, especially for care facilities serving smaller populations seeking assistance for these disorders, Study I in this thesis evaluated a group therapy intervention involving patients with TTM and SPD treated together within a single group.

The primary aim of Study I was to develop and assess the feasibility and preliminary efficacy of ACT-enhanced group behavior therapy delivered in a mixed group format for adult patients with TTM and/or SPD in routine psychiatric care. Additionally, we aimed to investigate the preliminary long-term efficacy of the treatment, assessing outcomes up to 12 months after the conclusion of the treatment period.

3.2 Study II: Internet-delivered acceptance-enhanced behavior therapy for TTM and SPD: A pilot trial

To further increase the availability and accessibility of BT for TTM and SPD, the aim of Study II was to develop and investigate the feasibility and preliminary efficacy of therapist-guided internet-delivered AEBT for patients with TTM and/or SPD in routine psychiatric care. In addition, we also aimed to investigate whether the treatment outcomes were sustained in the long term (up to 12 months after the end of treatment).

3.3 Study III: Experiences of internet-delivered acceptance-enhanced behavior therapy for TTM and SPD: A qualitative study

The aim of Study III was to investigate the participants' experiences of therapist-guided internet-delivered AEBT for TTM and/or SPD in order to ameliorate and refine the treatment protocol for Study IV.

3.4 Study IV: Internet-delivered acceptance-enhanced behavior therapy for skin-picking disorder: A randomized controlled trial

The aim of Study IV was to further evaluate the feasibility and efficacy of therapist-guided internet-delivered AEBT for adult patients with SPD compared to a wait-list condition in a randomized trial. Furthermore, we aimed to investigate the long-term effects of treatment (up to 6 months after the end of treatment).

4 The empirical studies

4.1 STUDY I

4.1.1 Methods

Study I was an open, uncontrolled trial designed to evaluate the feasibility and efficacy of ACT-enhanced group behavior therapy (AEGBT) for mixed-diagnosis groups. This included patients with TTM and SPD, within the context of routine psychiatric care. A total of 40 adult patients with TTM and/or SPD were enrolled in the study, and assessments were conducted from baseline up to 12 months following treatment. The intervention consisted of 10 weeks of AEGBT, and included both traditional interventions (e.g., HRT and stimulus control) as well as more recent acceptance-based techniques (e.g., embracing the urges and mindfulness). The treatment was followed by five booster sessions during the subsequent year. The primary end-point was post-treatment. The primary outcome measure for TTM was the Massachusetts General Hospital Hairpulling Scale (MGH-HPS), and for SPD the Skin Picking Scale-Revised (SPS-R), assessed at pre-treatment, post-treatment and right before the start of each booster session. Secondary outcomes included treatment response and remission according to the Clinical global impression-severity and -improvement scales (CGI-S, CGI-I) (Guy, 1976).

4.1.2 Main results

The result demonstrated a high group attendance and a low degree of treatment dropouts. The group format facilitated therapists in seeing 25% more patients in comparison to an individual treatment format. Additionally, the results indicated significant decreases in hair-pulling and skin-picking severity from baseline to post-treatment, with large effect sizes observed at post-treatment (MGH-HPS, $z(19) = 8.36$, $p < .05$, $d = 0.77$; SPS-R, $z(27) = 10.27$, $p < .001$, $d = 1.24$). These improvements were significantly sustained at the 12-month follow-up for patients with SPD (SPS-R, $z(27) = 10.07$, $p<.001$, $d = 0.73$), but not for patients with TTM (MGH-HPS, $z(19) = 10.28$, $p = 0.672$, $d = 0.19$). At the post-treatment assessment, 18 of the participants (45%) were classified as responders, and this response rate was maintained at the 12-month follow-up. Four participants (21%) with TTM and three participants (11%) with SPD were considered to be in remission at the post-treatment assessment.

