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**FROM EFFICACY TO IMPLEMENTATION:
APPLYING INTERNET-DELIVERED COGNITIVE
BEHAVIOURAL THERAPY IN THE TREATMENT
OF OCD**

Lina Lundström



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From efficacy to implementation: Applying internet-delivered cognitive behavioural therapy in the treatment of OCD

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To my "Mormor Barbro", advocate of women's educational rights, member of Tanzanian parliament and "Mama Barbro" to the whole Tanzanian nation. 1912-1999.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Tvångssyndrom (OCD) och dysmorfofobi (BDD) är två psykiatriska diagnoser inom kategorin OCD-spektrumtillstånd. Utan behandling är OCD och BDD ofta kroniska sjukdomar med en negativ inverkan på flertalet livsområden. I dagsläget är kognitiv beteendeterapi (KBT) den rekommenderade psykologiska behandlingen för både OCD och BDD, men ett problem är den låga tillgängligheten av KBT runtom i världen.

Internetförmiddad KBT (IKBT) är en form av KBT som innehållsmässigt är likvärdig med ansikte-mot-ansikte KBT, men som förmedlas via internet. Internetformatet gör behandlingen mer flexibel och lättillgänglig, vilket innebär att fler personer kan få hjälp. Det övergripande syftet med denna avhandling var att utvidga den tidigare forskning som gjorts inom området IKBT för OCD och BDD, med målet att nå ut till fler patienter som lider av dessa psykiatriska tillstånd.

I **Studie I** ville vi undersöka ifall IKBT med terapeutstöd och IKBT utan terapeutstöd var likvärdig eller inte sämre än traditionell ansikte-mot-ansikte KBT för OCD, samt genomföra en hälsoekonomisk analys av behandlingarna. 120 deltagare slumpades till antingen ansikte-mot-ansikte KBT, terapeutledd IKBT eller icke-terapeutledd IKBT och mättes före, varannan vecka och efter behandlingen samt 3 månader och 12 månader efter behandlingen. Deltagarna i alla tre behandlingsgrupperna förbättrades efter behandlingen men resultaten kring ifall IKBT är likvärdig eller inte sämre än ansikte-mot-ansikte behandling var inte entydiga. Både terapeutledd och icke-terapeutledd IKBT var kostnadseffektiva behandlingar jämfört med ansikte-mot-ansikte KBT, framförallt utifrån lägre behandlingskostnader för IKBT.

I **Studie II** utvärderade vi effekten av IKBT för OCD och BDD när behandlingarna gavs som en del av behandlingsutbudet i den svenska sjukvården. Fyrahundratrettiofyra deltagare genomgick IKBT för OCD och 163 deltagare behandlades med IKBT för BDD. Deltagarna mättes före, varje vecka och efter behandlingen. Patienterna förbättrades och minskade sina OCD och BDD symtom efter behandlingen. En stor andel av deltagarna genomförde de huvudsakliga delarna av behandlingen och skattade att de var nöjda med behandlingen. Implementeringen av behandlingarna minskade också markant antalet patienter som stod på väntelista för att få olika typer av ansikte-mot-ansikte behandlingar på den mottagning där implementeringen genomfördes.

I **Studie III** ville vi undersöka karaktärsdrag samt behandlingsutfall med IKBT för OCD hos en kategori av OCD patienter som har en underliggande känsla av ofullständighet (incompleteness). Studien använde 167 personer från **Studie II**, som genomgått IKBT behandlingen för OCD. En känsla av ofullständighet var förknippat med svårare grad av OCD, högre grad av samsjuklighet med andra psykiatriska diagnoser samt associerat

med symmetri/iordningställande symptom. Dessutom hade individer med höga nivåer av ofullständighet sämre behandlingsutfall med IKBT för OCD.

Sammanfattningsvis visade **studie I** att både terapeutledd och icke-terapeutledd IKBT är kostnadseffektiva behandlingar jämfört med ansikte-mot-ansikte KBT, men frågeställningen kring ifall IKBT är likvärdig eller inte sämre än ansikte-mot-ansikte KBT fick inte ett entydigt svar. **Studie II** visade att IKBT för OCD och BDD är effektiva behandlingar som kan implementeras i det svenska hälso- och sjukvårdssystemet. **Studie III** identifierade att en känsla av ofullständighet kan vara ett viktigt kliniskt karaktärsdrag inom OCD, som också är relaterat till sämre behandlingsutfall med IKBT.

ABSTRACT

Background: Obsessive Compulsive Disorder (OCD) and Body Dysmorphic Disorder (BDD) are closely related psychiatric conditions associated with functional impairment across various life domains, an increased risk of suicide, and a significant societal and economic burden. If left untreated, these disorders often become chronic. While Cognitive Behavioural Therapy (CBT) and medication with selective serotonin reuptake inhibitors (SSRIs) are first-line treatments recommended for both OCD and BDD, the availability of CBT is limited in most parts of the world.

Aims: The overall aim of this thesis was to extend previous evaluations of internet-delivered CBT (ICBT) for OCD and BDD, in order to demonstrate the applicability and effectiveness of the treatments and to reach out to a broader spectrum of patients suffering from these disorders. More specifically, the aims of each study were: **Study I**, to investigate whether therapist-guided and unguided ICBT were non-inferior and cost-effective compared to face-to-face CBT; **Study II**, to evaluate the effectiveness of ICBT for OCD and BDD when implemented in the Swedish health care system; **Study III**, to examine the clinical characteristics of incompleteness and to use it to predict treatment outcome with ICBT for OCD.

Methods: **Study I** was a randomised controlled non-inferiority trial that enrolled 120 participants. The participants were randomly assigned to receive 14 weeks of either face-to-face CBT, therapist-guided ICBT, or unguided ICBT for OCD. The primary outcome measure was the clinician rated Yale Brown Obsessive-Compulsive Scale (Y-BOCS) and the non-inferiority margin was set to 3 points on the Y-BOCS. Symptom severity was measured pre, bi-weekly, post, 3-month (primary end-point) as well as 12 months after treatment. **Study II** was an effectiveness study with repeated measures (pre, weekly, posttreatment). The RE-AIM implementation framework was used to measure implementation variables according to the elements of reach, effectiveness, adoption, implementation and maintenance. Four-hundred and thirty-four participants were included and received ICBT for OCD (OCD-NET) and 163 participants were included and received ICBT for BDD (BDD-NET). The primary outcome measures for effectiveness were the clinician-rated Y-BOCS and the Y-BOCS for BDD (BDD-YBOCS). **Study III** used a subsample (n= 167) of participants from **Study II** who received ICBT for OCD. Baseline incompleteness (feelings of something being not just right or incomplete) was measured with the Obsessive-Compulsive Trait Core Dimensions Questionnaire (OCTCDQ). The primary outcome measure was the clinician rated Y-BOCS and participants were measured pre-, weekly and post-treatment.

Results: In **Study I**, both therapist-guided and unguided ICBT were found to be cost-effective compared to face-to-face CBT. However, the non-inferiority results were

inconclusive because the confidence intervals crossed the pre-specified non-inferiority margin of 3 points on the Y-BOCS at the primary endpoint (therapist-guided ICBT, mean Y-BOCS difference= 2.10 points, [90% CI, -0.41 to 4.61]; $p=0.17$; unguided ICBT, mean Y-BOCS difference= 5.35 points [90% CI, 2.76 to 7.94]; $p < .001$). In **Study II**, OCD-NET and BDD-NET led to significant reductions in OCD and BDD symptom severity (mean Y-BOCS reduction= -8.8 points; mean BDD-YBOCS reduction= -11.4 points) and large within-group effect sizes posttreatment (OCD-NET, $d=1.94$; BDD-NET, $d=2.07$). Eighty-seven percent of participants receiving OCD-NET and 78% of participants receiving BDD-NET were treatment completers and participants in both treatment groups reported a high treatment satisfaction at posttreatment (OCD-NET= 87%, BDD-NET= 79%). The implementation also influenced treatment delivery at the clinic and dramatically decreased (by 60–70%) the mean number of patients waiting to receive face-to-face treatment options. In **Study III**, the underlying emotional construct of incompleteness was positively associated with OCD severity and a higher degree of comorbidity at baseline as well as with symmetry/ordering symptoms. Furthermore, elevated levels of incompleteness predicted worse treatment outcomes with ICBT ($B=0.13$, $SE=0.04$, [95% CI 0.05 to 0.21], $p=0.002$) assessed with the clinician-rated Y-BOCS. Participants with a high degree of incompleteness had lower probabilities than individuals who scored low on incompleteness of being classified as responders (39% vs. 52%) and remitters (10% vs. 34%).

Conclusions: The results suggest that therapist-guided and unguided ICBT are cost-effective alternatives to face-to-face CBT in the treatment of OCD. Future research should focus on investigating the effects and cost-effectiveness of a stepped-care approach to deliver ICBT. The findings further indicate that ICBT for OCD and BDD are effective, acceptable, and safe treatments that can be successfully implemented within the Swedish healthcare system. More research is needed to explore the effectiveness of ICBT in a less specialised implementation context, such as primary care. Incompleteness seems to be an important clinical characteristic in OCD that deserves further investigation and higher levels of incompleteness were found to predict a worse treatment outcome with ICBT.

