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EMOTION REGULATION AS A TRANSDIAGNOSTIC CONSTRUCT: NOVEL APPROACHES TO PSYCHIATRIC DIAGNOSTICS

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Emotion regulation as a transdiagnostic construct: Novel approaches to psychiatric diagnostics
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By

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"… it is a mistake to say that we suffer from feelings. We suffer from the defective contingencies of reinforcement responsible for the feelings."

– B.F. Skinner

Popular science summary of the thesis

Mental health problems are common in our society. To study, treat, and communicate problems that cause distress or impairment in a clinically significant way, researchers and healthcare staff use diagnostic classification systems to sort symptoms into categories (for example intense and excessive fear coupled with avoidance of spiders would be classified as specific phobia). If a person fulfills certain criteria for a disorder (here defined according to the Diagnostic and Statistical Manual of Mental Disorders), they can usually be diagnosed and potentially be provided with help by health care services. Research has shown that individuals fulfilling diagnostic criteria for one disorder often fulfill criteria for one or more additional disorders, something referred to as diagnostic co-occurrence. This tendency for mental health problems to co-occur can for example make treatment decisions more difficult, since much of treatment research historically has been based on investigating one disorder category at a time (for example, testing treatments adapted towards persons who only have specific phobia). Importantly, diagnostic co-occurrence has been shown to be associated with poorer outcomes for those affected, in comparison to individuals who experience problems within only one disorder category.

Researchers have argued that the fact that psychiatric diagnostic co-occurrence is common motivates also doing research that cuts across diagnostic boundaries, commonly referred to as "transdiagnostic". Transdiagnostic research means studying for example risk factors and treatments that could be relevant for several different types of mental health problems. One example of a transdiagnostic factor that has been studied is emotion regulation, which is an individual's ability to identify, react, and respond to their emotions in a helpful way. To what extent individuals successfully regulate their emotions is thought to be an important factor for several types of mental health problems (such as anxiety, eating disorders, and self-injurious behavior). Some behaviors could even be seen as serving the purpose of regulating emotions (for example drinking to get rid of anxiety).

This thesis aims to address some of the questions related to diagnostic co-occurrence and the relevance of emotion regulation to psychiatric problems in different ways. To date, research has to a large extent investigated how psychiatric diagnoses co-occur at a specific time point. Less research has investigated how individuals transition between different mental health problems over time, and what risk factors are associated with this "shifting". Furthermore, although emotion regulation has been well examined in previous research, many ways of defining the concept exists and some areas are still unexplored. More research is needed on how we currently define and measure emotion regulation to better understand what we are capturing with our measures. More

research is also needed which explores emotion regulation across a spectrum (at different levels) of mental health problems.

To understand if individuals shift between different mental health problems over time, two studies were done with data from questionnaires available in Swedish registries. In **Study I**, data from eating-disorder clinics was used (from the Stepwise registry). This included adults with eating disorders who had, upon admission to the clinic and 12 months after admission, filled out various questionnaires about their mental health, including eating disorder-related behaviors, emotion regulation difficulties, and other psychiatric symptoms (such as depression and anxiety). In this study, a novel method of studying symptom change was proposed and named "symptom shifting". Results showed that 13% of individuals in the sample had shifted between different eating disorders-related behaviors over time, a number that increased to 19% when also examining whether individuals also shift to other risky behaviors (self-injurious behaviors and substance use). Individuals whose symptoms had shifted reported more emotion regulation difficulties and more psychiatric symptoms, compared to those who did not symptom shift. In **Study II**, symptom shifting between eating disorder and substance use symptoms was further investigated using data from the Swedish Twin Registry. In this general population group, measured twice between 18- and 24-years age, 2% of individuals fulfilled criteria for a symptom shift. When comparing individuals who had reported symptom shifting with other groups, such as individuals without symptoms of eating disorders or substance use disorders, they similarly to Study I reported more psychiatric symptoms and had a genetic profile indicating higher risk for developing psychiatric problems.

To further develop our knowledge of emotion regulation as a transdiagnostic factor, two studies were performed including data on adults from the US. Two main samples were studied, one from the general community and one with individuals in residential treatment for substance use problems. In **Study III**, two of the most well-used questionnaires measuring emotion regulation were evaluated and compared to one another using psychometric methods (statistical analyses to evaluate reliability and validity) in the community sample. Results suggested that both measures were related to one another in expected ways and showed acceptable psychometric properties (also including a short version of one of the measures). However, one of the measures showed a greater association with psychiatric symptoms, suggesting it could be more relevant to use in clinical contexts. In **Study IV**, the residential treatment sample was added to the community sample and the relationship between emotion regulation and different levels of substance use (ranging from no use to heavy use) was explored. Results suggested that there was an association between emotion regulation difficulties and using substances more often, which resembled an approximate dimensional relationship

(meaning the more frequent and severe the substance use, the more emotion regulation difficulties and vice versa).

The studies in this thesis contribute with 1) a new way of studying psychiatric symptom fluctuation across different problem areas over time, which adds knowledge on our understanding of mental health problems and their manifestations, and 2) filling out relevant gaps in the literature on emotion regulation, which adds knowledge on its measurement as well as its relevance to different severities of mental health problems. A short summary of the literature on transdiagnostics, as well as discussions of the results and suggestions for future research, are also included in the thesis.

Abstract

Diagnostic co-occurrence among mental health problems is common. It has been suggested that more research which incorporates analysis on the symptom level and cuts across categorical diagnostic boundaries is needed. This type of transdiagnostic research could have the potential to further increase our understanding of psychopathology and how we can improve treatment outcomes. Emotion regulation is one transdiagnostic process which is thought to be of relevance to several types of mental health problems. These problems include eating disorders and substance use disorders, two areas that both show a significant overlap and are associated with emotion regulation difficulties. The current thesis thus aimed to contribute to the further understanding of (a) symptom-level change and (b) measurement of emotion regulation and its role across different levels of mental health problems (with a focus on eating- and substance use disorders).

The aim of **Study I** was to investigate symptom change over time, by assessing if treatment-seeking adults with eating disorders (N = 3159) demonstrated "symptom shifting" (simultaneously decreasing in some symptoms whilst increasing in others). Individuals demonstrating symptom shifting were then compared to nonshifting individuals on various indicators of mental illness. In the sample, 13% were found to demonstrate symptom shifting among eating disorder-related behaviors. The proportion of patients with symptom shifting increased to 19% when including shifts to deliberate self-harm or substance use (in addition to eating disorder-related behaviors). Individuals with symptom shifting reported significantly higher levels of other psychiatric symptoms (such as depression and anxiety), clinical impairment, and emotion regulation difficulties compared to nonshifting individuals. It was concluded that individuals with symptom shifting could be a group in need of tailored monitoring in clinical practice, as well as treatment approaches targeting several types of risky behaviors.

The aim of **Study II** was to further investigate symptom change over time, by investigating if symptom shifting occurred between symptoms of eating- and substance use disorders in a general population sample (N = 3315). Individuals with symptom shifting were also compared to other individuals with different temporal symptom profiles. A small group of individuals (2% of the whole sample) demonstrated symptom shifting (which represented 10% of individuals who suffered persistent problems in any or both areas). Individuals with symptom shifting reported higher levels of psychiatric symptoms (such as depression, anxiety, suicidality) and demonstrated higher polygenic risk scores for psychiatric disorders. Levels were comparable to individuals who suffered persistent co-occurring problems with eating- and substance use disorder symptoms over time. The results contribute to the understanding of the overlap between eating- and substance use disorders, and again highlight the need for health care services and treatments that address several problem areas simultaneously.

The aim of **Study III** was to evaluate psychometric properties and contrast two of the most used measures of emotion regulation, for which a community sample of adults residing in the US was used (N = 843). The Emotion Regulation Questionnaire (ERQ) and the Difficulties in Emotion Regulation Scale (DERS; including its short form DERS-16) were evaluated using correlations and confirmatory factor analyses. The measures were found to converge in expected ways. Satisfactory fits were found for the ERQ and DERS-16, but not for the original DERS. The DERS showed greater concurrent validity with

psychiatric symptoms (depression, anxiety, stress, substance use) than the ERQ. It was concluded that the validity of both measures to assess emotion regulation was supported, and that the DERS–16 with its shorter format is a clinically useful tool to assess emotion regulation in practice.

The aim of **Study IV** was to investigate the relationship between emotion regulation difficulties across different levels of substance use, and the role of co-occurring psychiatric symptoms. Data from two main sources were used, including the community sample in Study III (n = 843) and two substance use disorder populations from residential treatment clinics in the US (n = 415). Emotion regulation was significantly associated with both substance use frequency and severity across a variety of substances. Of the different facets of emotion regulation (DERS subscales), difficulties controlling impulsive behaviors was found to be specifically associated with greater substance use severity. No significant moderating effect of psychiatric symptoms (depression, anxiety, stress) was found. Results suggested that emotion regulation difficulties are of increasing relevance across the spectrum of substance use, from no use, to misuse, to poly–substance dependence.

The studies could contribute to method development in the area of symptom–level change and furthers our understanding of emotion regulation as a relevant transdiagnostic construct. They also could contribute by highlighting important clinically relevant outcomes (such as symptom shifting), which could have potential implications in psychiatric research and clinical practice/health care. Studying common functions of risky behaviors, such as eating disorder-related behaviors, substance use, and deliberate self-harm, from an emotion regulation perspective is suggested to be of importance to consider in future research.

List of scientific papers

I. **Garke, M.**, Sörman, K., Jayaram-Lindström, N., Hellner, C., & Birgegård, A. (2019). Symptom shifting and associations with mental illness: A transdiagnostic approach applied to eating disorders. *Journal of Abnormal Psychology*, *128*(6), 585–595. https://doi.org/10.1037/abn0000425

II. **Garke, M.Å.**, Molero, Y., Birgegård, A., Lichtenstein, P., Bulik, C.M., Sörman, K., Hellner, C., Larsson, H., Lundström, S., & Jayaram-Lindström, N. Symptom shifting between eating- and substance use disorders: A transdiagnostic approach applied to a general population sample. Manuscript.

III. Sörman, K., **Garke, M. Å.**, Hentati Isacsson, N., Jangard, S., Bjureberg, J., Hellner, C., Sinha, R., & Jayaram-Lindström, N. (2022). Measures of emotion regulation: Convergence and psychometric properties of the Difficulties in Emotion Regulation Scale and Emotion Regulation Questionnaire. *Journal of Clinical Psychology*, *78*(2), 201–217. https://doi.org/10.1002/jclp.23206

IV. **Garke, M. Å.**, Hentati Isacsson, N., Sörman, K., Bjureberg, J., Hellner, C., Gratz, K. L., Berghoff, C.R., Sinha, R., Tull, M.T., & Jayaram-Lindström, N. (2021). Emotion dysregulation across levels of substance use. *Psychiatry Research*, *296*, 113662. https://doi.org/10.1016/j.psychres.2020.113662

Scientific papers not included in the thesis

Garke, M.Å., Hentati Isacsson, N., & Kaldo, V. (2021). A possibly mean mean: The importance of considering heterogenous change in discrete symptoms when defining outcomes of cognitive behavioral therapy for patients with anxiety and mood disorders. Preprint available at PsyArXiv, doi: 10.31234/osf.io/q6532

Garke, M.Å., Hentati Isacsson, N., Kolbeinsson, Ö., Hesser, H., & Månsson, K.N.T. Improvements in emotion regulation during cognitive behavioral therapy predicts subsequent social anxiety reductions. Submitted manuscript.

Contents

List of abbreviations

DSM	Diagnostic and Statistical Manual of Mental Disorders
ICD	International Classification of Diseases
RDoC	Research Domain Criteria
HiTOP	Hierarchical Taxonomy of Psychopathology
ED	Eating Disorder
SUD	Substance Use Disorder
ERQ	Emotion Regulation Questionnaire
DERS	Difficulties in Emotion Regulation Questionnaire
EDE-Q	Eating Disorder Examination Questionnaire 4.0
DSHI	Deliberate Self-Harm Inventory
AUDIT	Alcohol Use Disorder Identification Test
PRS	Polygenic Risk Score
CATSS	Child and Adolescent Twin Study in Sweden
EDI-2	Eating Disorder Inventory-2
DUDIT	Drug Use Disorder Identification Test
MDD	Major Depressive Disorder
ADHD	Attention-Deficit Hyperactivity Disorder
PTSD	Post-Traumatic Stress Disorder
CES-D	Center for Epidemiological Studies Depression Scale
SCARED	Screen for Child Anxiety Related Emotional Disorders
BOCS	Brief Obsessive Compulsive Scale
DERS-16	Difficulties in Emotion Regulation Scale 16-item
STAI	State Trait Anxiety Inventory
PSS	Perceived Stress Scale
ASI	Addiction Severity Index
DUQ	Drug Use Questionnaire
DASS-21	Depression Anxiety and Stress Scale 21-item
S-DERS	State Difficulties in Emotion Regulation Scale

Introduction

We are yet to gain a full understanding of what psychiatric disorders are, and what factors cause the development and maintenance of mental health problems. What human mental suffering is and how we can quantify it is an ongoing discussion. Still, it is abundantly clear that people suffer from such issues, and that more effective and precise treatments are needed.