4.2 Study II

4.2.1 Methods

Study II was an open, uncontrolled trial of therapist-supported internet-delivered ACT-enhanced behavior therapy (iBT) with the objective of investigating the feasibility, acceptability, and preliminary efficacy for patients with TTM and/or SPD in a routine psychiatric setting. Twenty-five adult patients referred by clinicians, with TTM (n = 7) and/or SPD (n = 18), received 10 weeks of therapist-supported iBT. The treatment was followed by four booster modules. Similar to the intervention in Study I, the iBT program incorporated both HRT, stimulus control and acceptance-based techniques. The primary end-point was post-treatment. Clinician- and self-rated outcomes were assessed at pre-treatment, post-treatment and immediately before the delivery of each booster module. The MGH-HPS served as the primary outcome measure for TTM, while the SPS-R was utilized for SPD. Response and remission rates were part of the secondary outcome measures, and these were rated according to the CGI-S and CGI-I (Guy, 1976).

4.2.2 Main results

The results demonstrated high ratings of satisfaction and credibility by most of the participants. On average, participants completed 7.2 out of 10 internet modules, and only five participants prematurely terminated the treatment. There were significant decreases in the severity of hair-pulling and skin-picking symptoms on the primary outcome measures from pretreatment to post-treatment, with large within-group effect sizes (MGH-HPS, $z(7) = 8.49$, $p < .001$, $d = 0.89$; SPS-R, $z(18) = 12.75$, $p < .001$, $d = 1.75$). For participants with SPD, the positive changes in symptom reduction remained significant up to the one-year follow up (SPS-R, $z(14) = 13.18$, $p < .001$, $d = 1.2$), while the improvements for participants with TTM remained significant up to the 6-month follow up (MGH-HPS, $z(5) = 8.37$, $p < .044$, $d = 1.3$). Forty-eight percent (n = 12) of the participants were classified as responders at post-treatment, a figure that decreased to 20% (n = 5) at the 12-month follow-up. One participant with TTM was considered to be in remission both at post-treatment and at the 12-month follow-up. The

comparable figure for SPD was 22% (n = 4) at post-treatment, and this remission rate was maintained at the 12-month follow-up.

4.3 Study III

4.3.1 Methods

Study III constituted a qualitative follow-up study investigating the participants' experiences of undergoing iBT (from Study II). Ten participants were randomly selected from the feasibility trial of iBT and underwent semi-structured telephone interviews. These interviews followed an interview guide shaped by prior research, were recorded, and subsequently transcribed. The data underwent coding and thematic analysis, a versatile qualitative approach (Braun & Clarke, 2006).The coding process systematically followed a structured six-step procedure encompassing data familiarization, systematic coding, theme identification, theme review, theme definition and naming, and integration of themes into a comprehensive report.

4.3.2 Main results

Five major themes emerged: Treatment program, Therapist contact, Treatment components, Participant readiness, and Treatment effects, each with several sub-themes. The analysis unveiled that most participants regarded iBT as beneficial and efficacious. While some appreciated the treatment's flexibility, others conveyed a need for increased support. Furthermore, the analysis hinted at potential enhancements, such as streamlining the textual content of the program and simplifying the terminology. A considerable number of participants noticed repetition in the volume of homework assignments, which, on occasion, elicited stress and felt burdensome rather than being conducive to the treatment process.

4.4 Study IV

4.4.1 Methods

Study IV was a single-blind randomized controlled trial comparing iBT to a waitlist-control condition for adults with SPD conducted in an academic medical

center. A total of 70 self-referred adult participants were included and assessments were conducted from baseline up to 12 months post-treatment. Additionally, the feasibility and acceptability of iBT were evaluated. Participants randomized to the intervention group received 10 weeks of therapist-supported iBT, while those in the control group were placed on a waitlist. The control group was offered iBT directly after the 1-month follow-up assessment. The primary end-point was at post-treatment. The primary outcome measure was the Skin Picking Scale – Revised (SPS-R). Response rates were reported according to the CGI-I (Guy, 1976). Furthermore, self-rated remission, based on the cut-off proposed by Snorrasson et al. (2022), and clinician-rated remission, determined during the clinician post-assessment, were also reported.