LIST OF SCIENTIFIC PAPERS

- I. **Lundström, L.***, Flygare, O.*, Andersson, E., Enander, J., Bottai, M., Ivanov, V. Z., Boberg, J., Pascal, D., Mataix-Cols, D., & Rück, C. (2022). Effect of Internet-Based vs. Face-to-Face Cognitive Behavioral Therapy for Adults With Obsessive-Compulsive Disorder: A Randomized Clinical Trial. *JAMA Network Open*, *5*(3), e221967. *joint first author.
<https://doi.org/10.1001/jamanetworkopen.2022.1967>
 - II. **Lundström, L.**, Flygare, O., Ivanova, E., Mataix-Cols, D., Enander, J., Pascal, D., Chen, L., Andersson, E., Rück, C. (2023). Effectiveness of Internet-based cognitive-behavioural therapy for obsessive-compulsive disorder (OCD-NET) and body dysmorphic disorder (BDD-NET) in the Swedish public health system using the RE-AIM implementation framework. *Internet Interventions*, *31*:100608.
<https://doi:10.1016/j.invent.2023.100608>
 - III. **Lundström, L.**, Ivanova, E., Mataix-Cols, D., Flygare, O., Rück, C., Andersson, E. (2023). Incompleteness as a clinical characteristic and predictor of treatment outcome in a sample of individuals with obsessive-compulsive disorder. *Unpublished manuscript*.
- Appendix: Rück, C., Lundström, L., Flygare, O., Enander, J., Bottai, M., Mataix-Cols, D., Andersson, E. (2018). Study protocol for a single-blind, randomised controlled, non-inferiority trial of internet-based versus face-to-face cognitive behaviour therapy for obsessive-compulsive disorder. *BMJ Open*, *8*(9):e022254.
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LIST OF ABBREVIATIONS

- AAI** Appearance anxiety inventory
- ACC** Anterior cingulate cortex
- ACT** Acceptance and Commitment Therapy
- ADHD** Attention-deficit/hyperactivity disorder
- BDD** Body dysmorphic disorder
- BDD-YBOCS** Yale-Brown Obsessive-Compulsive Scale for BDD
- CBT** Cognitive behavioural therapy
- CFT** Compassion-Focused Therapy
- CR** Conditioned response
- CS** Conditioned stimuli
- CSTC** Cortico-striato-thalamo-cortical circuit
- CT** Cognitive Therapy
- DBS** Deep brain stimulation
- DSM-5** Diagnostic and Statistical Manual of Mental Disorders, fifth edition
- ERP** Exposure with response prevention
- GWAS** Genome-wide association study
- HA** Harm avoidance
- ICBT** Internet-delivered cognitive behavioural therapy
- INC** Incompleteness
- IU** Intolerance of Uncertainty
- KTA** Karolinska Trial Alliance
- MADRS-S** Montgomery-Åsberg Depression Rating Scale – Self report
- MBCT** Mindfulness-Based Cognitive Therapy
- NJRE** Not Just Right Experience
- OCD** Obsessive-compulsive disorder
- OCI-R** Obsessive-Compulsive Inventory – Revised
- OCS** Obsessive-compulsive symptoms
- OCTCDQ** Compulsive Trait Core Dimensions Questionnaire
- OFC** Orbitofrontal cortex
- RCT** Randomised controlled trial
- RE-AIM** Reach, Effectiveness, Adoption, Implementation and Maintenance
- RDoC** Research Domain Criteria
- SNP** Single nucleotide polymorphism
- SRIs** Serotonin reuptake inhibitors
- SSRIs** Selective Serotonin reuptake inhibitors
- TIC-P** Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry
- Y-BOCS** Yale-Brown Obsessive-Compulsive Scale

1 INTRODUCTION

“You can’t change someone who doesn’t see an issue in their actions”

In my opinion, the fundamental key to change in any psychological treatment is to motivate the patient to make that change. Without it, psychologists can spend hours introducing evidence-based treatments, but with no success. Conversely, when that motivation is there, patients are suddenly able to face dreadful anxiety provoking situations and practice new treatment skills, to reach the change they are longing for.

What struck me when I started working with OCD, in my early years of psychology practice, was that these patients often came to the clinic with a predefined motivation to change, something that I had not encountered in the same way working with many other disorders. The OCD patients could articulate a clear suffering from their obsessions and time-consuming compulsions and wanted help to change what they considered “was not them”. This, in combination with my ability as a therapist to offer an effective treatment, made me specifically interested in working with OCD.

Digging deeper into the lives of patients with OCD, I realised the tremendous suffering these patients had, and how the disorder also negatively affected the people around them. Many individuals who came to the clinic had suffered from OCD for years without adequate treatment. At the time, internet-delivered CBT (ICBT) for OCD had been developed by Erik Andersson and Christian Rück, and when I was asked to lead a project evaluating ICBT in comparison to face-to-face CBT (**Study I**), I immediately got interested. What if a digital format of the effective treatment I was delivering was equally effective? In my mind, this could enable access to treatment for those who would otherwise not receive help, as well as create an opportunity to position ICBT as a possible treatment alternative within the healthcare system.

With this first project, my PhD journey started, and little did I know then that these early thoughts would later be realised when ICBT for OCD and BDD was implemented within the healthcare system in Sweden (**Study II**). Through this journey, I hope that my research has contributed to forming ideas for how we look at psychological treatment delivery within Swedish healthcare, and I know that the implementation has already enabled access to treatment for OCD and BDD sufferers throughout the country. The treatments have also crossed international borders and have been translated into different languages. My hope for the future is that access to evidence-based care will continue to grow and enable help for those in need, independent of culture or socioeconomic status.

Stockholm, June 2023

2 LITERATURE REVIEW

2.1 OBSESSIVE-COMPULSIVE DISORDER

Obsessive-compulsive disorder (OCD) is a psychiatric condition affecting approximately 1.3% of the general population.¹ An individual with OCD experiences recurrent and persistent thoughts, urges, or impulses (obsessions) that are experienced as intrusive and unwanted, and causing substantial distress. The obsessions (e.g., I'm contaminated, what if I stab someone?) are often experienced as ego-dystonic, meaning that they are not consistent with the individuals' own beliefs or values. Compulsions are repetitive or ritualistic behaviours performed in order to reduce the anxiety and/or distress induced by the obsessions. Compulsions can be either overt, such as hand washing, or covert, such as counting. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) requires that either obsessions, compulsions, or both be present for a diagnosis of OCD, and that they cause clinically significant distress or impairment in social, occupational, or other areas of functioning.²

The mean age of onset for OCD is between 19–20 years of age and males make up a higher proportion of the early onset cases.³ However, women are at greater risk of developing OCD, with a lifetime prevalence rate of 1.5% compared to 1% among men.¹ While a diagnosis of OCD must meet specific criteria, obsessions and compulsions can occur on a spectrum and as many as 28% of individuals report experiencing obsessions or compulsions at some point in their lives.³

Comorbid conditions are common in individuals with OCD. In an American national comorbidity survey, up to 90% of respondents with OCD also met criteria for another lifetime diagnosis, with other anxiety disorders being the most common comorbid condition at 76%, followed by mood disorders (63%), impulse-control disorders (56%), and substance use disorders (39%).³ Neuropsychiatric disorders are frequently linked to OCD, with individuals diagnosed with OCD being 13 times more likely to have an autism spectrum disorder compared to the general population.⁴ Furthermore, approximately 20–30% of individuals with OCD exhibit concurrent or a past history of comorbid tics.⁵ Comorbidity with attention-deficit/hyperactivity disorder (ADHD) is more prevalent in youths and adolescents with OCD (19%), compared to adult samples (9%), but comorbidity rates vary significantly across different studies.⁶

2.1.1 Symptom dimensions

OCD is a heterogeneous disorder, often subdivided into different symptom dimensions based on the presentation of obsessions and compulsions. Numerous factor analytic studies have been conducted in OCD to identify the symptom dimensions with the best

fit and the most consistently replicated factors are the following four: contamination/cleaning, forbidden thoughts/checking, symmetry/ordering, and hoarding.⁷⁻¹²

In recent decades, some researchers have proposed categorisations of OCD according to underlying emotional and motivational factors that drive OCD behaviour, rather than categorising symptoms.¹²⁻¹⁵ Summerfeldt et al have proposed “The Core Dimensions Model of OCD” where OCD behaviour is thought to be motivated by the underlying emotional processes of harm avoidance (HA) and incompleteness (INC).¹³ Patients with harm avoidance often experience thoughts of inflated responsibility for preventing harm to oneself or others, which result in anxiety and compulsive neutralising behaviours to prevent something bad from happening.¹³ In contrast, patients with incompleteness often experience a feeling that something isn’t just right or feels wrong, and feel an urge to repeat an action over and over again until it feels right.¹⁴ In the literature, the term Not Just Right Experience (NJRE) is often used equivalent to incompleteness and these two terms are sometimes also called sensory phenomena.^{14,16,17}

A large body of research has replicated the findings that incompleteness has strong links to the symptom category of symmetry/ordering OCD.¹⁴⁻²¹ Incompleteness has further been specifically related to OCD features, rather than to other anxiety disorders,^{19,22} and positively associated with OCD severity, a higher rate of comorbidity, an earlier onset of OCD, lower functioning and higher levels of perfectionism.^{14-17,19,23} Researchers supporting the dimensional model of OCD agrees that incompleteness could have future treatment implications, where different underlying mechanisms of OCD might benefit from different treatment approaches.^{12,14,22}

2.1.2 Impact of the disorder

OCD has significant implications throughout an individual's life and spontaneous recovery is uncommon in OCD without adequate treatment.²⁴ OCD is associated with profound decreases in educational attainment, spanning from elementary school to postgraduate education, and the effects appear to be more pervasive for individuals with an early onset of OCD.²⁵ Upon entering the labour market, individuals with OCD experience further difficulties, with a higher likelihood of disability pension, long-term sickness absence or long-term unemployment.²⁶ Lower quality of life is common in people suffering from OCD, particularly in the work/social and emotional/family domains of life. Furthermore, individuals with OCD have a substantial risk of death by suicide, even after adjusting for comorbid psychiatric diagnosis.²⁷ Somatically, those diagnosed with OCD are found to have an increased risk for a broad range of cardiovascular diseases²⁸ and higher mortality rates compared to the general population.²⁹ These

findings emphasise the importance of timely diagnosis and treatment of OCD, in order to minimise the negative impact of the disorder on individuals' lives.