When trying to understand mental health problems we must firstly conceptualize and define them. For several decades, psychiatric disorders have been viewed as separate entities encapsuled in a dichotomy of health/sickness. However, in more recent years, complementary theoretical frameworks have been developed and initially tested. One prominent framework laid out within psychiatry and clinical psychology has been that of transdiagnostics. As suggested by the Latin prefix, transdiagnostics aims to cut across or beyond the boundaries of the classic categorical diagnoses as we know them today. Given the fact that psychiatric disorders frequently co-occur, the hope is that an increased understanding of processes that might drive the expression of several mental health problems, or common denominators among them, could advance our theoretical understanding of what mental illness is and in turn our ability to deliver effective treatments for some individuals.

This Ph.D. project came about from a collective desire among me, my supervisors, and colleagues to further our understanding of the scientifically and clinically observed overlap among some of the problem areas we study at the Centre for Psychiatry Research, including substance use disorders, eating disorders, and deliberate self-harm.

The thesis comprises two main overarching themes: development of transdiagnostic methods in psychiatry, and further understanding of emotion regulation as a transdiagnostic construct. These themes will be brought up and exemplified in relation to historical and recent scientific discussions within psychiatry, and in turn tied into the framework of the studies that constitute the current thesis.

During the scope of this thesis, I will use terms such as mental health problems, mental illness, psychopathology, psychiatric disorders, and psychiatric diagnoses. This does not necessarily tie to any personal ontological or epistemological standpoints. I appreciate the slightly different meanings associated to these terms but will take a pragmatic approach to the use of them to describe the issues we want to address when we try to understand and help individuals who are suffering. I am personally theoretically grounded in behavior science, and thus take a pragmatic stance that what helps the patient is useful.

Maria Åbonde Garke, Stockholm, August 2022.

1 Literature review

Psychiatric disorders are prevalent in society, and it is the rule rather than the exception that disorders co-occur (Kessler, Chiu, et al., 2005; McGrath et al., 2020). Furthermore, symptoms (or risky behaviors) associated with some specific diagnoses that the current thesis focuses on, such as binge eating/vomiting, substance use, and deliberate self-harm, usually tend to be positively associated with one another (Serras et al., 2010). Diagnostic co-occurrence, often referred to as co-morbidity in medicine, is not only associated with greater impairment for afflicted individuals, but has also been argued to question the validity (Kendell & Jablensky, 2003) of treating diagnoses as distinct categories as stated in the Diagnostic and Statistical Manual of Mental Disorders (DSM; American Psychiatric Association, 2013, 2022; Dalgleish et al., 2020). Much of previous research on the etiology and treatment of mental health problems has focused on investigating different psychiatric disorders separately (Hayes et al., 2020), resulting in knowledge relevant to the subgroup of individuals who fulfill diagnostic criteria for a single disorder at a given time (Hyman, 2010). Although categorical psychiatric diagnoses show utility in practice (Kendell & Jablensky, 2003), some individuals still fail to get relief from their symptoms with the diagnosis-specific treatments that are currently available (Barlow et al., 2017). The potentially variable validity of our current classification system and the fact that available treatments are only partly effective for some individuals, are suggested to be two interconnected issues.

These issues and their interconnection are the starting point for this thesis.

1.1 Diagnostic classification and transdiagnostic approaches

1.1.1 A short history of diagnostic classification and its critique

Psychiatric diagnostics has been a topic of scientific and clinical debate since the advent of psychiatry as a medical specialty. During the past decades, this discussion has had increasing focus around the prevailing system of descriptive classification of psychiatric diagnoses, manifested as the DSM (American Psychiatric Association, 2013, 2022) and the International Classification of Diseases (ICD; World Health Organization, 2019). During the debate thus far, one argument that has been put forward by critics of the prevailing system is that the current diagnostic classification system does not fully capture psychopathology, including the overlap between psychiatric conditions. This will be discussed in further detail in the proceeding section. Next, a historical background will be presented to contextualize the increased focus on transdiagnostic theories, meaning an approach to understand psychological disorders across and beyond the conceptual structure provided by the notion of diagnosis (Fusar-Poli et al., 2019).

The DSM was published in its first edition in 1952 by the American Psychiatric Association (Compton & Guze, 1995). At the time, the initiative and success in

structuring a diagnostic manual for psychiatric disorders was a big leap forward considering the many benefits of a unifying nomenclature. The introduction of the revised DSM–III during the latter part of the 20th century (American Psychiatric Association, 1980), vastly increased diagnostic reliability and proved a highly useful tool for clinicians and researchers alike. During this time, the focus also shifted towards atheoretical descriptive diagnostics in the context of the medical model. This was in contrast to previous editions who were mainly based in psychodynamic theory (Wilson, 1993). The approach applied in the DSM–III implicitly suggested that the symptoms listed under each diagnosis are caused by an underlying pathology, or are based in biological essences (Kendler, 2016). Taken to its extreme, each disorder was thus thought to be a separate entity with its own etiology. This viewpoint further entailed that treating the underlying pathology (e.g., insufficient levels of neurotransmitters) would result in relief of symptoms and thus "cure" the disease. The DSM and its way of classifying and establishing mental health problems as medical disorders has since its advent permeated our society, certainly so in the West, including how we view and treat mental disorders as well as how we structure healthcare (Dalgleish et al., 2020).

Although the prevailing diagnostic system has proven to be useful in many respects in both research and clinical practice, researchers within the fields of psychiatry and clinical psychology have proposed that the nosology as presented in the DSM may have some theoretical limitations (e.g., Andersson & Ghaderi, 2006; Brown & Barlow, 2009; Caspi et al., 2014; Cuthbert & Insel, 2013; Follette & Houts, 1996; Hyman, 2010; Lilienfeld & Treadway, 2016; Maj, 2018). These limitations include for example (*i*) the heterogeneity of diagnoses, (*ii*) the high rates of co-morbidity, and (*iii*) the reification of diagnoses (i.e., diagnoses being treated as real entities) across time (Hyman, 2010). In other words, the nosology perhaps does not carve nature at its joints nor supports an essentialist view of psychiatric disorders (Kendler et al., 2011). An example of such heterogeneity are the DSM diagnostic criteria for posttraumatic stress disorder, where the possible symptom combinations can lead to no less than 636 120 ways of fulfilling diagnostic criteria (Galatzer-Levy & Bryant, 2013). The reification of psychiatric diagnosis also risks researchers falling into circular reasoning, where the diagnosis becomes the explanation of the symptoms that made up the diagnosis in the first place (see also *Figure 1*). Furthermore, researchers participating in the discussion regarding psychiatric diagnostics and nosology have argued that a direct causal relationship between an underlying physiological dysfunction and the symptoms of mental illness we observe is unlikely (Kendler, 2014b, 2016), which could fundamentally question the way we view and treat psychiatric disorders. Researchers have interconnectedly argued that potential limitations of the DSM could contribute to individuals not reaching satisfactory treatment results (Hershenberg & Goldfried, 2015; Wong et al., 2010). Hypothetically, if selection of participants to treatment research rests on certain categorical diagnoses

which do not fully capture the nature of mental illness, the results may naturally not be generalizable depending on the treatment's model of action (R. Cooper, 2014).

1.1.1.1 *The phenomenon of diagnostic co-occurrence*

One topic of relevance to this thesis is that of diagnostic co-occurrence, or co-morbidity. Psychiatric co-morbidity (as in fulfilling diagnostic criteria for more than one disorder) has been shown to be highly prevalent (Clark et al., 2017; Kessler, Chiu, et al., 2005), being the rule rather than the exception. The term began being increasingly used in psychiatry and psychology during the late 20th century, coinciding with the publication and use of the DSM-III (Lilienfeld et al., 1994). Although co-morbidity is a common and expected phenomenon among medical diagnoses in general, co-morbidity in the realm of psychopathology usually also encapsulates the fact that having one psychiatric disorder increases the risk of having or developing other psychiatric disorders (Hyman, 2019; Krueger & Markon, 2006). The frequent correlation among psychiatric disorders is of relevance to further study, and this way of thinking about co-morbidity is the one referred to in this thesis (which more broadly will be referred to as co-occurrence). In addition to fulfilling diagnostic criteria for more than one disorder at a given point in time, individuals could also undergo diagnostic transitions over time (Copeland et al., 2013). In a prospective large-scale population study investigating such transitions during childhood, adolescence and young adulthood, some individuals both transitioned within one disorder category (meaning fulfilling criteria for a disorder was predictive of having the same disorder at a later stage) as well as between different disorder categories (Copeland et al., 2013). Naturally, as diagnostic categories are composed of individual symptoms, symptoms across diagnostic categories also tend to co-occur. Endorsement of individual symptoms within one or more diagnostic categories also fluctuate over time, including fluctuations in the context of treatment (Garke et al., 2021). However, symptom transitions between different problem areas over time have been less studied. In summary, psychopathology and mental health problems are inherently complex (Kendler, 2016), and how we best describe it is an empirical question (Kendler, 2014a).

1.1.2 **Alternative transdiagnostic conceptualizations of mental illness**

Some recent developments have been made to try to address the above stated limitations of the prevailing psychiatric nosology and diagnostic classification systems. These types of alternative and/or complementary frameworks for understanding and studying psychopathology contribute in different ways to the growing body of discussions on transdiagnostic perspectives. The common denominator across these alternative frameworks is the focus on a symptom level analysis cutting across diagnostic boundaries, with the aim to possibly complement (or even replace) the current diagnostic system in the future.

A short summary of three of the more well-known alternative frameworks are presented. See *Table 1* for an overview and comparison of these frameworks.

1.1.2.1 *Research Domain Criteria*

The Research Domain Criteria (RDoC) initiative, emanating from the National Institute of Mental Health, was a reaction to the growing critique of the DSM (Cuthbert & Insel, 2010). Stemming from biological psychiatry, the RDoC initiative has during the past decade created a sketch of a new type of research program, meant to be developed over time (Cuthbert & Insel, 2013; Insel, 2014). This classification system of sorts (referred to as a "matrix") rests on "dimensions" of relevant constructs making up the basis of human functioning, with these basic functions meant to range from normality to pathology (Elmer et al., 2016). Dimensions (with examples of constructs in parentheses) currently included are negative valence systems (anxiety, fear), positive valence systems (reward learning), cognitive systems (perception, language), systems for social processes (attachment, social communication), arousal/regulatory systems (arousal, sleep/wakefulness), and sensorimotor systems (motor actions) (Sanislow et al., 2022). This framework provides a contrasting bottom-up approach to how we understand the etiology of psychiatric disorders, compared to the top-down approach utilized in the DSM (see *Figure 1*). This method of understanding and studying psychopathology is agnostic to psychiatric nosology and can therefore be applied transdiagnostically, disregarding diagnostic categories altogether. However, critique has also been raised towards the RDoC system. For example, researchers have argued that it is too reductionistic with an overemphasis on biologically-based units of measure (Lilienfeld, 2014; Parnas, 2014). Nevertheless, research based in the RDoC framework has been ongoing since its launch, and the hope of its proponents is that it may inform future nosology (Cuthbert, 2022b).
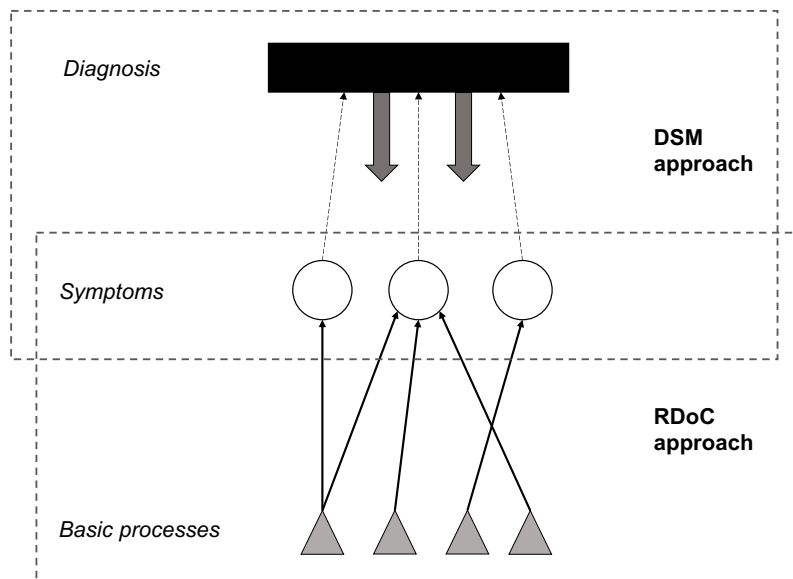
Figure 1. Illustration of the bottom-up approach of the RDoC framework vs the top-down approach taken within the framework of the DSM (bold dark grey arrows illustrating the risk of circular reasoning that comes with the reification of diagnoses).