4.4.2 Main results

At the post-treatment assessment, the iBT group exhibited significantly greater improvement in SPD-symptoms compared to the control group (between-group difference -5.1 points, $F = 9.69$, $p < .001$). The between-group effect size fell within the large range, with a bootstrapped *d* of 1.3 (95% CI = 0.92-1.69). In the iBT group, 43% of the participants were classified as responders, while no participants in the control group met the criteria for response. In terms of remission, 31% of the participants in the iBT group achieved remission, in contrast to only 3% in the control group. At the 6-month follow-up, SPD symptoms had increased compared to post-treatment, although the improvement from pre-treatment remained significant. Additionally, the results indicated high levels of treatment satisfaction, credibility, and a positive working alliance.

4.5 Ethical considerations

To ensure ethical guidelines were followed and ethical considerations were adequately addressed before commencing the studies, all studies included in this thesis obtained ethical approvals from one of the following ethical authorities: the Regional Ethical Review Board in Stockholm (Study I) and the Swedish Ethical Review Authority (Study II-IV). All involved researchers were trained in the principles of Good Clinical Practice (*Good Clinical Practice*, 2001)

and the declaration of Helsinki ("World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects," 2013).

Prior to inclusion in any of the four studies, participants received both verbal and written information, and informed written consent was obtained from all participants. In the informed consent, participants were explicitly informed that their participation in the study was entirely voluntary and that they had the option to withdraw their consent at any time without the need to provide an explanation. Results from all the included studies were analyzed at a group level, and all individuals were pseudonymized to prevent the identification of individual participants.

Ethical considerations played a pivotal role in determining the study designs as well. In both Study I and II, treatment formats (group treatment and internet-delivered treatment) that had not been comprehensively evaluated previously were explored. For this reason, it was essential to initiate our evaluations of these formats with smaller pilot studies. These pilot studies aimed to assess feasibility, acceptability, and ensure the absence of any harmful side effects associated with the treatments.

All the studies involved the management of sensitive data, which inherently carries certain risks. To ensure participant integrity, data handling and storage procedures strictly adhered to the regulations set forth by Karolinska Institutet and Region Stockholm. In studies I-II, all clinical information pertaining to the participants was documented in their medical records, and any other sensitive materials, such as case report forms, were securely stored in locked archive rooms within the clinic where the studies were conducted. In studies II-IV, special ethical considerations were taken into account to safeguard patient integrity, particularly in relation to the technical interventions. The treatment platform employed a double authentication procedure for both participants and therapists. All platform data was securely encrypted and stored on a server, including the digital case reports in study IV.

In Study I, II, and IV, measures were implemented to safeguard the integrity of the recruitment process. Participants underwent a comprehensive evaluation before enrollment, which encompassed a diagnostic interview and an examination of their medical history. This evaluation aimed to ascertain that participants indeed carried a primary diagnosis of TTM or SPD and did not concurrently exhibit any acute mental health conditions necessitating immediate treatment, such as

suicidal tendencies or substance abuse issues. Most of the data collected in these studies, including demographic information and clinician and self-ratings of TTM/SPD and comorbidity, are normally collected during routine psychiatric care as well and serve the purpose of ensuring the safety of the recruitment process as described above. However, certain additional data, including assessments related to work alliance, treatment credibility, and psychological flexibility, typically fall outside the scope of routine psychiatric care. This additional load of assessments could potentially have been perceived as burdensome by the participants and might have had a negative impact on them. Therefore, when selecting the instruments to be used, deliberate efforts were made to minimize the length and quantity of structured interviews and scales.