2.2 ETIOLOGY AND MAINTENANCE

2.2.1 Etiology

At present, the etiology of OCD can best be explained by an integrative model, where genetic, environmental and neurobiological factors interact.³⁰ It is crucial to further investigate the factors underlying the development of OCD in order to optimise prevention, early diagnosis and treatment strategies for this debilitating disorder. With current advancements in the field of genetics, risk genes for OCD may be identifiable in the future.

2.2.2 Genetic contribution

Genetic and twin studies have found OCD to be a heritable disorder^{30–33} and research consistently confirm that OCD run in families.³⁰ First-degree relatives of people with OCD are about 4–5 times more likely to have the disorder, compared to relatives of unaffected controls,³² and the risk of OCD is significantly higher for relatives to people with childhood-onset OCD.³⁰ In a meta-analysis investigating the heritability of obsessive-compulsive behaviours among twins, additive genetic effects (additive genes are genes working together to code for the same trait) accounted for approximately 40% of the phenotypic variance (the variability in traits or characteristics) in obsessive-compulsive behaviours. Non-shared environment (environments that are not shared among twins or siblings) accounted for approximately 50%.³³ Although OCD is heritable, no single gene has yet been identified as a major causal factor for the disorder, and studies indicate that OCD is polygenic, with many genes contributing to an increased risk for developing OCD.³⁰

Recent advances in the search for genetic contributions to the development of psychiatric disorders are Genome-Wide Association Studies (GWAS), where associations between certain traits and single-nucleotide polymorphisms (SNPs) from DNA are analysed. So far, the sample sizes for the GWAS studies in OCD have been too small to identify risk genes^{34,35} and only one study investigating variations in obsessive-compulsive symptoms (OCS) found a single SNP that reached the level of statistical significance.³¹ Hopefully, GWAS studies will add knowledge to the genetic contribution of OCD in the future.

2.2.3 Environmental risk factors

Several potential environmental risk factors such as perinatal complications, reproductive cycle, and stressful and traumatic life events have been proposed for OCD,

but a systematic review of the field concluded that most studies have investigated associations rather than causations. Data have often been collected retrospectively without twin or other types of family-based designs to control for genetic factors, which limits the conclusions that can be drawn from the findings.³⁶ In a subsequent population-based Swedish cohort study, a range of perinatal risk factors were associated with OCD (e.g., breech presentation, birth weight, smoking during pregnancy, Apgar distress scores at 5 minutes) independent of shared familial confounders, suggesting a causal pathway for these environmental risk factors.³⁷ In a Danish population-based cohort study investigating early-life family composition and parental socioeconomic status as potential risk factors for OCD, being an only child was associated with a higher risk for OCD in both sexes. Higher maternal age and birth order were risk factors for OCD in males and parental education, occupation, and income risks were more pronounced risk factors for OCD in females.³⁸ Future research in the field of environmental risk factors should aim to employ quasi-experimental family and twin designs to explain causation rather than association between risk factors and OCD.³⁶

2.2.4 Neurobiology

A large body of evidence suggests that neurobiologically, OCD is associated with a dysfunction of the cortico-striato-thalamo-cortical loop (CSTC).^{30,39,40} Studies have identified abnormally high activity throughout the frontal cortex and subcortical structures in people with OCD, such as the orbitofrontal cortex (OFC), thalamus, insula, striatum and anterior cingulate cortex (ACC). Each of these brain regions likely performs its distinct role within this loop, while closely cooperating with each other.^{39,40} The OFC is thought to serve as a monitor of appropriate behaviour in social contexts, the ACC functions as an action monitor and regulator, the caudate nucleus of the striatum acts as a gateway between the limbic and frontal cortices, and the thalamus acts as an information filter.³⁹

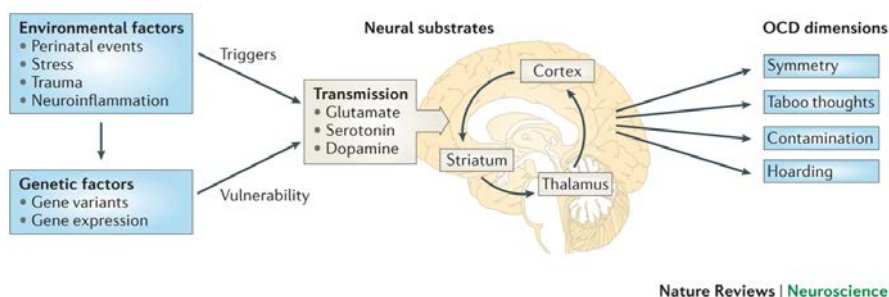
The CSTC comprises a direct (excitatory) and an indirect (inhibitory) pathway, which is balanced in healthy individuals but considered to be hyperactivated in individuals with OCD.³⁹ The altered balance of activity in these pathways is believed to either facilitate or impede the selection of suitable sequences of behaviour.⁴¹ Obsessions have been associated with increased activity in the OFC, while the repetitive character of compulsions are thought to be influenced by activity in the striatum.⁴² Brain imaging studies have also found that the activity in brain regions of the CSTC normalises in patients with OCD after successful CBT treatment.⁴³

Serotonin, dopamine and glutamate have all been suggested as neurotransmitters involved in OCD, and genetic studies suggest that gene variants in each of these systems could increase the risk for OCD.^{30,40} An integrative model of OCD proposes that

a genetic vulnerability to the impact of environmental factors might trigger modifications of neurotransmitter-related genes through epigenetic mechanisms. As a result, neuroanatomical expressions of these modifications produce an imbalance of the CSTC, expressed in phenotypes of obsessions and compulsions (see figure 1 below).³⁰

In summary, the etiology of OCD is gradually being uncovered, and it appears that genetic, environmental, and neurobiological factors interact in the development of the disorder. However, identifying risk genes for OCD will require larger sample sizes in GWAS studies, and such international efforts are currently underway. Additionally, to draw causal conclusions about environmental risk factors, researchers have emphasised the need for more prospective data collection and twin-design studies. By continuing to examine the complex interplay of risk factors, we will hopefully gain a better understanding of the mechanisms that drive the onset and maintenance of OCD in the future.

Figure 1. An integrative model for the expression of OCD



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2.2.5 Psychological models

2.2.5.1 The cognitive-behavioural model of OCD

The two-factor theory, postulated by Mowrer in the 1950s, remains a prominent psychological theory of OCD and forms the basis for exposure-based therapies for OCD. This theory combines classical and operant conditioning behavioural principles to explain the development and maintenance of anxiety disorders.⁴⁴ According to this theory, the obsession is considered a conditioned stimulus (CS) that elicits the anxiety/distress response (CR). The anxiety/distress is in turn a discriminative stimulus for compulsive behaviour, which is performed in order to reduce anxiety/distress in the short term (negatively reinforced) but maintains the CS-CR relation and increases compulsive behaviour in the long term.⁴⁴ E.g., a patient has an obsessional thought that

he/she has germs on the hands (CS) which elicits a anxiety/distress response of becoming ill (CR), which in turn makes the individual perform compulsions in order to get “clean” (negatively reinforced) but this behaviour maintains the handwashing behaviour over time (CS–CR).

The cognitive model of OCD, developed by Salkovskis and Rachman in the 1980s and 1990s,^{45,46} was based on studies that revealed a high prevalence of intrusive thoughts in the general population, with no difference in content from the obsessional thoughts experienced by OCD patients. As a result, the cognitive approach to OCD suggests that the problem lies in how individuals with OCD interpret the meaning of their obsessions, rather than the thoughts themselves.^{47,48} For instance, an obsessional thought may signal to a patient with OCD that something is wrong, making it their responsibility to prevent something bad from happening and resulting in an urge to perform a compulsion. In contrast, a person without OCD might view the same thought as unpleasant but normal, without feeling the need to take further action. The two-factor theory and the cognitive model together form the cognitive-behavioural model of OCD, which is illustrated in Figure 2 below.

Figure 2. Cognitive-behavioural model of OCD

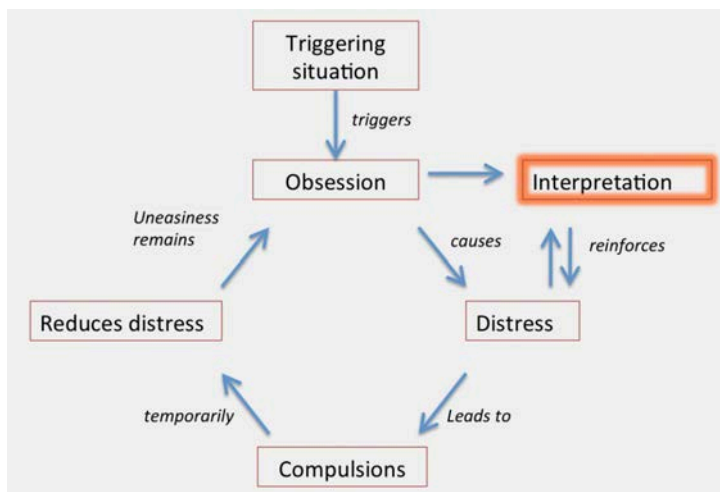


Figure caption: A triggering situation evokes obsessions (CS), which cause distress (CR). The obsessional thought is misinterpreted, resulting in further distress. The individual is compelled to perform compulsions in an effort to temporarily alleviate the distress. The reduction in distress is negatively reinforced, thereby maintaining long-term uneasiness (CS–CR). The provided image is a screenshot from the BASS4 internet platform.