1.1.2.2   *HiTOP and the p-factor*

Another theoretical idea ascribing to a transdiagnostic view of psychopathology is the Hierarchical Taxonomy of Psychopathology, or HiTOP for short (Kotov et al., 2017). Based in clinical psychology, the consortium behind the HiTOP propose an alternative taxonomy and reorganization of the current classification system, using statistical models to derive groupings and higher order dimensions of psychopathology (Kotov et al., 2017). This alternative framework highlights the importance of understanding syndromes as dimensional phenomena, in concordance with the RDoC initiative. However, the HiTOP is proposed to be a purely quantitative atheoretical classification of symptoms and higher-order dimensions specifically applied to psychopathology, using factor analysis as the main tool to group symptoms and syndromes into a hierarchy including both broader spectra and all the way down to narrow symptoms/components. The hierarchical and dimensional way of classifying psychopathology tries to solve the main issues with the DSM classification system, such as removing thresholds based on "clinical significance" and incorporating diagnostic co-occurrence by allowing higher-order spectra across different disorders (Kotov et al., 2017; Krueger et al., 2018; Lahey et al., 2021). The proponents of modeling psychopathology hierarchically suggest that there is a higher-order factor, also referred to as the p-factor or general factor of psychopathology (Caspi et al., 2014). This general factor could be of potential relevance in our attempt to understand and treat psychopathology, since it both mirrors the co-variance among mental disorders and could be used to reflect a general level of distress and impairment (Pettersson et al., 2021). However, more research is needed to explore

whether this statistical latent variable has a physical base in for example genetics (Fried et al., 2021).

This line of research is in its infancy, but due to the framework being more of a "remodeling" of the current nosological system rather than a completely novel ontological approach to psychopathology, researchers have suggested ways in which the HiTOP could be currently implemented into clinical practice (Ruggero et al., 2019). Researchers have pointed out some noteworthy limitations with the HiTOP approach as well. For example, it has been argued that it is simply a "factor-analytic articulation of the content of the DSM" (Haeffel et al., 2022, p 286). The fact that it, similarly to the DSM, is descriptive and atheoretical in terms of etiological processes could equally hinder development of our understanding of what processes underly mental health problems (Haeffel, Jeronimus, Kaiser, et al., 2022).

1.1.2.3   Network approach to psychopathology

A further theoretical idea ascribing to a transdiagnostic view of psychopathology is the "network approach to psychopathology" (Borsboom, 2017). Network analysis is a method that has been applied in a wide variety of settings, such as for modeling social phenomena (Borgatti et al., 2009). The rationale for applying network analysis to psychopathology suggests that monocausal explanations of mental health problems are unlikely, and that models that can incorporate the multifactorial and transdiagnostic mechanisms behind psychopathology are needed (Borsboom et al., 2019). This type of analysis does not view symptoms as indicators of a latent condition (as in for example the medical model of psychiatric disorders), but rather views symptoms as components able to affect one another in their own right. The researchers, in other words, suggest that psychiatric symptoms likely have direct causal inter-relationships, with symptoms interacting with one another in different ways across different individuals and over time (Fried et al., 2017). This fits well with the idea presented previously, that the concept of co-morbidity within mental disorders also incorporates the fact that symptoms or diagnoses are associated with one another (McNally, 2021).

The researchers behind the network model approach to psychopathology have shown, using statistical network modeling of the psychiatric symptoms included in the DSM, that symptoms across diagnoses are tightly connected and related to each other in various ways (Borsboom et al., 2011). The network model approach to psychopathology has been applied to various symptoms both inside and outside those included in the DSM, and has for example tried to estimate which symptoms are the most central ones (based on symptom interconnectivity) (Robinaugh et al., 2020). To exemplify, initial studies applying network analysis to eating disorders (ED) cross-sectionally has shown that body- and shape concerns seem to be central in ED symptom networks (Smith et al., 2018), suggesting they may be important targets for treatment. Research applying

network analysis to substance use disorders (SUD) is largely lacking, with only one study analyzing symptom relations cross-sectionally across the DSM-criteria (Rhemtulla et al., 2016). Overall, this line of research is relatively new and more studies with a longitudinal design are needed to understand temporality of symptom relations, and how symptoms may fluctuate over time (McNally, 2021).

Table 1. Overview and comparison of alternative frameworks

	TYPE OF TRANS-DIAGNOSTIC APPROACH	RESEARCH TRADITION	ONTOLOGY	CLINICAL APPLICATIONS
RESEARCH DOMAIN CRITERIA	Foregoes DSM taxonomy, research-focused	Medicine, biology, psychiatry	Assumes realism of mental illness, reductionism	Has mainly informed study design so far (Cuthbert, 2022a; Pacheco et al., 2022)
HIERARCHICAL TAXONOMY OF PSYCHOPATHOLOGY	Could forego DSM taxonomy, descriptive	Clinical psychology, psychiatry	Atheoretical, empirical	Could be applied in the clinic, potentially ready for use during 2022 (DeYoung et al., 2022)
NETWORK APPROACH TO PSYCHOPATHOLOGY	Foregoes DSM taxonomy	Psychology, clinical psychology	Opposes reductionism, proponents of pluralistic accounts	Mainly contributions to method development (Borsboom, 2022)

1.1.3   Current status of transdiagnostic theory and future relevance

Taken together, these alternative frameworks attempt to investigate psychopathology using a symptom-level analysis, complementing the existing diagnosis-level analysis, to further our understanding of psychopathology. Researchers have also suggested that a dimensional perspective could be worth considering to complement the dichotomous classification of illness vs no illness (Brown & Barlow, 2009; Kapur et al., 2012; Zachar & First, 2014). The idea of dimensionality has been around for a long time in the field of psychology, with one recognizable example being the concept of personality (John &

Srivastava, 1999). For example, the idea of dimensionality was incorporated in the DSM–5 to some extent (American Psychiatric Association, 2013, 2022). Dimensionality can be visualized as a gliding scale with two endpoints, where individuals could hypothetically be mapped on different symptoms and/or processes to create an individual profile. One current example can be found in Section III of the DSM–5 (emerging models and measures) for the diagnosis of personality disorders, which combines a categorical and dimensional approach (J. L. Anderson et al., 2018). An example of a treatment that has been developed founded on a dimensional classification of anxiety and mood disorders in line with the HiTOP (Brown & Barlow, 2009), is the Unified Protocol (Ellard et al., 2010). The Unified Protocol has shown promising results for the treatment of both anxiety and mood disorders (Cassiello-Robbins et al., 2020), and performs similarly when compared to standard treatments targeted specifically at the respective condition (Barlow et al., 2017). These results are interesting in the context of the concerns raised against descriptive diagnoses in the treatment of psychiatric disorders, as they suggest that a transdiagnostic treatment also can produce comparable treatment results across different anxiety and mood disorders.

Working within alternate frameworks as one line of research could aid our understanding of issues such as high rates of co-morbidity, the overlap, and potential common ground across different risky behaviors. It could also help us understand how common processes across categorical diagnoses could be implicated in the development and maintenance of psychiatric disorders, since it is likely that psychopathology is caused by a multitude of complex factors ranging from genes to peer influence (Berenbaum, 2013). Perhaps these common processes could also serve as useful treatment targets. Much more research is needed to contribute to our understanding of processes at the symptom level, taking a dimensional perspective on psychopathology, and further investigating transdiagnostic treatment targets. Different targets have been suggested to be implicated in the development and/or maintenance of psychiatric disorders, such as impulsivity and negative urgency (Cyders et al., 2016), rumination (McLaughlin & Nolen-Hoeksema, 2011), and psychological inflexibility (Levin et al., 2014). The investigation of the dynamic nature of psychiatric symptoms has only begun, and research is needed not only to investigate how symptoms co-vary, but also how they fluctuate over time as well as how these temporal symptom patterns might be associated with relevant transdiagnostic constructs.

1.2   Emotion regulation as a transdiagnostic construct

1.2.1   Definitions of emotion regulation in the current thesis

Emotion regulation is one of many constructs, or psychological processes, that have been put forward as relevant for psychiatric disorders transdiagnostically. Research on emotion regulation has, since its starting point within developmental psychology,

become an area with a dramatic increase in attention sometimes described as the "affect revolution" (Adrian et al., 2011). Research on emotion regulation has shown that it could be considered an important basic psychological function in everyday life, as well as of transdiagnostic importance to psychopathology in the form of emotion dysregulation (Fernandez et al., 2016; Sheppes et al., 2015). With the accumulation of research pointing to the diagnostic co-occurrence among psychiatric disorders, attention towards transdiagnostic constructs such as emotion regulation has naturally increased (Aldao et al., 2016). Multiple definitions of emotion regulation exist, and the construct itself could be considered broad and encompassing several dimensions, processes, and strategies. A common definition is:

"… the extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying emotional reactions, especially their intensive and temporal features, to accomplish one's goals." (Thompson, 1994, p 27)

During the past decades, additional definitions and ways of viewing the construct have been developed. A suggested way of broadly categorizing definitions of emotion regulation has been into two major frameworks: 1) emotion regulation as encompassing the strategies that are used to regulate emotions, and 2) emotion regulation as general emotional functioning (Sloan et al., 2017). One of the more common definitions within the framework of emotion regulation as strategies is the cognitively focused comprehensive theory, which the Emotion Regulation Questionnaire (ERQ) is based on. The ERQ focuses two specific covert cognitive emotion regulation strategies, cognitive reappraisal and expressive suppression (Gross & John, 2003). Within the framework of emotion regulation as general emotional functioning, one of the more common definitions is the one proposed by Gratz & Roemer in the development of the self-report instrument Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004). This contributed with a more comprehensive definition, which comprises awareness and acceptance of emotions, ability to engage in goal-directed behaviors in the presence of negative emotions without impulsive actions, as well as perceived access to effective emotion regulation strategies (Gratz & Roemer, 2004). Having difficulties in these above-mentioned areas would imply difficulties in regulating negative emotions, or emotion dysregulation. The framework has also been expanded to incorporate the regulation of positive emotions (Weiss, Gratz, et al., 2015). This definition fits within a cognitive-behavioral and acceptance-based framework grounded in functional contextualism, which highlights the importance of the context when understanding behaviors associated with emotion regulation.

1.2.1.1   *Working definition of emotion regulation in the current thesis*

A practical working definition of emotion regulation that best describes how emotion regulation has been viewed within the current thesis is: *what individuals do (both in*

overt and covert behavior) in the presence of emotions to alter the emotional experience, and to what capacity they are able to do this in a functional way. This is largely in line with the framework proposed by Gratz & Roemer (2004). From a behavioral perspective, several behaviors could be considered serving the function of regulating for example negative emotions, and thus being maintained due to negative reinforcement (Baker et al., 2004; Nock, 2009). The areas in focus in the current thesis, which is behaviors related to EDs and SUDs, can be understood from this perspective as well.

1.2.2 Measurement of emotion regulation and dysregulation

Due to the broad nature of the emotion regulation construct and its varying definitions, several ways of operationalizing and measuring it exists. In addition, different measures place differing weight on emotion regulation vs. emotion dysregulation and usually assumes that these are opposites. However, there is disagreement on whether these terms are actually two sides of the same coin (Cole et al., 2019). In terms of self-report scales, a consensus around a golden standard of measurement of emotion regulation is lacking. Across studies in both normal and clinical populations, the choice of definition and measurement varies widely (Gross & Jazaieri, 2014; Sloan et al., 2017).

One of the most commonly used self-report assessments of emotion dysregulation, or emotion regulation difficulties (hereon used interchangeably), is the DERS (Gratz & Roemer, 2004). The DERS encompasses six subscales aiming to measure the previously stated definition, referred to as Clarity, Impulse, Awareness, Strategies, Goals, and Acceptance. It was developed with a focus on the clinical utility of the scale and has been widely investigated in clinical and psychiatric samples. The scale was initially developed and evaluated with regards to psychometric properties in an undergraduate sample, and a six-factor solution was suggested resulting in the six subscales (Gratz & Roemer, 2004). Further, results from the initial study indicated that the measure had good internal consistency, test-retest reliability, and demonstrated construct validity (Gratz & Roemer, 2004). Since the first published study, psychometric evaluations performed in varying samples have yielded mixed results, specifically with regards to the factor structure. Some studies have shown support for the original six-factor structure (e.g., Fowler et al., 2014). Yet, several studies have suggested a five-factor solution excluding the Awareness subscale to be the best fit (Hallion et al., 2018; Lee et al., 2016; Nordgren et al., 2020), and modifications of the scale have been put forward as potential solutions (Bardeen et al., 2016). For example, a short version of the DERS has been developed, excluding the Awareness subscale (DERS-16; Bjureberg et al., 2016). Nevertheless, previous studies have shown that the scale has good construct validity, showing positive associations with other problem areas such as symptoms of psychopathology (Fowler et al., 2014; Nordgren et al., 2020) which speaks to the clinical utility of the scale. A small experimental study carried out to test emotion regulation

(operationalized as behavioral unwillingness to experience emotional distress and ability to engage in goal-directed behavior), in patients with borderline personality disorder suggested an association between DERS self-ratings and behavioral outcomes such as willingness to stay engaged in a frustrating task (Gratz et al., 2006). Further research done on the behavioral measurement of emotion regulation has shown that worse performance on distressing behavioral tasks (such as the Mirror Tracing Task) as well as higher self-reported emotion dysregulation (measured by the DERS) is associated with higher levels of borderline personality disorder symptomatology in substance users enrolled in residential treatment (Bornovalova et al., 2008).