When evaluating new treatment approaches, it is imperative to carefully weigh the potential risks against the potential benefits of the intervention being studied. At the outset of this doctoral project, the specific form of behavior therapy (ACT-enhanced behavior therapy) evaluated in all three intervention studies within this thesis (Study I, II, and IV) had demonstrated its effectiveness or showed promising results in prior trials of individual therapy for TTM and SPD. Initially, ACT-enhanced behavior therapy might lead to a temporary increase in distress as participants are actively encouraged to trigger their impulses to pull or pick, allowing them to practice embracing these impulses rather than acting on them. This temporary increase in distress is considered an integral part of the treatment, as it is a prerequisite for learning a sounder approach to these impulses. In all studies included in this thesis, every participant was offered the active treatment intervention. The only distinction was that individuals in the control group of Study IV received their treatment one month after the intervention group had concluded their treatment. While this waiting period may have presented a challenge for the participants, it constitutes a crucial aspect of the study's design, motivated by the potential advantages of advancing the development and testing of a treatment that, in the long run, can improve access to treatment.

Additionally, to ensure participant safety, depressive symptoms were monitored through self-ratings every other week during the interventions. If significant changes in mood or signs of suicidality were detected, the therapist promptly contacted the participant for further evaluation. Potential adverse effects of the interventions were closely monitored and transparently reported in both Study II and IV.

As far as the ethical permits allowed, several efforts were made to conduct the studies according to open science principles (Munafò et al., 2017). Studies II-IV were preregistered on the Open Science Framework to ensure strict adherence to predetermined study executing strategies and to prevent any deviations or alterations that could potentially benefit the researchers. Unfortunately, Study I was not preregistered due to an administrative error. To enhance transparency, the results have been thoroughly reported, with supplementary data readily accessible in online appendices. Additionally, they have been made publicly available through open-access publications.

4.5.1 Ethical approvals

Study I: 2014-70231

Study II and III: 2019-06325, 2020-06126

Study IV: 2022-03296-01

5 Discussion

The primary objective of this thesis was to develop and evaluate novel approaches to deliver and scale up the treatment for individuals dealing with TTM and/or SPD.

5.1 Is ACT-enhanced group behavior therapy a feasible treatment for adults with trichotillomania and skin-picking disorder when conducted in a psychiatric setting?

The aim of **Study I** was to evaluate the feasibility, acceptability, and initial efficacy of ACT-enhanced group behavior therapy (AEGBT) for TTM and SPD within a routine psychiatric setting. The overall findings suggested that AEGBT was feasible, as evidenced by its positive reception, low dropout rate, and high attendance rates during the treatment period. Furthermore, the group format seemed to help alleviate feelings of stigma and shame. The results also indicated the preliminary efficacy of AEGBT in reducing symptoms of TTM and SPD when administered to mixed groups of individuals with these conditions in this clinical context. Post-treatment outcomes in our study align with prior research on behavior group therapy for TTM (Diefenbach et al., 2006; Toledo et al., 2015) and individual behavior therapy for SPD (Schuck et al., 2011); however, no previous studies have explored group treatment for SPD. As seen in most previous research (Ninan et al., 2000; van Minnen et al., 2003), only a minority of participants achieved complete abstinence from pulling or picking following treatment, and a small number were considered in remission post-treatment.

Although earlier studies have reported sustained treatment effects for up to 3 months (Schuck et al., 2011; Teng et al., 2006), the 12-month follow-up for SPD of **Study I** is the first of its kind. Treatment effects for TTM remained significant up to the 2-month follow-up, possibly influenced by the smaller number of TTM participants. However, this pattern is consistent with previous research, where relapse after treatment is common for TTM (Diefenbach et al., 2006; Keijsers et al., 2006; Woods, Wetterneck, et al., 2006).

A notable strength of **Study I** is its naturalistic psychiatric setting, along with the inclusion of participants with a diverse array of comorbidities, setting it apart from previous research. Importantly, self-referrals were not accepted, and all participants were derived from standard clinic referrals. Most of the referred

TTM and/or SPD patients were included in the study. However, it is imperative to acknowledge certain limitations in interpreting the findings of **Study I**. The deliberate choice of a small sample size and the omission of a control group, driven by the pilot nature of the trial, raises the possibility that the observed changes could have been influenced by factors unrelated to the treatment. These extraneous influences may include the mere passage of time or the attention and support from caregivers that were not specific to the treatment. Furthermore, our study lacked controls for changes in medication during treatment and the monitoring of treatment sessions, which may have allowed for deviations from the prescribed treatment protocol.