Intolerance of uncertainty and excessive habit formation theories of OCD

Intolerance of uncertainty (IU) is a cognitive construct involved in the maintenance of OCD, which involves a heightened sensitivity to uncertainty and a need for control.^{49,50} Individuals with OCD often have a low tolerance for uncertainty, which triggers a preoccupation with the possibility of danger or harm.⁵¹ This in turn generates a persistent urge to reduce such risks or seek reassurance that feared disasters have not occurred. The individual engage in compulsive behaviours to reduce their anxiety and gain a sense of control, however, these behaviours actually reinforce the belief that uncertainty is intolerable and lead to the development and maintenance of OCD.⁴⁹ In the treatment of OCD, the IU model has added important psychoeducational elements where the patients can be taught that they need to accept a certain level of uncertainty, since it is impossible to attain complete assurance that negative consequences will not happen.⁴⁹ Additionally, cognitive strategies can be included in the treatment process to challenge the patient's desire for absolute certainty.⁵²

The traditional explanation for OCD proposes that individuals perform compulsive behaviours voluntarily in response to obsessional distress, and that these behaviours are negatively reinforced by the reduction of anxiety.⁵³ However, there are counteracting theories to this model, proposing that compulsions should not be viewed as goal-oriented responses to obsessions, but rather as behaviours originating in excessive habit formation.^{53,54} The executive control system plays a critical role in OCD, and neurocognitive models highlights the imbalance between the goal-directed and habit systems, with overactivity in the habitual network and underactivity in the goal-directed network.⁵⁴ According to the excessive habit formation theory, compulsivity results from an overreliance on habitual responses, which leads to an imbalance between habitual and goal-directed behaviour. The model further implies that obsessions may develop as post hoc rationalisations of compulsive behaviours, rather than deliberate and goal-directed choices.^{53,54}

In summary, various theories and models attempt to explain the development and maintenance of obsessive-compulsive behaviour. The two-factor and cognitive theories remain the most prominent, as they together form the cognitive-behavioural model of OCD, the basis for CBT treatment. Over the years, new theories have emerged, such as the IU and excessive habit formation theories, which have contributed to insights as well as the potential for combining different theories to develop more comprehensive treatment strategies for OCD.

2.3 BODY DYSMORPHIC DISORDER

The main focus of this thesis is OCD. However, in **Study II**, ICBT was implemented for both OCD and body dysmorphic disorder (BDD) in the Swedish health care system. Therefore, the following section will briefly describe BDD, and the remaining sections will discuss OCD and BDD together.

An individual with BDD experiences a preoccupation with perceived physical defects, that are disproportionate in nature, and often not noticeable to others. The preoccupation is accompanied by repetitive behaviours (e.g., excessive grooming, mirror-checking, seeking reassurance) or mental acts such as comparing one's appearance to others to relieve anxiety caused by the perceived defect. In addition, the concerns about appearance needs to cause significant distress and impairment in different areas of functioning and should not be better explained by an eating disorder.²

The lifetime prevalence of BDD is approximately 1.9% in the general population and the disorder is more common among women, with a 2.6 women to men ratio in the community.⁵⁵⁻⁵⁷ BDD usually begins in adolescence and is often chronic if left untreated.⁵⁸ Functional impairment and lower quality of life is common among individuals suffering from BDD, with effects on academic and work functioning,⁵⁹ as well as a high rate of psychiatric hospitalisation and suicidality.^{60,61} BDD sufferers often seek plastic surgery instead of psychological treatment for their problems, leading to dissatisfaction with the surgery and continued appearance problems.⁶² Depression is the most commonly reported comorbid diagnosis to BDD (75%), followed by social phobia (38%), substance use disorders (30-50%), and OCD (33%).^{58,63,64}

2.4 TREATMENT

2.4.1 Pharmacological treatment of OCD and BDD

Clomipramine is a serotonin reuptake inhibitor (SRI), and it was the first medication proved effective in the pharmacological treatment of OCD.⁶⁵ Subsequent selective serotonin reuptake inhibitors (SSRIs) have been used since the 1990s and their therapeutic effect over placebo has been confirmed in several trials.^{66,67} Studies comparing Clomipramine with SSRIs in OCD have found equivalent efficacy between the two agents, but some studies indicate that clomipramine is associated with higher rates of adverse events and trial discontinuation.⁶⁸ A dose response relationship have been found for SSRIs, where higher doses have shown greater efficacy in OCD compared to low or medium doses.⁶⁹ The addition of antipsychotics to SSRIs is not standard practice but can augment the effect in treatment-resistant OCD cases.^{68,70}

SSRIs are the recommended pharmacological treatment for BDD,^{71,72} and different SSRIs have had a significant effect over placebo in several trials, with higher doses showing a greater effect.⁷³ The effect of additional anti-psychotics is less studied in BDD, but overall seems to have little or no extra effect over SSRIs alone.⁷⁴

2.4.2 Psychological treatment of OCD and BDD

Today, CBT is recommended as a first-line psychological treatment for both OCD and BDD.⁷² International guidelines suggest that a combination of SSRIs and CBT should be offered to patients with moderate to severe symptoms and functional impairments, while CBT alone should be offered to mild cases.⁷²

The efficacy of CBT in treating OCD is well established, with large effect sizes reported in randomised controlled trials (RCTs) and positive long-term effects. Studies comparing the effect of cognitive therapy (CT) and exposure with response prevention (ERP) based therapies have found similar effects for both CBT elements. However, ERP treatments have the largest evidence base to support their use in treating OCD.^{75–79} In the case of BDD, CBT has proven effective in several RCTs⁸⁰ and naturalistic follow-ups indicate that treatment gains are typically maintained long-term.^{81,82} Nonetheless, remission rates following CBT for BDD are often low, and further research is required to improve existing CBT elements and evaluate their long-term effects.⁸³

There are various modes of delivering CBT for OCD and BDD, including individual therapy, group therapy, internet-delivered treatments and self-help programs (described in more detail below). The intensity of treatment can also be adjusted without altering the actual content or mode of delivery. For example, a concentrated 4-day group CBT treatment for OCD has demonstrated promising results in effectiveness studies, with long-term benefits.^{84–86}

In ERP treatments for OCD and BDD, the patient is exposed to the conditioned stimuli (CS, i.e., situations, images, thoughts) while refraining from rituals, compensatory behaviours or safety behaviours. Through repeated exposure, the anxiety/emotional distress (CR) is thought to gradually extinguish (Figure 3).⁸⁷ From a cognitive perspective, ERP also corrects dysfunctional beliefs and provides the patient with information that feared negative consequences are unlikely to occur.⁸⁸ Additionally, ERP enhances self-efficacy and teaches the patient to tolerate emotional distress to a greater extent without relying on safety behaviours.⁸⁸ A key aspect for change in ERP treatments is thought to be habituation, which refers to the fact that the emotional response to a feared stimulus diminishes over time, both between and within sessions, and gradually extinguishes.⁸⁸ However, Craske and colleagues have challenged this assumption by proposing an inhibitory learning theory for exposure and extinction.⁸⁹

This theory posits that fear extinction is primarily driven by the formation of new associations between feared objects or situations and the absence of objective threat, and these newly formed associations are reinforced through exposure.⁹⁰ The original fear-memory association is not erased, but competes for retrieval with the new non-threat association.⁹¹ Evidence for this is that retention of parts of the original fear memory can be uncovered, even after repeated exposures. According to Craske, the target for ERP treatment should preferably be to enhance inhibitory learning during exposure and promote fear tolerance instead of fear reduction.⁹¹

Figure 3. Anxiety/distress curve in ERP treatment according to the CBT model of OCD

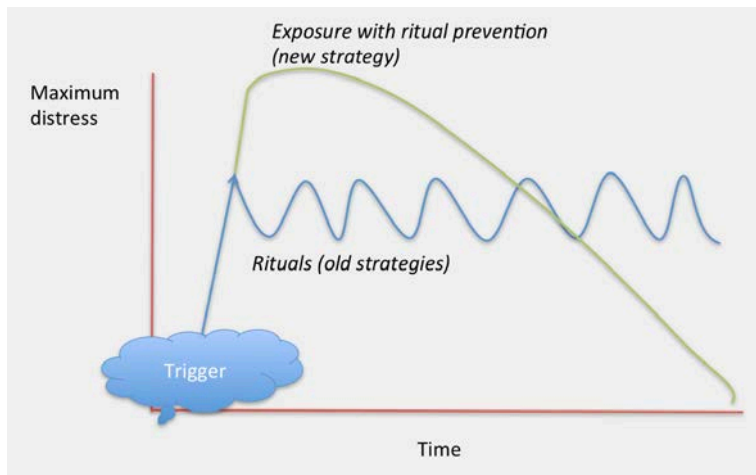


Figure caption: The trigger is the CS (situations, images, thoughts) that elicit an increase in anxiety/distress. The blue wavy line shows the temporary reduction in anxiety/distress, that happens when rituals are performed, but which maintains the anxiety/distress in the long-term (negatively reinforced). The green line illustrates the gradual decline in anxiety/distress (habituation) experienced when the patient remains in anxiety/distress-provoking situations, while refraining from engaging in rituals. The provided image is a screenshot from the BASS4 internet platform.