In contrast to the DERS, the ERQ serves to measure two specific covert emotion regulation strategies, namely suppression and reappraisal of emotions (Gross, 1998; Gross & John, 2003). In two subscales, the measure assesses the individual's tendency to rely on suppression of unwanted emotions (assumed maladaptive strategy) and to use reappraisal to shift perspective on the situation (assumed adaptive strategy), mainly in relation to negative emotions. In contrast to the DERS, the ERQ has not been widely evaluated in clinical samples, making it more difficult to draw conclusions with regards to the clinical utility of the scale (Sloan et al., 2017). It has however proven useful in basic research, and studies have demonstrated the disadvantages and benefits of using suppression and reappraisal respectively, to psychological well-being (Aldao et al., 2010; Hofmann et al., 2009; John & Gross, 2004). Results from studies in undergraduate as well as general community samples have demonstrated good psychometric properties and a stable two-factor solution (Melka et al., 2011; Preece et al., 2019).

1.2.2.1   *Current issues in the measurement of emotion regulation*

More work is needed to understand how to more precisely measure emotion regulation and dysregulation that is relevant for psychiatric disorders. Several dimensions warrant attention, such as 1) whether to place focus on self-reported emotion regulation or behavioral measures, 2) to further understand how we regulate positive emotions and implications for psychological wellbeing, 3) whether to focus on covert or overt strategies, or 4) what types of strategies that could be important to enhance outcomes of psychological treatment. Additionally, more research is needed on the psychometric properties of the DERS in different types of populations, based on previously mixed results and the usage of mainly undergraduate samples.

To mention one example of a relevant study on the measurement of emotion regulation, the study suggested that focusing on behavioral outcomes rather than specific cognitive emotion regulation strategies seems to explain psychiatric symptoms to a larger extent (Aldao & Dixon-Gordon, 2014). More specifically, this study investigated to what extent individuals used both covert and overt emotion regulation strategies, and how the endorsement of these different types of strategies explained reported

symptoms of psychopathology. The results showed that overt behaviors serving an emotion regulatory function (such as drinking or seeking advice) emerged as significant predictors of psychopathological symptoms, to a higher degree than covert strategies (Aldao & Dixon-Gordon, 2014). This example not only highlights the importance of behavior for the concept of emotion regulation, but also further supports the use of overt behavioral measurements of emotion regulation in conjunction with self-reports. However, one caveat is important to note here. Much of the theory and literature on emotion regulation strategies has generally categorized certain strategies as adaptive or maladaptive for individuals, such as the strategies encompassed in the ERQ (John & Gross, 2004). From a functional perspective, whether a strategy is ultimately useful or not is dependent on the context (Gratz, Weiss, et al., 2015). Therefore, measuring emotion regulation difficulties in relation to an individual's ability to engage meaningfully in their goals and using strategies flexibly is still of importance (Gratz & Tull, 2022).

1.2.3   Emotion regulation as a transdiagnostic construct in psychiatric disorders

Accumulating research has demonstrated that emotion regulation is associated with various types of psychiatric disorders and symptoms (Aldao et al., 2010; Cludius et al., 2020; Weiss, Sullivan, et al., 2015). To mention some, emotion dysregulation has been associated with heightened symptomatology within anxiety disorders (Hofmann et al., 2012; Turk et al., 2005), attention deficit hyperactivity disorder (Surman et al., 2013), post-traumatic stress disorder (Tull et al., 2007), borderline personality disorder (Gratz et al., 2013), and gambling disorder (Williams et al., 2012). Research has also pointed out the importance of emotion dysregulation within deliberate self-harm (Nock, 2009). Interestingly, individuals with co-occurring symptoms or risky behaviors, such as those of deliberate self-harm, substance use, and eating disordered behavior, report greater emotion regulation difficulties than individuals reporting only one symptom (Buckholdt et al., 2015). This ties into the previously mentioned research demonstrating a significant diagnostic overlap between EDs and SUDs (Bahji et al., 2019), where it is not impossible that emotion regulation difficulties could be one factor driving this expression of symptoms. Taken together, research on emotion regulation in the context of mental health problems indicates that emotion regulation difficulties are associated with higher psychiatric symptom loads.

1.2.3.1   *Emotion regulation and substance use disorders*

SUDs as well as EDs is of specific interest in this thesis. Emotion dysregulation has been shown to be associated with different types of SUDs (Dingle et al., 2018), although less research has investigated potential differences in emotion dysregulation profiles across individuals with different SUDs. In line with the classification of SUDs in the DSM being separate disorders (e.g., alcohol use disorder, cannabis use disorder), the disorders have previously commonly been investigated in isolation (Rounsaville et al., 2003). Studies

have reported heightened levels of emotion dysregulation in patients with for example alcohol use disorder (Fox et al., 2008; Petit et al., 2015), and emotion regulation skills could have predictive value for levels of alcohol use during psychological treatment (Berking et al., 2011). Emotion dysregulation has also been shown to be associated with alcohol misuse in general inpatient psychiatric samples (Garofalo & Velotti, 2015). Further pointing to the transdiagnostic relevance of emotion regulation, individuals with both alcohol use disorder and one or more co-occurring emotional disorders reported higher levels of emotion regulation difficulties than individuals with only alcohol use disorder (Bradizza et al., 2018).

In a broader perspective, research pointing to the importance of emotion dysregulation in substance use is in line with the theoretical framework highlighting that using drugs can be negatively reinforced by providing relief from negative affect (Baker et al., 2004). It is also in line with research pointing to the role of stress, loss of reward, and negative affect in promoting drug use behavior (Koob, 2013). Findings from a study using ecological momentary assessment in marijuana-using adolescents lends support to this notion. Results showed that negative affect was associated with marijuana use, and that individuals meeting criteria for dependency had an increase in positive affect after use (Ross et al., 2018). In another study, the bidirectional relationship between alcohol and marijuana use and emotion regulation strategies was tested among college students (Weiss et al., 2017). Results suggested interestingly that there is indeed such a relationship between substance use and the use of adaptive emotion regulation strategies, where the use of adaptive strategies decreased the odds of substance use whilst substance use decreased the odds of using adaptive strategies the following day (Weiss et al., 2017). Since studies suggest that emotion dysregulation in the context of substance use can be connected to the substance use behavior itself, there is also a need to study the dimensional relationship between emotion dysregulation and substance use across different substances (beyond diagnostic criteria).

1.2.3.2 *Emotion regulation and eating disorders*

In the field of EDs, the relevance of emotion dysregulation across different diagnoses (such as anorexia nervosa and bulimia nervosa) has been substantially assessed (L. K. Anderson et al., 2018; Lavender et al., 2015). Due to the somewhat limited diagnostic validity of the eating disorder diagnoses, where up to 60% of patients could fall under the Eating Disorder Not Otherwise Specified category stated in the DSM (Fairburn & Bohn, 2005), research on transdiagnostic constructs such as emotion regulation has naturally been prominent in this field. Patients with a range of different ED diagnoses show impaired emotion regulation as compared to controls (Brockmeyer et al., 2014), and no large differences in emotion dysregulation profiles between ED types have been shown (Monell et al., 2018). Furthermore, there is an association between improvements in eating disorder symptoms and improvements in emotion regulation difficulties when

measured before and after treatment (Mallorqui-Bague et al., 2018), although another treatment study utilizing repeated measures showed no association between emotion regulation and binge eating frequency (Bodell et al., 2019). Studies using ecological momentary assessment in patients with bulimia nervosa also show, similarly to results regarding marijuana use stated above, that negative affect precedes bingeing and purging behaviors, and that it decreases afterwards (Berg et al., 2013). In one of the longitudinal studies, negative affect was also shown to be associated with frequency of binge-eating episodes over time (Bodell et al., 2019). This also strengthens the rationale for eating disorder-related behaviors serving a function of down-regulating negative affect, and thus being negatively reinforced (Haynos & Fruzzetti, 2011).

1.2.3.3   Theoretical viewpoint on emotion regulation underlying the current thesis

As previously mentioned, there is a significant overlap between eating disorder-related behaviors and deliberate self-harm (Kostro et al., 2014), as well as substance use (Bahji et al., 2019; Bulik et al., 2004). With the literature review as a backdrop, the theoretical viewpoint saturating this thesis is as follows: these behaviors (substance use, eating disorder-related behaviors such as binge eating, deliberate self-harm) could, in certain contexts, serve a similar function of regulating emotions (e.g., by alleviating distress). This is illustrated in *Figure 2*. This way of thinking about risky behaviors has inspired the studies in the thesis.
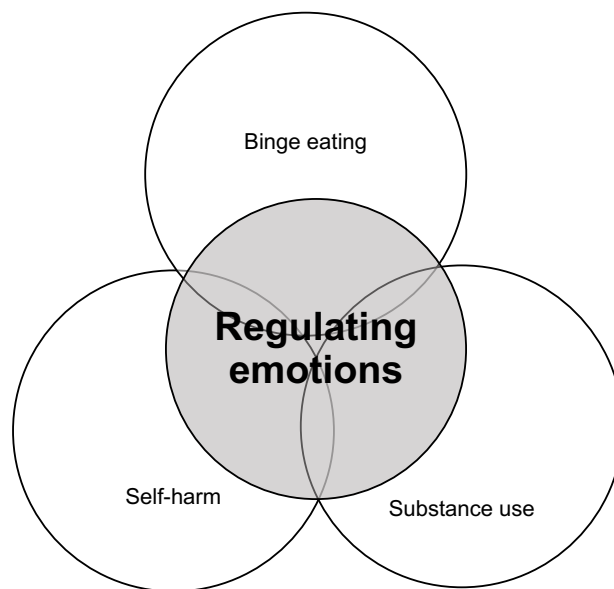

Figure 2. Sketch of the theoretical viewpoint informing the current thesis.

2 Research aims

2.1 Overall aims

The overarching aim of the thesis was to develop methods to study co-occurrence of different mental health problems and their underpinnings, and how we could further our current understanding of emotion regulation as a potential transdiagnostic process. More specifically, the aims were to:

1. Understand whether psychopathology, with a focus on EDs and SUDs, fluctuated over time utilizing a symptom level analysis, and how this was related to emotion dysregulation.
2. Contribute to the understanding of emotion regulation as a construct by investigating its measurement, as well as an increased understanding of the relationship to substance use across different levels of use/substances.

2.2 Specific aims of studies

The specific aims of the studies included in the thesis were to investigate:

I. Do individuals with EDs transition among symptoms over time? If a so called "symptom shift" is observed, is this related to heightened levels of emotion dysregulation and other mental illness indicators?

II. Do individuals shift between symptoms of EDs and SUDs in a general population sample? If so, are there differences in severity of psychiatric symptoms between such individuals with symptom shifting and individuals with other temporal symptom patterns?

III. What are the psychometric properties and convergence among two common measures of emotion regulation (i.e., the DERS and ERQ)? What is their concurrent validity with other psychatric symptoms?

IV. Is emotion dysregulation approximately dimensionally related to different levels of substance use (across a variety of SUD diagnoses), and does co-occuring psychiatric symptoms moderate this association?

3 The empirical studies

3.1 Study I

Study I was an observational study investigating if patients with EDs demonstrate "symptom shifting", defined as having decreased reliably in at least one ED-related behavior whilst simultaneously increased in another, during the course of one year. Shifts from ED-related behaviors to deliberate self-harm and substance use were also investigated. Individuals with symptom shifting were compared to the rest of the sample (referred to as "nonshifting") on levels of emotion dysregulation, and several other mental illness indicators such as impairment, depression, and anxiety.

3.1.1 Methods

3.1.1.1 Participants and procedure

The sample (N = 3159, age M = 26.47, female = 97%) consisted of patient data extracted from the Stepwise registry (recorded between 2005 and 2018), which covers specialized ED clinics throughout Sweden (Birgegård et al., 2010). All patients were ≥ 18 years of age, had been diagnosed with an ED, and an intent to treat was established at the clinic. Patients were measured twice with various self-report instruments and clinician assessments at baseline before treatment initiation, and at a 12-month follow-up. Not all measures were mandatory to complete, giving rise to differing numbers of available cases for each measure.

3.1.1.2 Measures

ED-related behaviors were measured using the *Eating Disorder Examination Questionnaire 4.0* (EDE-Q; Fairburn & Beglin, 1994). The EDE-Q includes both items rated on a 7-point scale, as well as ratings of the number of ED-related behaviors during the past month (including binge-eating, vomiting, laxative use, and compulsive exercise episodes). Deliberate self-harm was measured using the *Deliberate Self-Harm Inventory* (DSHI; Gratz, 2001), and substance use was measured using the *Alcohol Use Disorder Identification Test* (AUDIT; Saunders et al., 1993).