The group therapy approach and the mixing of TTM and SPD patients in the same treatment groups offer more efficient utilization of therapist time and the potential for increased dissemination and availability of evidence-based treatment for TTM and SPD. However, it is important to note that the group format may not inherently make treatment more accessible for individuals residing in geographically remote areas.

5.2 Is internet-delivered acceptance-enhanced behavior therapy a feasible and preliminary effective treatment for adults with trichotillomania and skin-picking disorder when conducted in a psychiatric setting?

In an effort to enhance accessibility to treatment for TTM and SPD, **Study II** built upon prior research on OCDRDs (Andersson et al., 2012; Enander et al., 2016), where iCBT has demonstrated feasibility and effectiveness, subsequently being incorporated into regional care for patients, irrespective of their geographical location. Building on this groundwork and leveraging the treatment protocol from Study I, we developed iBT for TTM and SPD. The aim of **Study II** was to evaluate the feasibility, acceptability, and initial efficacy of iBT for TTM and SPD within a routine psychiatric setting.

Overall, the results indicate high levels of participant satisfaction, treatment credibility, engagement, and therapeutic alliance, coupled with low dropout rates. These findings suggest that the treatment was both feasible and acceptable within the clinical context. However, it is noteworthy that a significant proportion of participants experienced increased stress during the treatment,

indicating the need for further treatment modifications, as discussed below (see section 5.3).

Substantial improvements were observed in the primary outcome measures for both TTM and SPD from pre-treatment to post-treatment, with large effect sizes comparable to prior meta-analyses of mostly in-person behavior therapy (Farhat et al., 2020; Selles et al., 2016). These positive effects were also reflected in the clinician-rated NIHM-TSS/TIS for TTM participants and the disorder-specific secondary outcome measures for SPD. However, it's important to note that only a small subset of participants achieved complete abstinence from pulling or picking, and few reached a state of remission. These findings are consistent with previous research and underline the need for ongoing development and enhancement of TTM and SPD treatments (Ninan et al., 2000; Schuck et al., 2011; van Minnen et al., 2003; Woods, Wetterneck, et al., 2006).

Strengths of **Study II** lie in its use of a routine psychiatric setting with clinically referred participants, distinguishing it from prior online studies that relied on self-referrals and/or self-reported data (C. A. Flessner et al., 2007; Gallinat et al., 2019b; Moritz et al., 2012; Mouton-Odum et al., 2006; Kate Rogers et al., 2014). The study included participants with a wide spectrum of comorbidities, including neuropsychiatric conditions, making the results more generalizable to patients with TTM and SPD in psychiatric care.

Nevertheless, **Study II** has its limitations. Similar to Study I, the intentionally small sample size and the absence of a control group reflect the primary aim of this pilot study — to explore the feasibility and acceptability of the new treatment format, rather than emphasizing its efficacy. However, this design choice opens the possibility that observed changes could be influenced by factors unrelated to the treatment, necessitating caution in interpreting the results. While the absence of a control group restricts conclusions about treatment efficacy, the chronic nature of TTM and SPD (Christenson, Pyle, et al., 1991; Wilhelm et al., 1999) (Wilhelm et al., 1999; Christenson et al., 1991) and the long duration of symptoms in our sample suggest that the treatment's effects are unlikely to be solely attributed to spontaneous remission or non-specific factors.

The lack of statistical power due to the small sample size may explain the non-significant 12-month follow-up effects for TTM participants. An alternative explanation could be the high relapse rates observed in participants with TTM, a pattern reported in previous studies (Diefenbach et al., 2006; Keijsers et al.,

2006; Woods, Wetterneck, et al., 2006). Another limitation of **Study II** was the absence of predefined feasibility assessment criteria, potentially introducing subjectivity into the conclusions. Hence, it is advisable to consider the study as exploratory within this context.