In the beginning of the 2000s, a "third wave" of CBT was introduced, which included several interventions such as acceptance and commitment therapy (ACT), mindfulness-based cognitive therapy (MBCT), and compassion-focused therapy (CFT).⁹² These are relatively new approaches in the treatment of OCD and BDD that emphasise mindfulness, acceptance, and values-based action to develop a non-judgmental and accepting attitude towards intrusive thoughts and compulsive behaviours, while also working towards meaningful goals and values. Overall, the evidence for ACT and MBCT in the treatment of OCD and BDD is limited, but while more research is needed, the existing studies suggest that these treatments may be useful alternatives⁹³⁻⁹⁵ or

complementary approaches to traditional CBT.^{96,97} However, the evidence so far indicates that they do not outperform ERP treatments.⁹⁸

To summarise, evidence-based treatments for OCD and BDD include psychological treatments with CBT and/or pharmacological treatments with SSRIs.^{72,99} CBT can be administered in various modalities and intensities, with ERP being a key component of the treatment, involving the patient's exposure to feared stimuli while refraining from engaging in compensatory behaviours. In addition, other CBT theories, such as the inhibitory learning approach to exposure or the integration of "third wave" CBT elements, have emerged as useful complementary approaches in the treatment of OCD and BDD.

2.4.3 Access to CBT and the potential of ICBT

OCD and BDD have low probabilities of remission in the absence of effective treatment^{61,100} and unfortunately, a significant gap exists between the supply and demand of CBT for OCD and BDD.¹⁰¹ Common barriers that limit access to treatment include a shortage of trained CBT therapists,¹⁰² treatment costs,¹⁰³ geographical distances and the embarrassment associated with disclosing one's symptoms.¹⁰⁴ One possible solution to these challenges is ICBT, which is a form of CBT delivered over the internet and typically supported by a therapist or other healthcare professional. Therapist-guided ICBT has equivalent treatment content to regular face-to-face CBT, but it is more accessible and requires less therapist time.¹⁰⁵ During therapist-guided ICBT, patients work online with text-based self-help materials, CBT exercises, and homework assignments, typically through a secure website. Communication takes place within an internet platform, where the patient and therapist can send asynchronous messages to one another. The primary role of the therapist is to motivate the patient to engage in CBT exercises and provide support throughout treatment by troubleshooting any issues that may arise. Research has demonstrated that therapist-guided ICBT is an effective treatment option for both somatic and psychiatric disorders, with comparable efficacy to traditional face-to-face CBT.¹⁰⁶ Therefore, therapist-guided ICBT represents a promising solution to overcome the barriers associated with accessing CBT for OCD and BDD.

2.4.4 ICBT for OCD and BDD

ICBT for OCD has demonstrated positive results across cultures and age groups. In Australia, Wootton and colleagues and Mahoney and colleagues have both shown ICBT for OCD to be effective in randomised controlled trials^{107,108} and in Germany, Herbst and colleagues have tested ICBT for OCD with positive long-term effects.¹⁰⁹ ICBT has also shown to be efficacious in children and adolescents with OCD,^{110,111} and in comparison to face-to-face CBT using a stepped care model including ICBT.¹¹² Our therapist-guided ICBT treatment for OCD (OCD-NET), which was employed in **Study I, II** and **III** of this

thesis, was developed by Andersson et al (Table 1 and Figure 4).¹¹³ The treatment was initially evaluated through a pilot study (n= 23), where a large within-group effect size (d = 1.56) was observed posttreatment.¹¹⁴ Subsequently, a RCT was conducted (n= 101), comparing OCD-NET to an active control condition involving internet-delivered supportive therapy. Results indicated that OCD-NET outperformed the supportive therapy, exhibiting a large between-group effect size (d= 1.12)¹¹⁵ and treatment effects were also sustained for up to two years posttreatment.¹¹⁶ In a third study (n= 128), OCD-NET, with or without the addition of the partial NMDA-agonist d-cycloserine was investigated. While no significant impact of d-cycloserine on treatment outcomes was observed, large within-group improvements were observed for both OCD-NET groups (d-cycloserine group, d= 1.82; placebo, d= 2.20).¹¹⁷

The evidence base for ICBT in BDD is less established compared to OCD and apart from our therapist-guided ICBT treatment for BDD (BDD-NET, Table 1 and Figure 4) used in **Study II**, only an app-based CBT treatment with online and telephone coach support has been developed for adult BDD patients. Results from the app-based intervention indicate that the treatment is acceptable and feasible,¹¹⁸ with large effect sizes (d= 1.44) posttreatment compared to a waitlist control condition.¹¹⁹ Similarly, our BDD-NET treatment has demonstrated promising results in one feasibility study and one RCT, with large effect sizes (ranging from d= 0.95 to 2.01)^{120,121} and in a subsequent follow-up study, treatment gains were maintained up to 2 years after treatment.¹²² BDD-NET has also been tested globally with participants from various cultural backgrounds, and results suggests that BDD-NET can be effective when delivered to a culturally diverse sample.¹²³

Figure 4. Internet platform screenshot of the OCD-NET and BDD-NET treatments

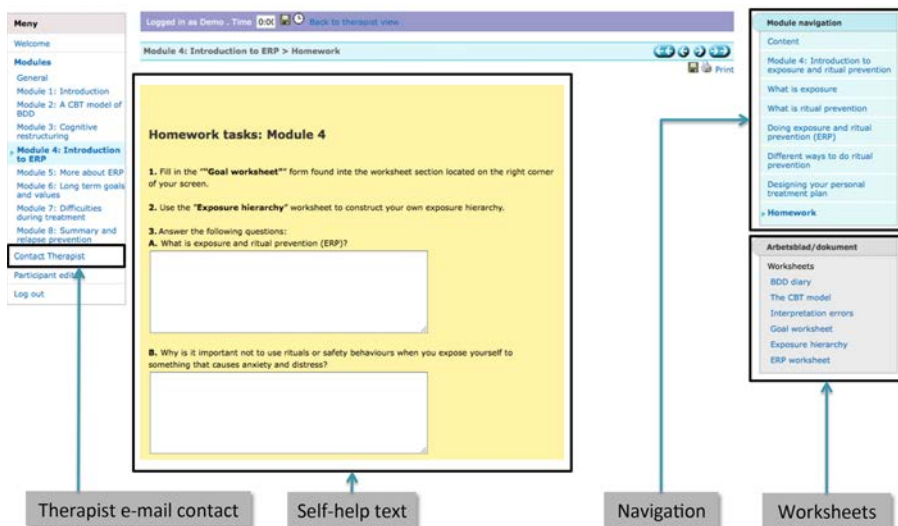


Table 1. Treatment content of OCD-NET and BDD-NET

OCD-NET: Module content	BDD-NET: Module content
Psychoeducation: Introduction to the treatment and information about OCD and the online CBT program	Psychoeducation: Introduction to the treatment and information about BDD and the online CBT program
A cognitive-behavioural conceptualisation of OCD: Psychological model of OCD with patient examples	A cognitive-behavioural conceptualisation of BDD: Psychological model of BDD with patient examples
Cognitive restructuring: Common OCD metacognitions and biases and unhelpful interpretations of thoughts	Cognitive restructuring: Self-defeating thoughts and maladaptive thinking maintaining BDD symptoms
Exposure with response prevention: Introduction to Exposure with response prevention (ERP) and goal formulation	Exposure with response prevention: Introduction to Exposure with response prevention (ERP) and goal formulation
More on ERP: Different aspects of ERP are highlighted, and a more in-depth explanation is given on how to work with ERP over time	More on ERP: Different aspects of ERP are highlighted, and a more in-depth explanation is given on how to work with ERP over time
Imaginal exposure: Introduction to imaginal exposure techniques	Values-based behaviour change: Value-based long-term goals and accepting standpoints against negative thoughts
Re-exposure: ERP exercises continues and instructions to re-exposure are given	Difficulties during treatment: Commonly encountered difficulties during treatment are presented and discussed
Difficulties during treatment: Commonly encountered difficulties during treatment are presented and discussed	Relapse prevention: The treatment is summarised and a plan for relapse prevention is constructed
Values-based behaviour change: Daily ERP continues with further exercises added including value-based goals	
Relapse prevention: The treatment is summarised and a plan for relapse prevention is constructed	

2.4.5 Unguided ICBT for OCD and BDD

Results from self-help treatments for OCD (bibliotherapy, internet-based and computerised formats), support the use of self-help interventions, but effect sizes have been larger for self-help treatments with minimal contact, compared to pure self-help interventions.¹²⁴ When self-help treatments are compared to face-to-face therapy, results usually favours face-to-face treatments¹²⁵ and patients receiving some therapist support tend to have better treatment outcomes and lower rates of attrition than those with no therapeutic contact.^{124,126}

ICBT can be delivered unguided (with no therapist support or with minimal therapist input), and two recent meta-analyses found that low-intensity digitally delivered self-help treatments for OCD were significantly more effective than a passive control condition.^{29,130} However, Lovell et al. found that none of two self-help programs for OCD (reading a book or a computerised program) reached statistical significance over a waitlist control condition.¹²⁹ Contrary, Wotton et al, found that unguided ICBT for OCD was effective compared to a waitlist control condition¹³⁰ and results from two previous open trials with unguided ICBT showed that treatment gains were maintained up to 12 months after treatment.¹³¹ While unguided ICBT for OCD appears to be a promising treatment format according to some studies, more research is needed, especially randomised controlled trials comparing unguided ICBT to other forms of treatment for OCD, such as face-to-face therapy. To the best of my knowledge, there have been no attempts yet to deliver unguided ICBT for BDD.