Measures of other mental illness indicators included: *DERS* (Gratz & Roemer, 2004) measuring emotion dysregulation; *Comprehensive Psychopathological Rating Scale Self-Rating* (Svanborg & Åsberg, 1994) measuring symptoms of anxiety, depression, and compulsivity; *ADHD Self-Report Scale Screener* (Kessler, Adler, et al., 2005) measuring symptoms of inattention and hyperactivity; *Clinical Impairment Assessment* measuring secondary functional impairment; and clinician ratings of global functioning (*Global Assessment of Functioning*; American Psychiatric Association, 2000).

3.1.1.3   Statistical analyses

Symptom shifting was, as a first step, defined as the occurrence of a reliable decrease in the frequency of one ED-related behavior and a reliable increase in at least one other ED-related behavior (based on all the above stated self-rated frequencies of behavioral episodes in the EDE-Q, making it possible for individuals to have shifted between various types of symptoms). Change scores were calculated by subtracting the baseline rating from the follow-up rating, and a Reliable Change Index (Christensen & Mendoza, 1986) was applied to the change scores to exclude low scores attributed to measurement error. See *Table 2* for an overview of the symptom shifting definition. The symptom shifting definition was extended to include shifting from one of the ED-related behaviors to deliberate self-harm and substance use respectively in two separate subsamples (n = 1012 with DSHI at both measurement points and n = 399 with AUDIT at both measurement points).

Table 2. Overview of the symptom shifting definition with fictional cases

	Binge eating episodes			Compulsive exercise episodes		
	Baseline	Follow-up	Δ	Baseline	Follow-up	Δ
Symptom shifting	30	10	**–20**	10	20	**+10**
Nonshifting	12	12	**0**	25	5	**–20**

Regression analyses with robust confidence intervals were used to compare those defined as having symptom shifted to the nonshifting group. All available data was used, resulting in separate analyses for each measure which applied listwise deletion. The *p*-values were not corrected.

3.1.2   Results

In the whole sample, 422 (13%) patients were categorized as having symptom shifted among ED-related behaviors. When extending the symptom shifting definition to also include shifting from ED-related behaviors to deliberate self-harm (in addition to shifting to other ED-related behaviors) in the first subsample, 197 (19%) demonstrated symptom shifting. Similar results were found when extending the symptom shifting definition to also include shifting to substance use, where 77 patients (19%) demonstrated symptom shifting in the second subsample.

With regards to comparisons between the symptom shifting and nonshifting groups, those who demonstrated symptom shifting among ED-related behaviors were found to report significantly higher levels of emotion dysregulation, as well as more symptoms of depression, anxiety, compulsivity, deliberate self-harm, impairment, and lower global functioning across baseline and follow-up. A significantly larger proportion of symptom shifting individuals were also found to have had increased in deliberate self-harm from baseline to follow-up. Results were similar when comparisons between symptom shifting and nonshifting individuals were performed on follow-up values, whilst controlling for baseline values.

3.2 Study II

Study II was an observational study investigating if young adults in the general population demonstrate symptom shifting (defined in Study I) between symptoms of ED and SUD. Furthermore, potential differences between individuals demonstrating symptom shifting and individuals with other temporal ED and/or SUD symptom profiles on psychiatric variables and psychiatric polygenic risk scores (PRS) were investigated.

3.2.1 Methods

3.2.1.1 Participants and procedure

Data originated from the Child and Adolescent Twin Study in Sweden (CATSS; see Anckarsäter et al., 2011), which is a currently ongoing study of twins born 1992 and later in Sweden. In the current study those who had participated in the two data collection waves conducted at 18 and 24 years of age were included, resulting in a sample size of *N* = 3315 (female = 62%). At these two measurement points, participants completed various self-report instruments detailed below[1]. A subsample of twins in CATSS had also been previously genotyped (*n* = 1668), thus providing data on PRS.

3.2.1.2 Measures

ED symptoms were measured using the "ED symptom index" in the *Eating Disorder Inventory-2** (EDI-2; Garner, 1991), where a total score of ≥ 21 was used as a cut-off for presence of ED problems (Nevonen & Broberg, 2001). SUD symptoms were measured using the total scores of the *AUDIT** (Saunders et al., 1993) and *Drug Use Disorder Identification Test** (DUDIT; Berman et al., 2005). Cut-off scores of ≥ 8 for men and ≥ 6 for women were used as indication of heavy drinking using the AUDIT, and cut-off scores

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[1] Variables measured at both 18 and 24 years marked with an asterisk (*), variables measured at 18 years marked with a dagger (†), all other variables measured at 24 years.

of ≥ 6 for men and ≥ 2 for women were used to indicate presence of drug-related problems using the DUDIT.

Other psychiatric variables measured were *suicidality* (self-reported occurrence yes/no of suicidal ideation and suicide attempts lifetime and past 12 months), symptoms of depression (*Center for Epidemiological Studies Depression Scale**, Radloff, 1977), symptoms of anxiety (*Screen for Child Anxiety Related Emotional Disorders*[†], Birmaher et al., 1997; *Hospital Anxiety and Depression Scale*, Zigmond & Snaith, 1983), obsessive compulsive symptoms (*Brief Obsessive Compulsive Scale*[†], Bejerot et al., 2014; *Obsessive-Compulsive Inventory-Revised*, Foa et al., 2002), and personality dimensions (Self-Directedness and Cooperativeness in the *Temperament and Character Inventory*[†], Cloninger et al., 1993).

PRS were used for eight psychiatric diagnoses: schizophrenia, bipolar disorder, major depressive disorder (MDD), autism, attention-deficit hyperactivity disorder (ADHD), ED (anorexia nervosa), post-traumatic stress disorder (PTSD), and anxiety disorders. They were previously derived from summary statistics emanating from genome-wide association studies (Taylor et al., 2019).

3.2.1.3 Statistical analyses

Symptom shifting was defined, in accordance with Study I, as the occurrence of at least one reliable increase in ED symptoms (according to the EDI-2) and a simultaneous reliable decrease in SUD symptoms (according to the AUDIT and/or DUDIT), or vice versa, between the measurement points.

To compare individuals who demonstrated symptom shifting to other temporal symptom profiles, individuals who did not fulfill criteria for having symptom shifted (i.e., nonshifting) were further categorized into groups of clinical and theoretical relevance based on presence or absence of ED and/or SUD symptoms. The following groups were defined: "No symptoms" (no ED or SUD symptoms above cut-offs at any time point), "Single domain" (ED or SUD symptoms above cut-offs at one of the time points), "Single persistent" (symptoms of ED or SUD above cut-offs at both time points), "Co-occurring domain" (symptoms of ED and SUD above cut-offs at one of the time points), and "Co-occurring persistent" (symptoms of ED and SUD above cut-offs at both time points).

Missing data (mostly on the item level) in the self-rating instruments was imputed using predictive mean matching and polytomous regression (Van Buuren, 2018). Generalized estimating equations were then used to investigate group differences in the psychiatric variables among the following groups: Symptom shifting, No symptoms, Single persistent, and Co-occurring persistent. *P*-value correction for multiple comparisons was made.

3.2.2　Results

The proportion of individuals demonstrating a symptom shift according to the definition was 2%, both among complete cases and in imputed data. Individuals who had symptom shifted represented 10% of those who suffered persistent problems (corresponding to individuals in the Single persistent, Co-occurring persistent, and Symptom shifting groups).

In imputed data, individuals in the Symptom shifting group overall scored similarly to individuals in the Co-occurring persistent group on the other psychiatric variables, and there were no significant differences among mean scores between the groups (see *Figure 3* for an overview of measures at 18 years). Compared with the No symptoms group, individuals in the Symptom shifting group scored significantly higher on depressive symptoms and anxiety symptoms, reported higher rates of suicidal ideation and attempts, and scored lower on the personality dimensions self-directedness and cooperativeness. Compared with the Single persistent group, individuals in the Symptom shifting group scored significantly lower on the personality dimension self-directedness.

When comparing PRS for psychiatric disorders across the groups in the subsample who had been previously genotyped, individuals in the Symptom shifting group had significantly higher PRS for anorexia nervosa and ADHD compared with individuals in the No symptoms group. Compared with the Single persistent group, individuals in the Symptom shifting group demonstrated higher PRS for bipolar disorder, anxiety disorders, MDD, anorexia nervosa, and schizophrenia. When comparing to the Co-occurring persistent group, the Symptom shifting group showed higher PRS for schizophrenia and MDD. The Symptom shifting group demonstrated lower PRS for autism in one instance, when compared to the No symptoms group.
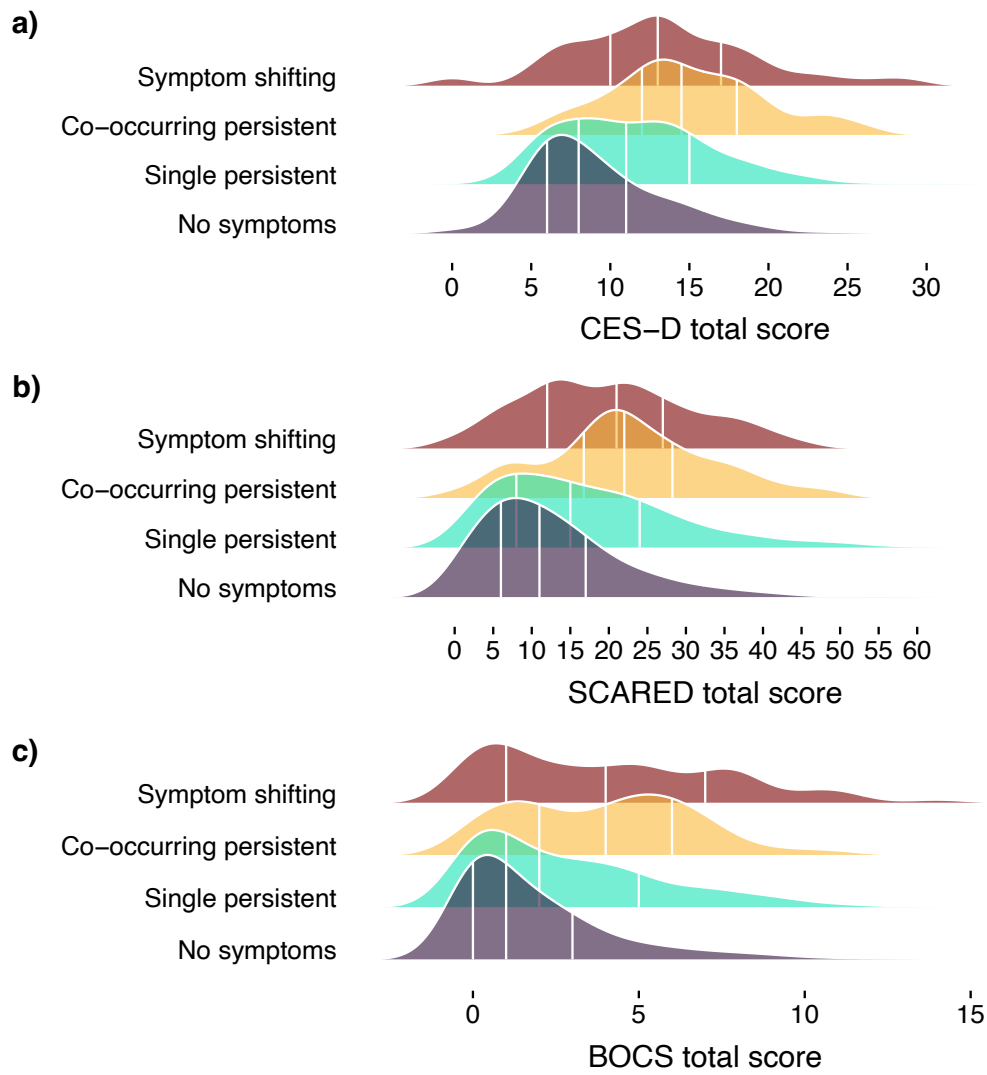
Figure 3. Distributions of a) depressive symptoms (CES–D), b) anxiety symptoms (SCARED), and c) obsessive–compulsive symptoms (BOCS) across groups, measured at 18 years. White lines represent the lower quartile, median, and upper quartile respectively.

3.3 Study III

Study III was a cross-sectional study investigating the psychometric properties and convergent validity of the DERS (including the abbreviated DERS 16-item) and the ERQ. Potential differences in concurrent validity (i.e., association with related constructs including common psychiatric symptoms) between the two scales was explored.

3.3.1 Methods

3.3.1.1 Participants and procedure

The sample consisted of N = 843 community-residing individuals (age M = 30.05, range 18–64 years, female = 54%) in Connecticut, US. Exclusion criteria included head injuries, psychotic disorders, acute medical or psychiatric conditions, current use of opiates or opioid use disorder treatment. Participants completed diagnostic interviews and a range of self-report instruments on site.