5.3 What are the participants experiences of internet-delivered acceptance-enhanced behavior therapy for trichotillomania and skin-picking disorder?

Study III aimed to assess participants' experiences with iBT and explore ways to enhance treatment effectiveness and its utilization for individuals with TTM and SPD. Thematic analysis yielded five themes labeled as follows: 1) Treatment program, 2) Therapist contact, 3) Treatment components, 4) Participant readiness, and 5) Treatment effects.

In the "Treatment program" theme, most participants reported a positive overall experience, citing the program's helpfulness and relevance. These findings align with the positive outcomes observed in Study II (Asplund et al., 2022). Participants exhibited diverse perspectives on the utility of the treatment format. While some valued the flexibility of the digital format, finding it easy to follow, others faced challenges with self-discipline and motivation.

In the "Therapist contact" theme, participants viewed the contact positively, considering it integral to treatment. Preferences for additional support varied, with some participants desiring physical meetings, video sessions, or phone calls. The importance of therapist support aligns with prior TTM-research, indicating a preference for supported interventions (Arabatzoudis et al., 2021). Furthermore, iCBT trials for various psychiatric disorders also indicate that supported online interventions tend to be more effective than non-supported interventions (Baumeister et al., 2014). For individuals desiring increased support, blended CBT - a treatment format combining the benefits of face-to-face with online interventions, could be worth exploring. Previous research suggest that blended CBT may save both therapist time, lead to decreased drop-out rates and sustained long-term effects. (Erbe et al., 2017)

The "Treatment components" theme highlighted varied experiences with different treatment components. Psychoeducation and reading about fictional patient characters were generally helpful, but some found the provided

examples to be repetitive. Components from HRT and ACT were perceived differently by participants. This highlights the need for further research on the efficacy of each component, in particular to what degree the different components are effective based on the individuals' pulling/picking style.

In the "Participant Readiness" theme, individuals with high daily life stress perceived the treatment's workload as burdensome. Some desired more time, emphasizing the need for a comprehensive assessment of participants' readiness before treatment. Adapting treatment based on individual needs was recommended. Additional practical support, as has been offered in previous iCBT trials for adult patients with ADHD and youth dealing with OCD and autism spectrum disorder could potentially aid these individuals to digest the treatment material and comply with the treatment to a higher extent. Another solution, inspired by a trial on iCBT for insomnia (Forsell et al., 2019) could be to assess the risk of treatment failure early in treatment, and then augment support for those at-risk of treatment failure.

The "Treatment Effects" theme revealed improved understanding and heightened awareness for many participants. Essential strategies were adopted to reduce or cease pulling/picking behavior. While perceived as effective by many, some participants faced challenges, resulting in feelings of failure.

Limitations of **Study III** include the limited diversity of participants, who primarily were females with a university-level education. However, the study's primary aim was not generalization of the results, but to gain insights into experiences, guiding future refinement of iBT.

Insights gained from **Study II** and **III** yielded significant information regarding the feasibility and participant experiences related to iBT. Subsequently, several modifications to the treatment program were implemented before the initiation of Study IV. A brief overview of the key modifications follows.

In response to reported heightened stress levels during iBT, we streamlined the program's content, simplified homework exercises, and introduced the option for audio presentations to facilitate participant focus on core treatment components. To enhance participants' visibility of progress throughout the treatment weeks, we integrated a dynamic visual graph that evolved as participants logged the time spent on pulling/picking each week. Addressing participant requests, we introduced SMS notifications to alert them whenever a

therapist sent a message through the treatment platform. Additionally, the platform underwent updates, featuring a more visually appealing layout and the flexibility to adjust text size.