To summarise, the recommended psychological and pharmacological treatments for both OCD and BDD are CBT and SSRIs. CBT can be delivered in different formats and intensities, where ICBT is one way of delivery, that can enable access to individuals who otherwise would not get help. ICBT for both OCD and BDD has shown positive results in research settings. Findings from the few effectiveness studies on ICBT for OCD indicate promising results, whereas the results from unguided treatment formats seems more ambiguous and requires further investigation. In BDD, effectiveness studies and trials of unguided ICBT are lacking, and more research is needed in this field.

2.5 COST-EFFECTIVENESS OF ICBT FOR OCD AND BDD

Cost-effectiveness analysis assesses the additional benefits of a treatment relative to its additional costs and compares it to alternative treatments or other control conditions. Such analyses are critical when implementing a new treatment into the health care system and can be used to provide policy makers with information to guide

treatment selection, so that as many patients as possible can be helped and treated effectively with the available funds. Costs can be estimated from various perspectives, e.g., the health care organisational perspective (intervention costs), the direct medical (medication usage and health care visits) and the societal perspective (sick-leave and absenteeism from work).¹³² Costs are usually calculated in monetary units, whereas the advantages of a treatment can be assessed in a variety of metrics such as life expectancy, reduction of symptoms or improvement in quality of life.¹³³

Only a few studies have investigated the cost-effectiveness of therapist-guided ICBT for OCD. Andersson et al. compared therapist-guided ICBT to online supportive therapy and found ICBT to be cost effective from a healthcare organisational and societal perspective.¹³⁴ In children and adolescence with OCD, therapist-guided ICBT has proven to be cost-effective when compared to a control condition¹³⁵ and in a stepped care model comparing ICBT to in person face-to-face CBT.¹³⁶ The only adult study comparing ICBT with face-to-face CBT found ICBT to be a cost-effective treatment alternative. However, this study used no direct comparison between the treatments since simulated data from different literature sources were used to estimate treatment effects and costs for the face-to-face treatment.¹³⁷ Thus, a direct comparison between ICBT and regular face-to-face CBT is still needed in adult samples. In BDD, one study of BDD-NET proved it to be a cost-effective treatment alternative compared to a supportive therapy control condition.¹³⁸

Taken together, ICBT may be a cost-effective treatment alternative for OCD but the cost-effectiveness in relation to standard face-to-face treatment is still not fully explored. Little is known regarding the cost-effectiveness of ICBT for BDD. More research is needed in this field, in order to inform and guide policymakers in their decisions regarding which treatments to implement in healthcare settings.

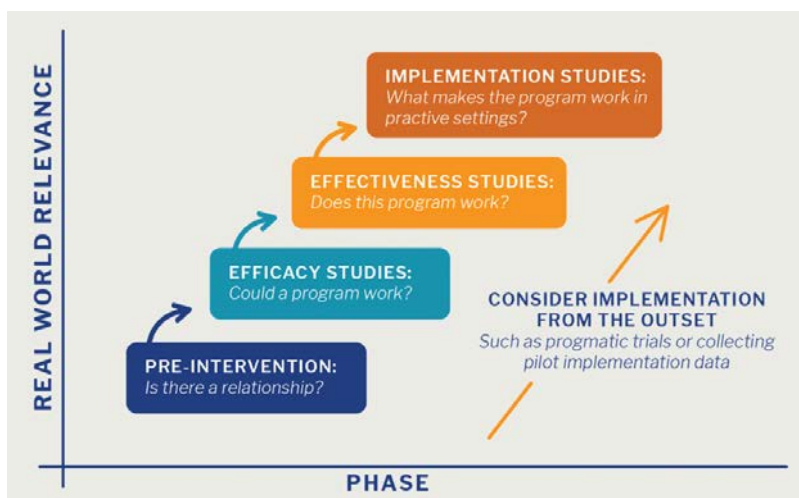
2.6 IMPLEMENTATION OF ICBT FOR OCD AND BDD IN HEALTH CARE SETTINGS

There is a significant delay for scientifically proven interventions to get implemented in real-world settings. On average, it takes 17 years for new evidence-based findings to reach clinical practice.^{139,140} Implementation science is the study of methods to advance this synthesis of research results into healthcare practice and there are numerous frameworks to be used for implementation evaluations.¹⁴¹ One of them is the RE-AIM implementation framework (used in **Study II**), that focuses on implementation from the different dimensions of reach, effectiveness, adoption, implementation and maintenance. The RE-AIM framework has been extensively employed in public health settings, with an emphasis on external validity rather than internal validity and short-term efficacy.^{142,143}

Most studies on ICBT for OCD and BDD have been efficacy trials in research settings, reducing the generalisability to a broader population. In contrast, effectiveness studies evaluate a treatment when it is delivered or implemented in a clinical setting, usually as part of routine care. These trials often have less strict inclusion and exclusion criteria, and treatment delivery is generally more flexible, thereby increasing the generalisability of the results. The effectiveness of ICBT for OCD when delivered as part of routine care has been investigated by a few research groups.

Lovell and colleagues found that a digital CBT program for OCD delivered in routine care, did not reach a pre-specified level of clinical significance compared to a control condition of patients waiting to receive therapist-led CBT. Nonetheless, the treatment reduced the proportion of patients requiring therapist-led CBT.¹²⁹ Luu et al. evaluated an online ICBT course delivered in routine care and found medium within-group effect size reductions between pre- and posttreatment ($g = 0.61$).¹⁴⁴ Another ICBT program for OCD delivered in routine care was associated with meaningful improvements in OCD symptoms (posttreatment, $g = 0.57$ and 3-month follow-up, $g = 0.90$), but these effects were considerably smaller than those of previous randomised trials.¹⁴⁵ Our OCD-NET treatment was tested in Improving Access to Psychological Therapies (IAPT) services in England and significant reductions of OCD symptoms ($d = 1.77$)¹⁴⁶ were found, in the same range as in the previous published clinical trials.^{115–117,147} OCD-NET has also been implemented and tested in an outpatient research clinic in New York City, USA and results from this effectiveness study showed large effect sizes ($d = 1.38$) posttreatment.¹⁴⁸ To the best of my knowledge, ICBT for BDD has not been evaluated when delivered in a clinical healthcare setting.

Figure 5. Different phases of research implementation



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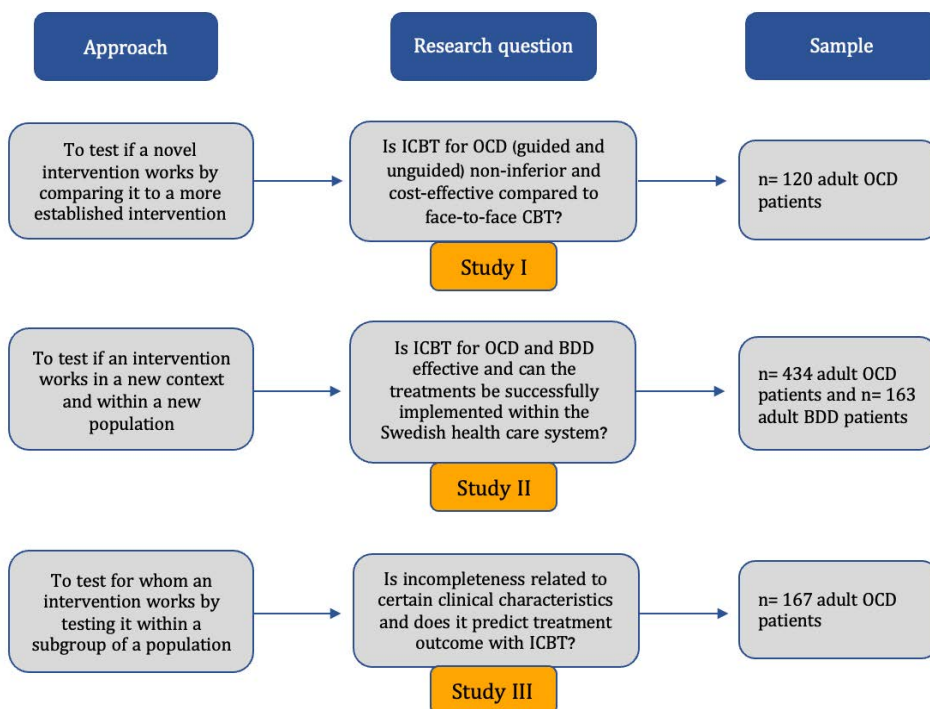
2.7 REMAINING EVIDENCE GAPS

Although studies support the efficacy of ICBT for OCD and BDD, several critical issues remain to be addressed before ICBT for OCD and BDD can be widely implemented. First, it is unclear if therapist-guided and unguided ICBT for OCD are non-inferior to regular face-to-face CBT, which is the current treatment of choice according to national and international guidelines. Second, cost-effectiveness studies on ICBT for adult OCD patients are scarce, and it is crucial to conduct a full health economical evaluation of ICBT versus standard face-to-face CBT (**Study I**). Furthermore, the effectiveness of ICBT for OCD and BDD needs to be established when the treatments are implemented in a regular healthcare setting (**Study II**). Finally, ICBT may not be suitable for all OCD patients, and it is important to identify predictors of treatment outcome with ICBT to guide future treatment development and selection (**Study III**).