3.3.1.2 Measures

Emotion regulation was measured using the *DERS* (Gratz & Roemer, 2004) and the *ERQ* (Gross & John, 2003). The DERS includes six subscales (Nonacceptance, Goals, Impulse, Awareness, Strategies, Clarity), and the 36 items are rated on a scale of 1 (Almost never, [0%–10%]) to 5 ("Almost always [91%–100%]). Item responses are summed (after adjusting reversed items) into scores across subscales, as well as a total score where greater values indicate more emotion regulation difficulties. The short form, *DERS-16* (Bjureberg et al., 2016), was derived from the full scale and includes all original subscales except Awareness. The ERQ includes two subscales (Cognitive Reappraisal, Expressive Suppression) measured across 10 items rated on a scale of 1 ("Strongly disagree") to 7 ("Strongly agree"). Items are summed into scores reflecting the two emotion regulation abilities, where a higher score is indicative of a greater tendency to use reappraisal and suppression respectively.

For the analyses of concurrent validity, the *CES-D* (Radloff, 1977) was used to measure depressive symptoms, the *State Trait Anxiety Inventory* (STAI; Spielberger, 1983) was used to measure anxiety symptoms, the *Perceived Stress Scale* (PSS; Cohen et al., 1983) was used to measure stress symptoms, and the *Addiction Severity Index* (ASI; McLellan et al., 1992) Drug Use subscale was used to measure substance use.

3.3.1.3 Statistical analyses

Due to the ERQ being added later during the study, 55% of participants had available data on this measure. All analyses were conducted on available data. The ASI data was transformed based on the *Drug Use Questionnaire* (DUQ; Hien, 1991) which has a 6-point response format (ranging from 0 = "Never" to 5 = "4 or more times a week"). To form the substance use measure in this study, all substances were added together which

reflected substance use (across all substances; alcohol, cannabis, cigarettes, cocaine, opioids) over the past 30 days. Convergence between the DERS scales and the ERQ, as well as concurrent validity, was analyzed using bivariate Pearson correlations. To assess differences in concurrent validity between the DERS and ERQ, tests of significance were performed to explore differences in the correlation coefficients. Confirmatory factor analyses fit using full information maximum likelihood were used to assess the factor structures of the emotion regulation scales (based on previous research). To assess results from the confirmatory factor analyses, recommended goodness-of-fit estimates and cut-offs were used (Hu & Bentler, 1999).

3.3.2   Results

3.3.2.1   Internal consistency

All measures of emotion regulation and their subscales (DERS, DERS-16, and ERQ) as well as the other measures of psychiatric symptoms (CES-D, STAI, PSS) showed acceptable to excellent internal consistency (assessed using Cronbach's α).

3.3.2.2   Factor structures

Factor analyses performed for the DERS included 1) a correlated six-factor model, 2) a correlated five-factor model (excluding the Awareness subscale), and 3) a bifactor model including one general factor and five specific uncorrelated factors (also excluding the Awareness subscale). Goodness-of-fit values suggested overall than none of the models had an acceptable fit. The first model demonstrated the poorest fit, with the values improving incrementally across the second and third models. Factor analyses performed for the DERS-16 included 1) a correlated five-factor structure, and 2) a bifactor model. Results from these models suggested an inadequate fit for the first model, and an acceptable fit for the second model across most indices. The ERQ was evaluated using an orthogonal two-factor model (including the two subscales), which showed an acceptable fit across most indices.

3.3.2.3   Convergent and concurrent validity

With regards to convergent validity, correlations between the DERS and the ERQ (including all subscales across both measures) were in expected directions. The Reappraisal subscale was negatively associated with DERS and DERS-16 total scores and subscale scores, and Suppression was positively associated. Regarding concurrent validity, the DERS and DERS-16 demonstrated similar moderate correlations with symptoms of depression and anxiety and weak correlations with stress and substance use. The ERQ and its subscales overall demonstrated weak correlations with all other measures of psychiatric symptoms. When testing for statistically significant differences between correlation coefficients for the DERS, DERS-16, and ERQ subscale total scores, only two coefficients were not significantly different. These associations were between

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the Reappraisal and Suppression subscales and substance use, and between the DERS–16 total score and Reappraisal subscale and stress.

3.4 Study IV

Study IV was a cross–sectional study investigating the relevance of emotion regulation as a construct across different levels of substance use (both in terms of frequency and severity, close to the concept of dimensionality), irrespective of SUD diagnosis, and the potential moderating effect of co–occurring psychiatric symptoms in this relation.

3.4.1 Methods

3.4.1.1 *Participants and procedure*

The sample consisted of individuals from two main data sources; Sample 1 was the same community sample employed in Study III (see Study III for details), and Samples 2 and 3 consisted of patients residing at two residential SUD treatment facilities in Mississippi, US. The patient samples (N = 415, age M = 35.16, range 18–65 years, female = 43%) were recruited and assessed on site during the first two weeks of treatment. To be included patients had to have no cognitive impairment or current psychotic disorder, and Sample 3 had to have at least an alcohol and/or cocaine use disorder diagnosis.

3.4.1.2 *Measures*

Emotion regulation difficulties were measured using the *DERS* (Gratz & Roemer, 2004). Other psychiatric symptoms (depression, anxiety, and stress) were measured using the *CES–D* (Radloff, 1977), *STAI* (Spielberger, 1983), and *PSS* (Cohen et al., 1983) in Sample 1, and using the *Depression Anxiety and Stress Scale–21* (DASS–21; Antony et al., 1998; Lovibond & Lovibond, 1995) in Samples 2 and 3. In order to facilitate interpretation of other psychiatric symptoms across samples, scores on these measures were standardized.

Substance use was assessed with the *ASI* (McLellan et al., 1992) in Sample 1, and the *DUQ* (Hien, 1991) in Samples 2 and 3. As described in Study III, the data from the ASI was transformed to match the response format used in the DUQ. Two estimates of overall substance use were used in the study; *substance use frequency* over the past 30 days (represented by the sum of the DUQ score across the following substances: alcohol, cannabis, cocaine, and opioids), and *substance use severity*. Substance use severity was defined based upon classifying the whole study sample into three subgroups: "Community without substance misuse", "Community with substance misuse", and "SUD residential treatment". The Community without substance misuse (n = 276) constituted of individuals from Sample 1 who had no lifetime SUD diagnosis and no use of illicit substances during the past 30 days. The Community with substance misuse included individuals from Sample 1 who either had tested positive for illicit drugs (cannabis,

cocaine, or opioids), had a lifetime SUD diagnosis, or had a history of out- or inpatient, or detox, treatment for SUD. The SUD residential treatment group consisted of all participants in Samples 2 and 3, which all met criteria for one or more current SUD (most patients were dependent on multiple substances).

3.4.1.3   Statistical analyses

All participants in the study had data on the DERS. All other available data points in the other measures were used (with some measures including missing values). Bivariate Pearson correlations were used to investigate associations between all measures (including the DERS subscale scores). Linear hierarchical regression models were used to investigate the association of substance use frequency and substance use severity with the DERS total score. To investigate if there was a certain DERS subscale "profile" associated with substance use severity (i.e., if there was a pattern of functioning in the different dimensions of emotion regulation across the three groups), a logistic regression model was used. Furthermore, three linear hierarchical regressions were performed, one in each subgroup, to investigate potential moderation of psychiatric symptoms in the association between substance use frequency and DERS total score. Due to differences in age and gender composition across the subgroups, these variables were included as covariates in all regression analyses.

3.4.2   Results

3.4.2.1   Relationship between emotion regulation and substance use severity

Across the three levels of severity (meaning subgroups Community without substance misuse, Community with substance misuse, and SUD residential treatment), the DERS total scores increased significantly with increasing substance use severity (see *Figure 4* for an overview of the relationship). Worth noting is that substance use frequency also increased significantly with increasing substance use severity (can also be viewed in *Figure 5*).
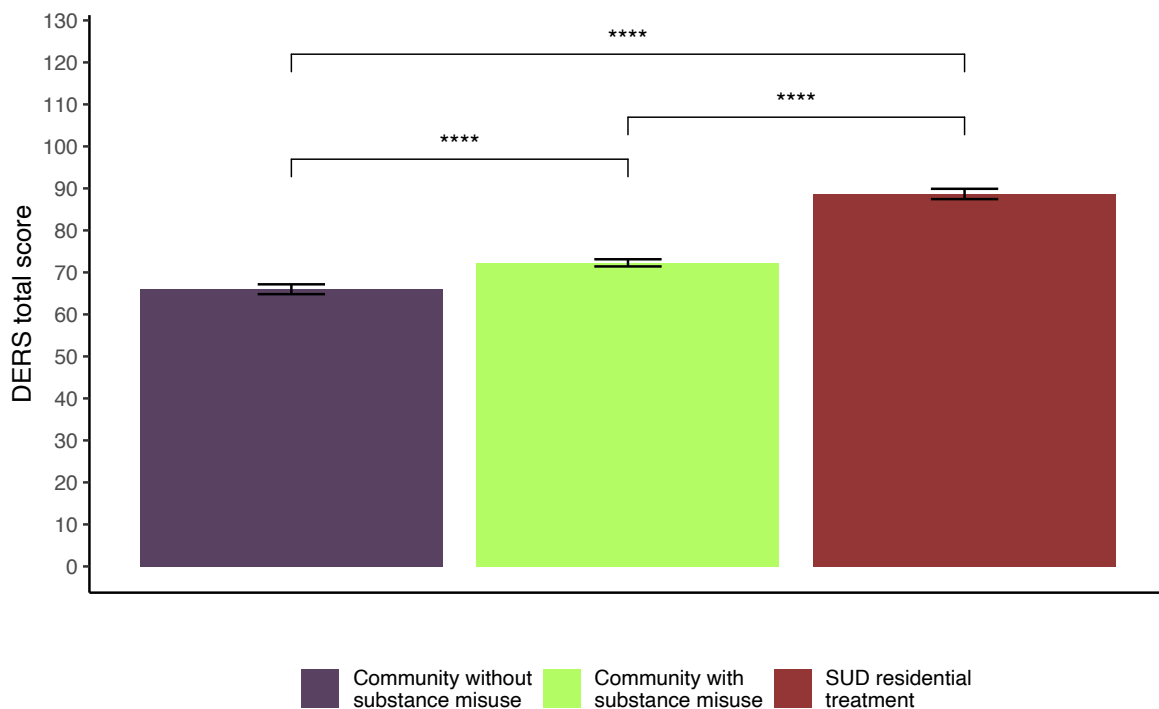
Figure 4. Bar graph illustrating the difference in emotion regulation difficulties across the levels of substance use severity. Error bars represent standard error, asterisks denote a *p*-value < .001.

3.4.2.2   Relationship between emotion regulation and substance use frequency

Across the whole sample, emotion dysregulation was weakly associated with substance use frequency (see *Figure 5* for a visual illustration of the relationship). This relationship was also present in the hierarchical regression model, where the DERS total score was significantly associated with substance use frequency whilst controlling for sex and age.

3.4.2.3   DERS subscale score profiles

When examining the DERS subscale scores (Nonacceptance, Goals, Impulse, Awareness, Strategies, and Clarity), the strongest relationship was found between both substance use frequency and severity and the Impulse subscale (controlling impulsive behaviors when distressed). Scoring higher on the Impulse subscale was associated with higher odds for belonging to the SUD residential treatment subgroup. Small but statistically significant odds for scoring higher on the Goals and Clarity were found for belonging to the Community with substance misuse group when compared to the Community without substance misuse group. Finally, small but statistically significant odds for scoring higher on the Awareness subscale were found for belonging to the SUD residential treatment subgroup when compared to the Community with substance misuse group.
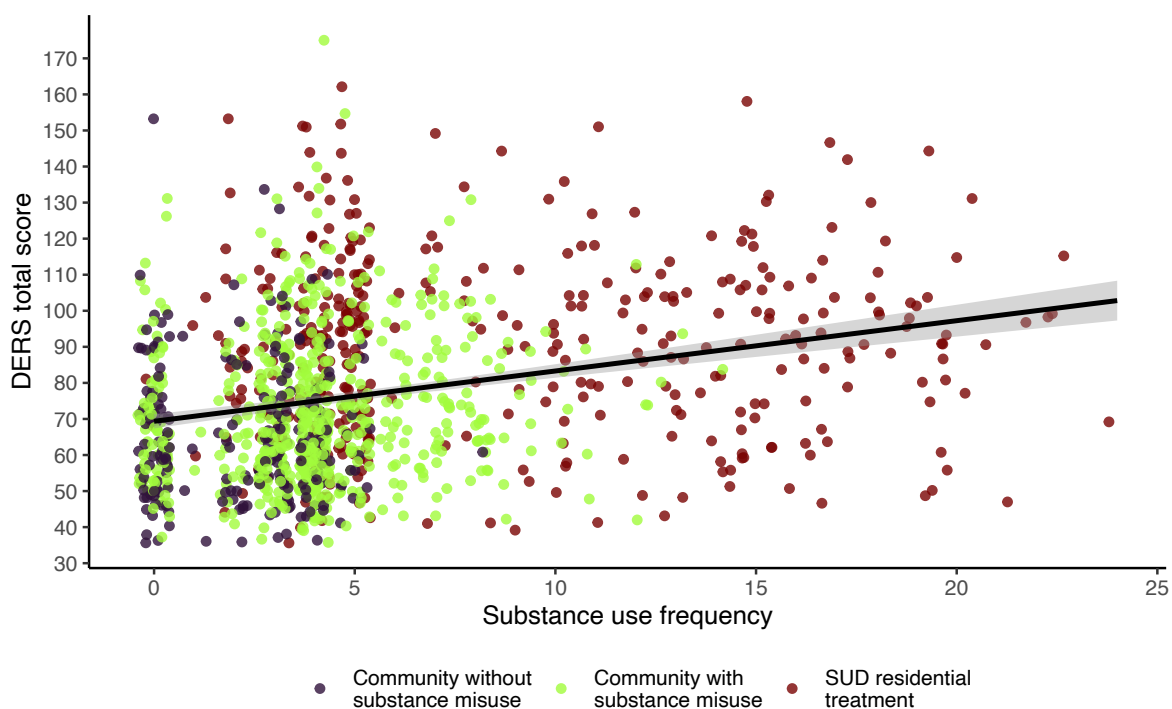
Figure 5. Scatterplot illustrating the relationship between emotion regulation and substance use frequency (also including substance use severity for reference, in color). Black line denotes the estimated regression line (with 95% confidence interval).