In sum, findings from Study III suggest that regular iBT might not suit everyone but could be viewed as an early intervention in a stepped care approach, where at-risk participants could be identified and offered intensified digital therapist support or even face-to-face therapy.

5.4 Is internet-delivered acceptance-enhanced behavior therapy disorder an effective treatment for adults with skin-picking disorder?

The aim of **Study IV**, was to evaluate the effectiveness of iBT compared to a waitlist control condition in reducing symptoms of SPD. As expected, our findings revealed that iBT led to significantly greater improvements in skin-picking symptoms compared to the waitlist condition. These improvements were evident in both clinician- and self-rated outcomes, with substantial between-group effect sizes observed immediately post-treatment and at the controlled one-month follow-up. In general, the between-group effect sizes in our study align with those reported in prior waitlist-controlled trials assessing traditional face-to-face behavior therapy for SPD (Schuck et al., 2011; Teng et al., 2006), and were generally larger than those found in previous studies of unguided online interventions (Gallinat et al., 2019b; Moritz et al., 2012; Moritz et al., 2023). This difference may be attributed to the therapist-guided nature of our iBT treatment, potentially leading to higher compliance rates. The incorporation of ACT-elements into traditional Habit Reversal Therapy (HRT) could also have increased participant engagement with the active exercises.

Furthermore, the findings also demonstrated high feasibility. Impressively, 80% of participants in the iBT group successfully completed all ten program modules. The majority of participants expressed satisfaction with the treatment, with over 90% stating they would recommend it to others. Few adverse events were reported, and none were severe. Participants found iBT highly acceptable and credible, with a positive perception of the working alliance.

Notable strengths of this **Study IV** include its large sample size, minimal data attrition, clinician-verified diagnoses, long-term follow-ups, and the use of

blinded assessors. However, several limitations should be noted and some of these are outlined below. Firstly, we employed a passive control condition, enabling control over factors like the passage of time and repeated assessments but precluding control over unspecific treatment effects such as expectancy or alliance effects. A logical next step would be to compare iBT against an active comparator and/or traditional face-to-face BT. Another limitation is the absence of controlled long-term follow-ups beyond one-month post-treatment. Self-referral of participants in the current study might affect the generalizability of the findings to SPD patients in psychiatric outpatient clinics, although the sample demographics did not significantly differ from the clinician-referred sample in Study II conducted within a psychiatric setting (Asplund et al., 2022).

5.5 Future directions

The findings derived from the studies included in this thesis offer valuable insights into existing research on TTM and SPD. Moreover, the execution of these studies has led to the emergence of new research inquiries, which will be delineated below as potential avenues for future investigation.

While participants in Studies I, II, and IV exhibited substantial improvements in the severity of TTM and/or SPD, only a few achieved remission. This trend aligns with prior research (Ninan et al., 2000; Schuck et al., 2011; van Minnen et al., 2003; Woods, Wetterneck, et al., 2006) and underscores the necessity for further innovations of TTM and SPD treatments.

One potential strategy to enhance the effectiveness of iBT could involve early identification of high-risk non-responders, followed by tailored adjustments or treatment scaling, as demonstrated in internet-delivered treatments for insomnia (Forsell et al., 2019). Identifying individuals with low treatment adherence during early intervention stages could indicate poor treatment response, as seen in face-to-face OCD, where early patient adherence significantly predicted treatment outcomes (Simpson et al., 2011). Offering additional forms of complementary support, such as video-sessions and SMS reminders, to individuals with low treatment adherence could potentially augment iBT effectiveness.

Another approach to increase patient engagement is the implementation of "modular treatments", tailored to address each participant's specific needs.

Allowing patients to focus on treatment components addressing their unique problems or type of pulling/picking might enhance motivation and effectiveness in iBT for TTM and SPD, consistent with studies on other psychiatric disorders (Chorpita et al., 2017). For instance, in the context of TTM/SPD treatment, a modular iBT program would enable patients whose pulling/picking behaviors are primarily triggered by emotional instability to forgo the stimulus control treatment component - considered short-term and ineffective by some - and instead concentrate on learning emotion regulation techniques, which they may find more beneficial.