3 RESEARCH AIMS

The overall aim of this thesis was to extend previous evaluations of ICBT for OCD and BDD in order to demonstrate the applicability and effectiveness of the treatments and to reach out to a broader spectrum of patients suffering from these disorders. The specific aims for each study are presented below.

Figure 6. Overview of the studies included in the thesis



3.1 STUDY I: Non-inferiority study comparing therapist-guided and unguided ICBT to face-to-face CBT for OCD

Study I aimed to investigate if therapist-guided and unguided ICBT were non-inferior compared to regular face-to-face CBT, to evaluate the cost-effectiveness of ICBT in relation to face-to-face CBT, and to investigate whether the source of referral (clinician or self-referral) affected treatment outcomes with ICBT.

3.2 STUDY II: Effectiveness and implementation of ICBT for OCD and BDD in the Swedish public health system

The primary aim of **Study II** was to evaluate the effectiveness of ICBT for OCD and BDD when delivered and implemented in Sweden's health care system. Secondary aims were to investigate the acceptability of the treatments in terms of treatment uptake and treatment satisfaction as well as if the introduction of ICBT correlated with reductions in waiting lists for other face-to-face treatment options at the clinic.

3.3 STUDY III: Incompleteness as a clinical characteristic and predictor of treatment outcome with ICBT

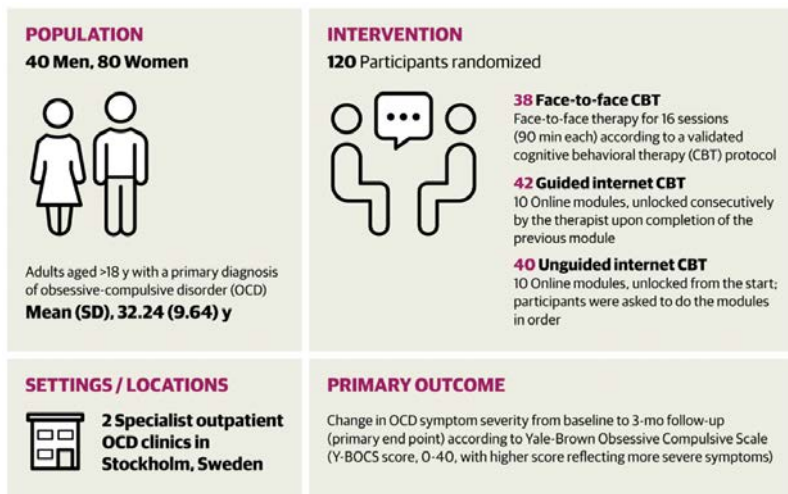
The primary aim of **Study III** was to investigate the underlying emotional construct of incompleteness in a clinical sample of OCD patients who underwent ICBT. Specifically, the study aimed to validate that incompleteness could be reliably assessed using the Obsessive-Compulsive Trait Core Dimensions Questionnaire (OCTCDQ), to investigate the positive association of incompleteness with specific baseline characteristics, and to investigate if elevated levels of incompleteness predicted worse treatment outcomes with ICBT for OCD.

4 METHODS

4.1 STUDY I

Study I was a single-blinded, non-inferiority, randomised clinical trial, comparing therapist-guided ICBT and unguided ICBT against individual face-to-face CBT for adult OCD patients. A full health economic evaluation of the two ICBT treatments compared to face-to-face CBT was performed and the study further investigated whether the treatment effects were moderated by the source of participant referral. The study was conducted at two specialist outpatient OCD clinics in Stockholm, Sweden, and the participants were either self-referred or referred by a clinician. Masked assessments were administered at baseline, biweekly during treatment, at posttreatment and 3 and 12-month after treatment, with the primary end-point being the 3 month follow-up assessment. The main outcome measure was the clinician-rated Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the margin of non-inferiority was set to 3 points on the Y-BOCS using a 90% confidence interval. One hundred and twenty participants were randomised to receive either therapist-guided ICBT (consisting of 10 modules delivered over 14 weeks, with therapist support throughout the treatment), unguided ICBT (consisting of the same 10 modules, delivered over 14 weeks but with no therapist support) or face-to-face CBT (consisting of 16 sessions á 90 minutes each, delivered over 14 weeks).

Figure 7. Methods overview of Study I



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4.2 STUDY II

Study II evaluated the effectiveness of ICBT for OCD and BDD when the treatments were implemented in the Swedish public health system. The RE-AIM implementation framework was used for the evaluation, with the elements of reach, effectiveness, adoption, implementation and maintenance. The study consisted of 434 individuals diagnosed with OCD and 163 individuals diagnosed with BDD, all of whom were either self-referred or clinically referred to an outpatient psychiatric clinic in Stockholm, Sweden, providing ICBT. Participants received guided ICBT for OCD (OCD-NET, consisting of 10 modules delivered over 12 weeks) or guided ICBT for BDD (BDD-NET, consisting of eight modules, delivered over 12 weeks) and had support from a therapist throughout the treatment. The primary outcome measures were the Y-BOCS and the Yale Brown Obsessive Compulsive Scale for BDD (BDD-YBOCS), respectively. The participants were assessed before treatment, weekly during treatment, and after treatment.

Table 2. Outcome measures for OCD-NET and BDD-NET using the RE-AIM implementation framework.

RE-AIM element	Definition	Metric
Reach	The number and percentage of those invited and eligible who participate and their representativeness	Numbers eligible/excluded and demographic characteristics of included participants
Effectiveness	Change in outcome measures and impact on quality of life and well-being	<p>OCD-NET: Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), self-rated Y-BOCS, Obsessive Compulsive Inventory-Revised (OCI-R), Montgomery - Åsberg Depression Rating Scale - self-report (MADRS-S), EuroQol 5-dimensions (EQ-5D), treatment response (Y-BOCS score reduction $\geq 35\%$ and CGI-I ≤ 2) remission (Y-BOCS score ≤ 12 and CGI-I ≤ 2), Negative Effects Questionnaire (NEQ), number of admissions to inpatient psychiatric care during treatment using medical records</p> <p>BDD-NET: Yale-Brown Obsessive-Compulsive Scale for BDD (BDD-YBOCS), Appearance Anxiety Inventory (AAI), Montgomery - Åsberg Depression Rating Scale - self-report (MADRS-S), EuroQol 5-dimensions (EQ-5D), treatment response (BDD-YBOCS score reduction $\geq 30\%$) and full or partial remission (BDD-YOCS score ≤ 16), Negative Effects Questionnaire (NEQ), number of admissions to inpatient psychiatric care during treatment using medical records</p>
Adoption	Treatment uptake and satisfaction of the participants	Percentage of participants completing core modules (completers), percentage of participants completing all modules, numbers discontinuing treatment and reasons why, treatment credibility scale (TCS), Client Satisfaction Questionnaire (CSQ)
Implementation and Maintenance	The extent to which a program is delivered consistently, the time and costs, and the long-term effects	Average therapist time spent per participant, number of messages sent during treatment, numbers waiting to receive different treatment options at the clinic and numbers allocated to ICBT

4.3 STUDY III

Study III investigated the associations between the underlying emotional construct of incompleteness and clinical characteristics (OCD severity, age onset, comorbidity, previous treatment with CBT and symmetry/ordering symptoms). In addition, the study investigated incompleteness as a predictor of treatment outcome with ICBT. The study used a subsample of 167 participants from **Study II**, where participants underwent 12 weeks of ICBT for OCD. The primary outcome measure was the clinician rated Y-BOCS, which was assessed pre- and posttreatment. The level of incompleteness was measured before treatment with the OCTCDQ Questionnaire. Before the primary analysis, a confirmatory factor analysis (CFA) was conducted to assess whether the items pertaining to the incompleteness and harm avoidance subscales of the OCTCDQ loaded high onto two distinct factors.

4.4 ETHICAL CONSIDERATIONS

Study I, II and III were approved by the Swedish Ethical Review Authority (formerly the Regional Ethics Committee in Stockholm) to ensure they followed ethical guidelines and that ethical considerations were adequately addressed before the studies began. In **Study I**, an external entity, the Karolinska Trial Alliance (KTA), monitored the study every six months during the study period to ensure that guidelines for good clinical practice were adhered to. Furthermore, all personnel involved in **Study I** attended a course in good clinical practice and received certification from the KTA.

Informed consent is one of the founding principles in research ethics, and participants should always be informed about the research and enter voluntarily. In all three studies, participants were informed in writing about the research they were asked to be part of and about their right to decline participation at any time. Before study inclusion, participants had to consent for their data to be used in research, by signing a written informed consent in **Study I** and by consenting to an opt-out informed consent in **Study II and III**. Results from all three studies were analysed at a group level, and all individuals were anonymised to ensure that identification of individual participants was not possible.

Ethical aspects were also considered when designing the studies. In **Study I**, we chose to have three active treatment conditions (ICBT or face-to-face CBT) instead of a waitlist control condition receiving no treatment. As the effect of ICBT is not as well-established as face-to-face CBT, non-responders in the two ICBT treatments were offered face-to-face CBT after the 3-month follow-up. Participants in **Study II and III** who dropped-out of ICBT or did not have sufficient effect after treatment termination, were offered other treatment options at the clinic. **Study I and II** were preregistered at ClinicalTrials.org and Open Science Framework, and the study protocol for **Study I** was

published before statistical analysis took place.¹⁴⁹ This was done to ensure that predefined strategies for study execution were followed and to prevent any deviations or changes made to the researchers' advantage.