3.4.2.4   Influence of psychiatric symptoms

Results showed no significant influence of psychiatric symptoms, nor the interaction between them and the DERS total score, in relation to substance use frequency in any of the subgroups.

3.5 Ethical considerations

The balance between doing good and avoiding harm is a central aspect when considering research ethics. It revolves around weighing potential benefits against any potential harm for the individual participant (World Medical Association, 2013). The respect for autonomy and justice for the individual participant is another central aspect related to the current thesis. The respect for autonomy revolves around informed consent and respect for privacy. These aspects are weighed in with regards to all studies in the thesis.

With regards to respect for autonomy, there are potential risks such as exposure of sensitive personal information that is highly relevant in the context of all studies within the thesis. Information such as alcohol use and other substance use is particularly important in this context due to the potential legal consequences that are involved, as

well as substance use problems being a stigmatized topic in our society. Safe data storage according to guidelines becomes a key factor to respect the privacy of the participants of all studies encompassed in the thesis. Needless to say, all studies included have been ethically vetted and all participants have provided informed consent before participating in line with the Declaration of Helsinki (World Medical Association, 2013). No direct personal information that identified the participants was handled in the studies.

For Study I, the risk of study participation causing any harm was small, given that the data was obtained from a national quality assurance registry of specialized eating disorder clinics. The data collection occurred in conjunction with diagnostic assessment at the clinics, where ultimately the data was saved in encrypted data bases. All patients have given informed consent before participation. The registry has been used in several previous studies, without any reports of harm to the involved patients. The same considerations apply in Study II as well, where data from the Swedish Twin Registry was used. The data used in this study consisted of mostly self-reported data on mental health, but also summaries of genetic psychiatric risk factors. Since the genetic information consisted of statistically derived PRS, it poses no risk for identification of the individual. The data analyzed in Study III and IV was received from two collaborating units in the US, where any personal information had been removed to avoid identification of individual participants. To summarize, although there always are risks posed with regards to collecting and handling sensitive information, the risks of participation were in all cases deemed small across the studies.

The potential benefits of the results obtained in the studies were deemed to outweigh the risks of causing harm to the individual participants. One point worth noting in this context is the potential benefits of utilizing already collected data. The participants have generously provided their time to participate in all data collections comprised in the current thesis. Therefore, to maximize the usage of their time and effort, as well as maximize usage of the funding often obtained from governmental sources backing the studies, it can be useful to appropriately utilize already existing data sources for secondary data analysis to answer research questions not already posed to those datasets.

4 Discussion

This thesis aimed to contribute to research within a broader transdiagnostic setting, by investigating (a) symptom transitions over time across different mental health problems, and (b) the association between emotion regulation and different symptom profiles. The main findings indicate firstly that a smaller subgroup of individuals (among both treatment-seeking patients and individuals from the general community) demonstrate a symptom pattern over time referred to as "symptom shifting", where they simultaneously decrease in one symptom area whilst increasing in another (**Study I–II**). Secondly, findings indicate that two commonly used self-report measures of emotion regulation show convergent validity, whilst one of them showed greater concurrent validity with clinically relevant psychiatric symptoms (**Study III**). Thirdly, findings indicate that emotion regulation is associated with substance use, both in terms of substance use frequency and severity, across a sample of individuals from the general community as well as patients in residential treatment (**Study IV**).

4.1 Do individuals with eating disorders shift between symptoms over time?

The findings from Study I suggest that, among patients with EDs admitted to specialized care, some individuals seem to decrease in some ED symptoms whilst increasing in other ED symptoms and/or risky behaviors such as deliberate self-harm and substance use. Firstly, it is important to note that power was limited for some analyses. Using a national care registry, it was not possible to conduct proper *a priori* power analyses, and not all measures were mandatory giving rise to varying group sizes available for analysis. Despite this, the study did indicate that there is a subset of individuals with persisting mental health problems. These individuals, and such symptom trajectories overall, could risk being missed in regular healthcare, where care usually is organized as separate specialties and clinics where the focus lies on the primary problem area or behavior (such as specialized ED clinics and specialized SUD clinics). The results from the study align with for example the research previously mentioned showing that some individuals undergo diagnostic transitions across time (Copeland et al., 2013), and that risky behaviors tend to co-occur (Serras et al., 2010). In line with the overarching theoretical viewpoint of the thesis, it is proposed that this symptom pattern could be understood for example from a functional perspective. Previous research has suggested that both ED-related behaviors, deliberate self-harm as well as substance use may serve the function of regulating emotions (Baker et al., 2004; Nock & Prinstein, 2004; Wang et al., 2021). For some of the patients demonstrating symptom shifting, one could hypothesize that an ED-related behavior serving the function of avoiding negative emotions could have been replaced with another behavior (e.g., deliberate self-harm) that serves a similar function for the individual.

Although to our knowledge this study was the first to define and study symptom shifting in this particular way, these types of symptom trajectories are of course not novel to either theorists or clinicians. Furthermore, that individuals may replace one symptom with another (referred to as symptom substitution) was discussed during the mid-20th century within both behavior theory and psychodynamic theory (Kazdin, 1982; Tryon, 2008). A related term within behavior theory is that of response covariation, which similarly poses that changing the probability of one behavior occurring could change the probability of other behaviors occurring (Sprague & Horner, 1992). One more recent study on a form of symptom transition worth mentioning, which was not brought up in the published paper of Study I, is a study investigating trajectories of self-injurious behavior and substance misuse in adolescents (Nakar et al., 2016). The results from the study suggest that some of the adolescents, on a group level, over time decreased in self-injurious behavior whilst substance misuse increased, approximating a symptom shift. Previous qualitative research based on interviews has also shown that some individuals report that they stopped engaging in deliberate self-harm due to the development of alternate behaviors such as substance use (Gelinas & Wright, 2013).

The research on symptom shifting, as defined in Study I, is just beginning and more research developing on this method as a way of understanding co-occurrence among mental health problems is needed. Some of the issues raised around the term symptom substitution several decades ago still need to be explored, such as how to determine if one symptom actually could be replaced by another (and if symptom substitution occurs for a subgroup of individuals with symptom shifting), and during what time frame a symptom shift should have occurred to be deemed a theoretically and clinically relevant symptom pattern (Kazdin, 1982). One example of research building on Study I is a study that investigated if patients with anorexia nervosa undergoing inpatient treatment demonstrated symptom shifting (Meule & Voderholzer, 2022). The study did not find evidence that patients who decreased in eating disorder-related symptoms showed simultaneous increases in obsessive-compulsive symptoms, a common co-occurring disorder. The authors did not however discuss if obsessive-compulsive behaviors serve similar functions as the ED-related behaviors for these individuals. Further studies complementing investigation of symptom shifting with a functional assessment of behaviors will be important going forward, which could renew the discussion on symptom substitution from an emotion regulation and contextual behavioral science perspective.

4.2 Does the concept of symptom shifting translate to the general population?

Study II provides a conceptual replication of the methodological framework in Study I, demonstrating that there is a subgroup of individuals, albeit small in size, in the general population that demonstrate symptom shifting between symptoms of ED and SUD.

Individuals in the symptom shifting group reported levels of psychiatric symptoms comparable to individuals with co-occurring persistent ED and SUD, which was in line with results from Study I. They also showed higher PRS for several psychiatric diagnoses. Worth mentioning early on is that the small group sizes for some of the groups could pose problems with statistical power, especially for the analyses of group differences for PRS. Replicating these results in a larger sample will be important to assess the robustness of the results.

The proportion of shifters varied markedly between Study I and II (13% vs. 2%), which is to be expected given the different populations studied. Furthermore, the material used for defining the symptom shifting group differed slightly from Study I. Whilst self-reported frequencies of certain behaviors were mainly employed in Study I, in Study II the total scores of scales were used instead. These aspects, in addition to other factors such as time frame and age of participants, are things that could potentially affect rates of symptom shifting across the two studies.

Tying into the overarching transdiagnostic theme of this thesis, Study II adds to the literature base on the overlap between EDs and SUDs by indicating that individuals may shift between symptoms within these problem areas over time. Furthermore, results from the group comparisons suggest that individuals who improve in one symptom area, but worsen in another symptom area (Symptom shifting group), report similar levels of other psychiatric symptoms and suicidal ideation to those individuals who have persisting problems in both symptom areas over time (Co-occurring persistent group). When examining the overall distributions of scores on the measures, there seemed to be an approximate dimensional structure (i.e., the mean scores are lowest in the No symptoms group, highest in the Symptom shifting and Co-occurring persistent groups, and in the middle for the Single persistent group). It is difficult not to draw parallels to the reasoning brought up in the Background section of this thesis, both in terms of the potential to understand mental health problems from a dimensional perspective (Kotov et al., 2017) as well as the burden associated with psychiatric co-morbidity (Watson et al., 2011).

Interestingly, the symptom shifting group showed higher PRS for MDD and anorexia nervosa compared to the other groups. This points to potential genetic risk factors that could be connected specifically to symptom shifting, which was not possible to investigate in Study I. However, these results should be interpreted with caution due to the uncertainty connected to the small group sizes. Study II points to the need for future research on symptom shifting to also assess potential genetic risk factors involved, as well as complement with prospective assessment of other transdiagnostic risk factors such as emotion dysregulation.

4.3 How do measures of emotion regulation relate to one another?

Results from Study III provided additional evidence of convergent validity among the DERS and ERQ, that stem from two overarching theoretical frameworks of emotion regulation. Unlike previous research evaluating the convergence among these self-report scales, the study contributes to the literature by evaluating psychometric properties in a relatively large sample with a broad age span (Zelkowitz & Cole, 2016). When examining concurrent validity with psychiatric symptoms, the DERS was shown to be more highly correlated with them than the ERQ. This is reasonable given that the DERS was developed with a clinically useful definition of emotion regulation in mind (Gratz, Weiss, et al., 2015). These results taken together support the validity of both scales, and further supports the position of the DERS as a clinically relevant tool.

The DERS-16 overall demonstrated similar results to the full-length DERS with regards to convergent and concurrent validity, and performed better than the full scale in confirmatory factor analyses. This adds further support for using a short version of the DERS, which can be helpful to save time and effort in both clinical and research contexts. Another study evaluating three different short forms of the DERS further suggests that the versions developed so far, including the DERS-16, perform similarly (Skutch et al., 2019). However, in contrast to the findings in Study III as well as other studies evaluating the factor structure the DERS (Nordgren et al., 2020), it was found that the omitted Awareness subscale in DERS-16 could potentially be valuable to keep (Skutch et al., 2019).

Although Study III aimed to address some questions relating to measurement of emotion regulation, many questions remain. As previously mentioned, many definitions of emotion regulation exist, as is the case for many psychological constructs overall. Although a construct being broad could be considered a rightful reflection of the complexity of emotion regulation processes, it can make it difficult to effectively unify and summarize the research in the field (Bloch et al., 2010). As exemplified by the discussion regarding the variety of different DERS short forms, there is a need for more research to establish what the gold standard of measuring emotion regulation should be. Going forward, it would be helpful if researchers in the field unite around a way of measuring emotion regulation difficulties with the DERS that is empirically supported and accepted.

Another remaining question regarding the measurement of emotion regulation, also raised in the published paper, is what aspects of state and trait-related factors are reflected in the DERS scores. Given the relatively strong correlation of the DERS with other psychiatric symptoms, a concern is that the DERS scores reflect more than the intended trait-related difficulties, such as more state-related general distress. A measure of state-based emotion regulation difficulties, based on the DERS, has been

developed (S-DERS; Lavender et al., 2017). Results from the initial study showed moderate correlations between the S-DERS and the DERS, which suggests that the measures reflect distinct aspects of state and trait emotion regulation at least to some degree (Lavender et al., 2017).