As relapse or deterioration post-acute treatment is common among TTM and SPD patients across treatment formats (Asplund et al., 2022; Diefenbach et al., 2006; Keijsers et al., 2006; Woods, Wetterneck, et al., 2006), future research should concentrate on methods to improve long-term motivation and outcomes. Our iBT program incorporates several booster modules as a means to bolster maintenance. However, while both Study II and IV demonstrated high average module completion during the acute treatment phase, adherence to booster modules was considerably lower. Long-term outcomes in both studies varied, and the study designs do not allow for in-depth conclusions from these results. To ascertain if long-term outcomes are improved by the inclusion of booster sessions, future research should compare a group receiving boosters with another not receiving them. If the addition of boosters proves beneficial in maintaining treatment outcomes, a subsequent step would be to explore ways to optimize booster adherence. Absent these results, a potential strategy to boost maintenance might involve identifying individuals who deteriorate post-treatment and offering tailored support. For instance, tailored booster sessions could encompass increased therapist dosage and more visual feedback on treatment gains (e.g., highlighting less visible hair regrowth/skin healing). Furthermore, providing additional guidance on the long-term benefits and the necessity of continued post-treatment exercises might also be advantageous.

Fortunately, as part of this thesis and in other studies, promising treatment alternatives have been developed, aiming to enhance the availability and accessibility of treatment for TTM and SPD. Nonetheless, a substantial number of individuals suffering from these disorders still lack access to appropriate care. Therefore, the primary and most significant challenge ahead involves disseminating these treatments to a broader population. One of the crucial next

steps in TTM and SPD research is thus to evaluate the effectiveness of iBT when delivered and implemented in regular healthcare systems.

Finally, to enable meaningful comparisons between trials, it is crucial to establish standardized criteria for defining response and remission after treatment. A precedent for such an initiative exists for instance in the field of OCD, where a multi-round, web-based survey resulted in global expert consensus on operationalized definitions of treatment response, remission, recovery, and relapse (Mataix-Cols et al., 2016). Using this approach for SPD and TTM could potentially ensure consistency and facilitate effective communication within the research community.

6 Conclusions

The overall aim of this thesis was to enhance accessibility and availability of evidence-based treatment for TTM and SPD by developing and evaluating the feasibility and effectiveness of innovative treatment approaches. Summarized below are the conclusions drawn from the four studies comprising this thesis.

Study I concluded that ACT-enhanced group behavior therapy (AEGBT) for mixed diagnosis groups, encompassing adult patients with TTM and/or SPD, proved to be a feasible, acceptable, and safe treatment approach within routine psychiatric care. The study offered initial evidence of the intervention's efficacy. Long-term outcomes varied based on diagnosis, favoring SPD-participants. However, further research is needed, including studies with larger sample sizes and active control conditions.

Conducted within a routine psychiatric setting, **Study II** similarly demonstrated the feasibility, acceptability, and safety of therapist-supported internet-delivered behavior therapy (iBT) for TTM and SPD patients. Study II revealed iBT as a preliminarily effective intervention in reducing TTM- and SPD-related symptoms post-treatment. Echoing **Study I**, long-term efficacy favored SPD participants over those with TTM.

Study III provided insights into the advantages and challenges associated with iBT, leading to crucial modifications in the iBT program applied in Study IV. Furthermore, Study III outlined areas for further research and enhancement to augment treatment efficacy and its applicability to a broader participant spectrum, including tailored treatments addressing individual needs.

In an academic setting, **Study IV** demonstrated the efficacy and sustained long-term benefits of iBT for adult SPD participants compared to a passive control condition. These findings further supported iBT as a feasible, acceptable, and safe intervention. Additional research, encompassing studies with active control conditions and non-inferiority trials, alongside cost-effectiveness analyses comparing face-to-face behavior therapy versus iBT, are warranted.

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