4.4 Are emotion regulation difficulties associated with increasing substance use frequency and severity?

In Study IV, it was found that there is an association between emotion regulation difficulties and substance use in line with previous research (Weiss et al., 2022). Although the study is restricted to assessing associations at one given time point, the study adds and develops on research in the area by providing a large sample with varying levels of substance use frequency and severity across different substances (Stellern et al., 2022). Individuals with a higher substance use severity, who used multiple substances and suffered from psychiatric co-morbidities, tended to report higher Impulse subscale scores (corresponding to more difficulties controlling impulsive behavior when distressed). This corresponds to previous research demonstrating persisting difficulties with controlling impulsive behaviors in individuals with alcohol and cocaine use (Fox et al., 2007, 2008).

The study did not find evidence of a moderating effect of other psychiatric symptoms in the relationship between substance use and emotion regulation. In the context of previous research, this result was more difficult to interpret. Given that there is an overall association and frequent co-morbidity between substance use and depression and anxiety (Bradizza et al., 2018), it was surprising that there was no association between substance use and psychiatric symptoms (depression, anxiety, and stress) in Study IV. There was however, in line with Study III, an association between psychiatric symptoms and emotion regulation difficulties. Although one can hypothesize potential reasons for these results given the specific characteristics of Study IV, it is important to note that there overall is a lack of studies empirically examining this relation (Weiss et al., 2022). Replications of these results are needed before drawing further conclusions beyond the study.

Beyond Study IV, research has shown support for the role of emotion regulation as a function of relevance to substance use. In other words, for some individuals, taking substances may serve functions of avoiding negative emotions or enhancing positive ones (M. L. Cooper et al., 2015). However, more truly transdiagnostic and dimensional studies are needed in the field of substance use and emotion regulation. Although Study IV did in some ways touch upon some of these aspects by investigating the relationship across substances (not focusing on one disorder only) and use frequencies and severities (resembling a dimensional nature), studies properly designed to address these questions are needed. Additional studies investigating functions of several

different types of risky behaviors (such as deliberate self-harm and ED-related behaviors) and the relationship with emotion regulation difficulties and other co-occurring psychiatric symptoms in the same study would be of interest.

4.5 General limitations

Some important limitations in the context of this thesis are worth noting. Limitations of self-report measures are applicable to all studies. It is clear that self-report assessments have many benefits; they are often readily available, as well as easy and fast to administer and complete for both researchers and participants. However, they are also hampered by some limitations. For example, they require certain language skills and capacity to reflect on oneself (i.e., verbal behavior), and in the context of emotion regulation it requires basic knowledge on one's emotional life. When measuring constructs using a self-report scale, it can generally be challenging to establish a degree of reliability and validity to understand what we are measuring and how the measurement we obtain relates theoretically to the construct (for a thorough discussion on measurement theory, see Borsboom, 2005). Unfortunately, none of the included studies used a complementary behavioral measure to provide more alternative sources of data. Also worth noting is that the studies included have to some extent relied on a between-individual group design, which limits possibilities to understand how within-individual variation over time contributes to mental health problems and associations with emotion regulation. It would be of great benefit to further study for example symptom shifting using more frequent and fine-grained measurement (e.g., using ecological momentary assessment).

Another limitation related to Study IV is the cross-sectional design, which did not allow us to investigate the temporality of the associations between emotion regulation and substance use. The relationship between emotion regulation and psychopathology has mostly been investigated using cross-sectional studies, thus we know less about to what extent emotion regulation skills affect the development and/or maintenance of mental health problems (Cludius et al., 2020). Most likely, emotion regulation skills contribute to both processes, but more longitudinal studies are needed investigating the predictive value of emotion regulation.

Unfortunately, none of these limitations could be considered unique in the context of research within psychiatry or psychology. The context in which we conduct research reinforces certain behaviors, and thus necessarily many studies suffer from similar shortcomings. There is also a longstanding tradition in the field of psychology/psychiatry of studying group differences using null hypothesis significance testing, which could be problematic given that with a large enough sample size one can always find a statistically significant difference if there is a measurable one (Meehl, 1990). Finding ways to change contingencies in the research context to promote more studies with

longitudinal and measurement-intensive designs will be important going forward. These could for example include both changing research funding schemes to facilitate longitudinal study designs, as well as developing more easily accessible technological tools that make it simple for researchers and participants to assess behaviors in real time. The four-year limit of a doctoral education makes certain research designs necessarily hard to conduct, but the time could with advantage be used to do for example replication studies and secondary data analysis to complement projects which involve new data collection.

5 Conclusions

This thesis aimed to contribute to the development of methods to study the co-occurrence of mental health problems on a symptom level, as well as develop on emotion regulation as a potential transdiagnostic construct. The included studies concluded the following:

Study I: A meaningful subgroup of treatment-seeking individuals with EDs demonstrated "symptom shifting", decreasing in some symptoms whilst increasing in others, over time. Individuals with symptom shifting reported more psychiatric symptoms and emotion regulation difficulties, suggesting they could need more careful monitoring and tailored treatment.

Study II: A small subgroup of individuals in the general population demonstrated symptom shifting between symptoms of EDs and SUDs over time. These individuals also reported higher levels of psychiatric symptoms and demonstrated higher PRS for psychiatric disorders, levels comparable to individuals with persistent co-occurring symptoms of EDs and SUDs. These results conceptually replicate those in Study I.

Study III: Two common measures of emotion regulation, the ERQ and DERS, converged in expected ways and to expected degrees, which supports the validity of the scales. The DERS and DERS-16 demonstrated higher concurrent validity with psychiatric symptoms than the ERQ. This strengthens their status as clinically useful measures.

Study IV: Emotion regulation was associated with both frequency and severity of substance use, across a range of different substances. However, a moderating effect of psychiatric symptoms could not be established. Difficulties controlling impulsive behaviors when distressed was of specific importance to individuals with a higher substance use severity.

6 Points of perspective

6.1 What does the future of psychiatric research hold?

Reading the Background section of this thesis, it is easy to be swayed to think that the solution to understanding psychopathology is throwing out the status quo and replacing it with new promising frameworks. However, it is essential to note that a paradigm shift in psychiatry probably is an unlikely and unwanted scenario (Stein et al., 2022). Many of the frameworks offer interesting complementary perspectives on theory, but of course have significant limitations in of themselves (nothing is perfect). Although new ways of understanding and studying mental health problems has the potential to help us in the goal of preventing suffering and providing effective treatments, it should preferably be done in a way that builds upon what we already know.

One interesting aspect worth thinking about, relating to the critique posed towards the DSM, is the relative validity of different DSM diagnoses. It is unlikely that all diagnoses suffer the proposed limitations of the DSM in the same way. This is summed up in a quote by Stein et al (2022):

"...schizophrenia and bipolar disorder may be genuine disease entities, but our syndromic definition lacks specificity, and there are likely different causal pathways that lead to clinically meaningful subtypes of these disorders. Major depressive disorder, on the other hand, is likely to be a hodgepodge of mood syndromes, some non-dysfunctional (i.e., nondisorders) or nonspecific (i.e., combining depressive with anxiety symptoms), including only a few true but potentially diverse disease entities (e.g., melancholia, psychotic depression)." (p 398).

Similarly, different mental health problems may be more or less suited to be viewed from a dimensional perspective (Haeffel, Jeronimus, Kaiser, et al., 2022). Personality disorders could be one example of where dimensional models could be more useful, but this is also an empirical question. The perhaps slightly disappointing, but most realistic, conclusion is that a one-size-fits-all approach to mental health problems is likely to inadequately describe what we want to address. There will always be a need for a common nomenclature that works well enough in clinical practice defined on a (perhaps arbitrary) dichotomy, and most importantly is useful for clinicians to guide treatment and provide a basis for decisions relating to resource allocation. In other words, we are still in need of a tool such as the DSM or ICD! I however consider it of importance that psychiatry and clinical psychology as research fields continue building upon theories of psychopathology, that may in the future inform and potentially improve on the current nosology.

One example of an interesting consequence that the discussion around the RDoC initiative has already brought, is shifting the focus of treatment targets from diagnoses to specific symptoms in pharmaceutical research (Cuthbert, 2022a). I want to take the opportunity here to again acknowledge the importance of considering the philosophy of psychiatry when conducting research (where I think the discussion around the current nosology has beneficially brought and spread philosophical knowledge as a consequence). As mentioned in the Background section, what we mean to target in treatment is tightly connected to how we view mental health problems, and therefore affects the hypothesized treatment mode of action (R. Cooper, 2014). To give an example, the incorporation of the medical model and DSM nosology in the cognitive behavioral therapy field has resulted in a plethora of treatment manuals directed towards specific disorders. The treatment mode of action could here be described as a "shotgun", where we with a variety of different techniques hope to target at least some symptoms/mechanisms of relevance for helping the patient. If the diagnoses we aimed to treat were valid and helped us select individuals that would benefit from the specific treatment, this treatment mode of action would not necessarily be problematic. If there however was a significant heterogeneity in the patients within a diagnostic category, it is natural that some patients will not benefit from treatment. A shift in perspective towards, for example, mechanisms underlying specific symptoms (of which emotion regulation as a common function for certain behaviors could be one such) is already ongoing in psychiatric research and could be of value also for future research.

6.2 Clinical implications

Although this thesis did not evaluate any applications in clinical settings per se, some potential clinical implications of the studies are worth noting.

Some of the most imperative clinical implications stem from the work on symptom shifting in Study I and II. Although in practice many clinicians already work transdiagnostically, health care (as well as research) has been organized to a degree based on diagnostic categories. For the subgroups of patients with overlapping problems (especially between EDs and SUDs), this can cause problems in getting effective care. The fact that some individuals seem to shift between different symptoms or symptom areas over time suggests that ways of monitoring progress as well as tailoring treatment approaches is duly needed in practice. The aspect of improving monitoring is likely easier to implement directly, by broadening the scope of symptoms investigated at treatment follow-ups. One example where such reasoning was applied was in a study evaluating treatment for deliberate self-harm done by colleagues, where engagement in risky behaviors was followed up to assure symptom shifting did not occur as an unintended consequence (Bjureberg et al., 2018).

Implementing tailored treatments based on this research in practice will likely take more time. Our knowledge of what risk factors underlie or what things that could trigger symptom shifting, or even diagnostic co-occurrence at a higher level, needs further development. From a functional perspective of a behavior therapist, working with specific behaviors and their functions is more straightforward in individuals who have already developed mental health problems. However, developing medications or preventative strategies is less straight forward from this perspective, unless we find a way to profile individuals effectively in order to match the right patient to the right intervention (as is the goal in precision medicine; Friston et al., 2017). It would be interesting if function could be one such way of classifying individuals, that could be helpful in treatment selection (see for example Wang et al., 2021), in line with the theoretical viewpoint underlying this thesis.

Studies III and IV suggest, in line with a growing body of research, that emotion regulation is a transdiagnostic process of relevance to several mental health problems. Furthermore, emotion regulation difficulties seem to increase as severity of problems increase (Study IV). Emotion regulation improvements has also been shown to be associated with symptom improvement for some individuals who undergo psychological treatment (e.g., Garke et al., submitted manuscript). One suggestion consequently put forward as a clinical implication based on this research is to evaluate the effect of addressing emotion regulation difficulties in treatment. This could be done either as focusing on emotion regulation as part of a larger treatment (e.g., Axelrod et al., 2011), or as a whole emotion regulation–focused treatment program (e.g., Gratz, Bardeen, et al., 2015). Although some studies have shown promising results of addressing emotion regulation in the context of psychological treatment (e.g., Berking et al., 2008), one risk worth considering is that we still get stuck in the "shotgun" treatment mode of action. In other words, although emotion regulation seems to be of relevance on a group level, for some individuals, emotion regulation will not be a relevant factor in the maintenance process (given that we still select patients based on topography rather than function). Providing more individualized care based on careful assessment of specific difficulties and then addressing these difficulties in treatment, rather than adding more "shots to the shell", will be relevant to consider when moving ahead in this field.

6.3 Open science statement

During my doctoral studies my knowledge of issues relating to open science and reproducible research has increased successively (which is reflected in the extent to which these practices have been applied). Transparency is important, therefore I state what and how open science practices have been applied relating to the studies in this thesis.

Study I and IV did not apply open science practices. Study II was not preregistered due to the exploratory nature of the study. I however plan to make the analysis code available and publish the article openly. Study III was not preregistered, and analysis code was not made available, but it was published open access.

The more recent studies not included in, but of relevance to, the thesis have been preregistered where appropriate, code has been/will be made available, and published with open access. Due to the sensitive nature of the data, it is unfortunately rare that it is possible to make these kinds of datasets openly available (often due to constraints in older ethical permits, or that it consists of registry-based data as was the case for Study I and II). This is increasingly made possible however by methods such as making synthetic versions of datasets (as applied in Garke et al., 2021) as well as developments in regulations relating to legal aspects of data sharing.

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