Since ICBT treatments are remote treatment formats, it is important to carefully monitor participants' well-being and potential suicidal ideation. In **Study I**, participants in all treatment arms were contacted bi-weekly during treatment, and their OCD symptom severity and potential suicide risks were assessed. If a participant expressed suicidal ideation, the assessor conducted a structured suicide risk assessment. If there was an urgent need for care, the participant was booked for a face-to-face psychiatric appointment at the clinic. In **Study II** and **III**, automated self-assessments with Montgomery-Åsberg Depression Rating Scale self-rated (MADRS-S) were administered weekly in the internet platform. If a participant scored four or more on the item measuring suicidal ideation, the treating psychologist was automatically informed and contacted the participant for a structured suicide risk assessment. If there was an urgent need for care, the participant was booked for a face-to-face appointment with a psychiatrist at the clinic, or contact was made with the nearest emergency psychiatric unit where the patient lived. Potential adverse events and negative effects related to the treatments were also collected through self-rated questionnaires at the end of treatment in all three studies.

Ethical considerations to ensure the integrity of all participants are crucial when conducting research within a technical support system. To make the treatment login and online assessments safe, double authentication was used, where the participant's and study personnel's login and password were confirmed via a telephone text message. All platform information was stored encrypted at a server, and other sensitive material like case report forms were stored in locked archive rooms at the clinic where the studies were conducted.

5 RESULTS

5.1 STUDY I

Participants in all three treatment groups had improved at the primary end-point (3 month follow-up), but the main non-inferiority results were inconclusive. The mean difference between therapist-guided ICBT and face-to-face CBT at the primary end-point was 2.10 points on the Y-BOCS (90% CI, -0.41 to 4.61 points; $p=0.17$), a non-significant difference favouring face-to-face CBT, but the confidence intervals included both 0 and 3 points, rendering an inconclusive main result. The difference between unguided ICBT and face-to-face CBT was 5.35 points (90% CI, 2.76 to 7.94 points; $p < .001$), favouring face-to-face CBT. This difference was significant, but the lower end of the confidence interval included 3 points, also producing an inconclusive result. The health economic analysis showed that both guided and unguided ICBT were cost-effective treatments compared to face-to-face CBT. The estimated treatment costs were \$6795 for face-to-face CBT, \$603 for therapist-guided ICBT and \$249 for unguided ICBT. When expanding to a full societal perspective, the cost savings for therapist-guided ICBT were \$6153 (95% CI, \$4536-\$7563; $p < .001$) and for unguided ICBT \$5761 (95% CI, \$4145-\$7298; $p < .001$) compared with face-to-face CBT. Source of referral did not moderate treatment outcome (time-by-source of referral interaction effect, $Z=0.03$ [95% CI, -0.06 to 0.13]; $SE=0.05$; $p=0.53$).

Figure 8. Mean Y-BOCS scores from pre-treatment up to the 3-month follow-up

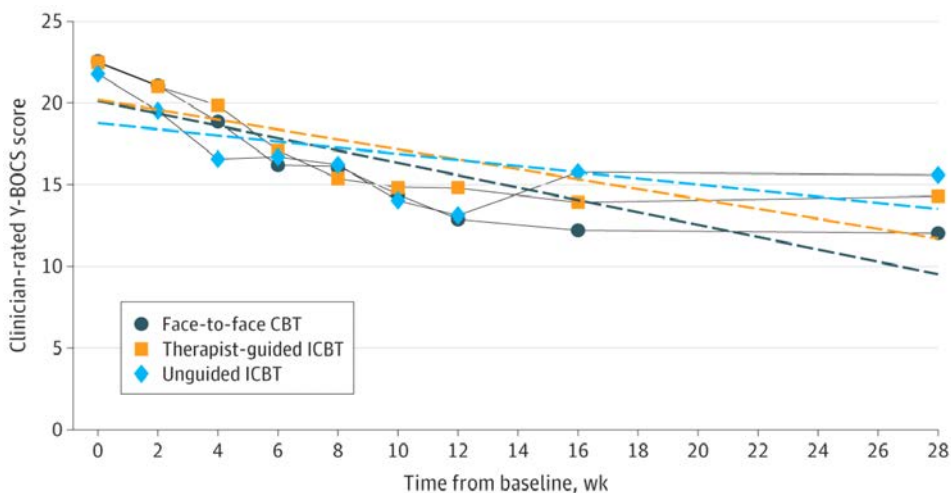


Figure caption: Clinician-rated observed (solid lines) and estimated (dashed lines) Y-BOCS scores from before treatment to the 3-month follow-up. Reproduced with permission from Jama Network Open.

Figure 9. Estimated differences between face-to-face CBT and the two ICBT treatments at the 3-month follow-up

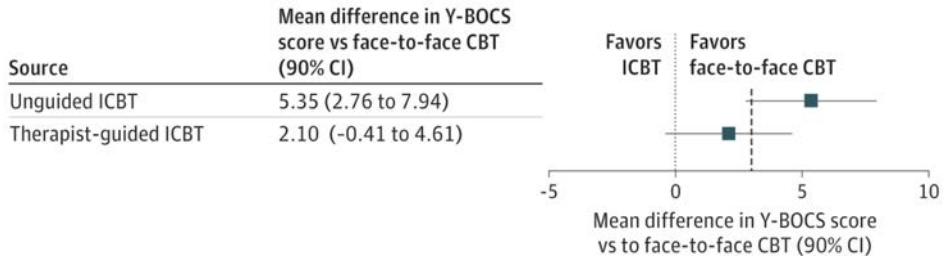


Figure caption: Estimated differences between face-to-face cognitive behavioral therapy (CBT) and the two internet-based cognitive behavioral therapy (ICBT) treatments at the 3-month follow-up. The dotted line indicates the prespecified noninferiority margin of 3 points on the Y-BOCS. Reproduced with permission from Jama Network Open.

Figure 10. Cost effectiveness planes of therapist guided ICBT and unguided ICBT compared to face-to-face CBT at the 3-month follow-up

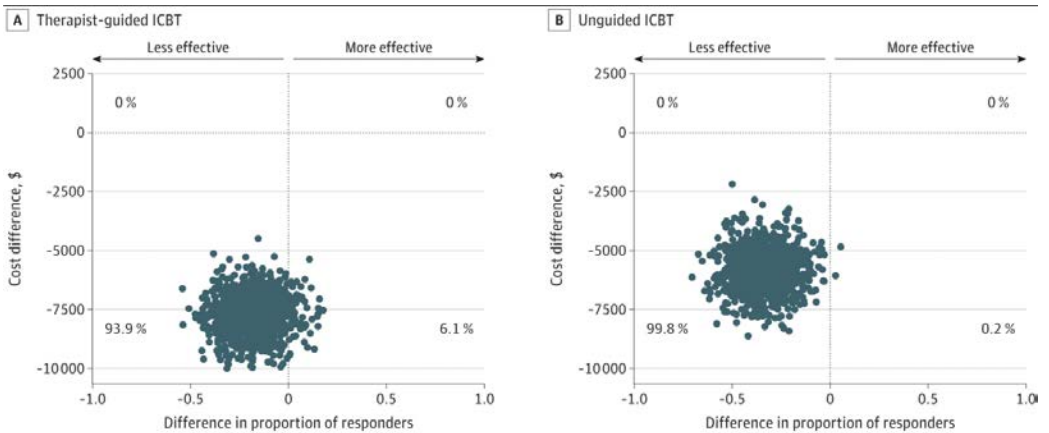
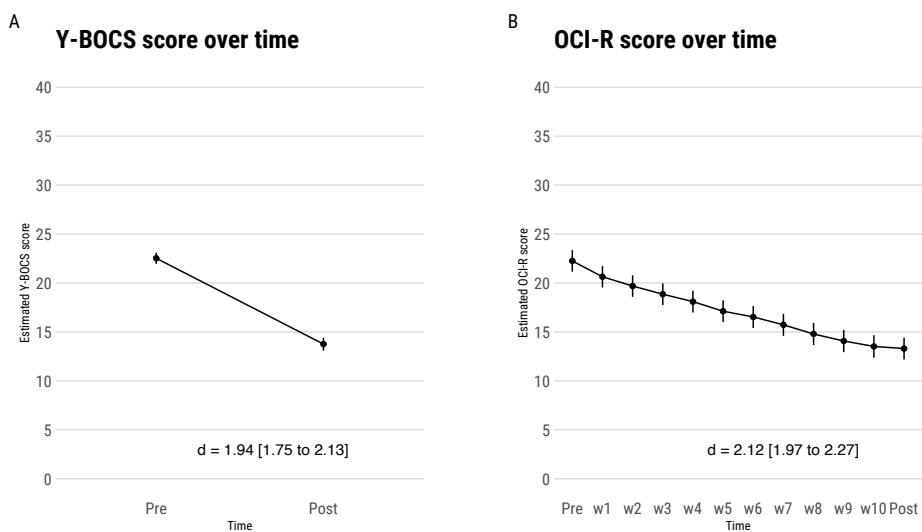


Figure caption: The comparator is the face-to-face CBT treatment condition=0. Cost difference is from a societal perspective and presented in US dollars (\$). Costs are based on the Trimbo and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TIC-P).¹⁵⁰ Effect is shown as the rate of response (Y-BOCS \geq 35% and CGI-I \leq 2).¹⁵¹ Reproduced with permission from Jama Network Open.

5.2 STUDY II

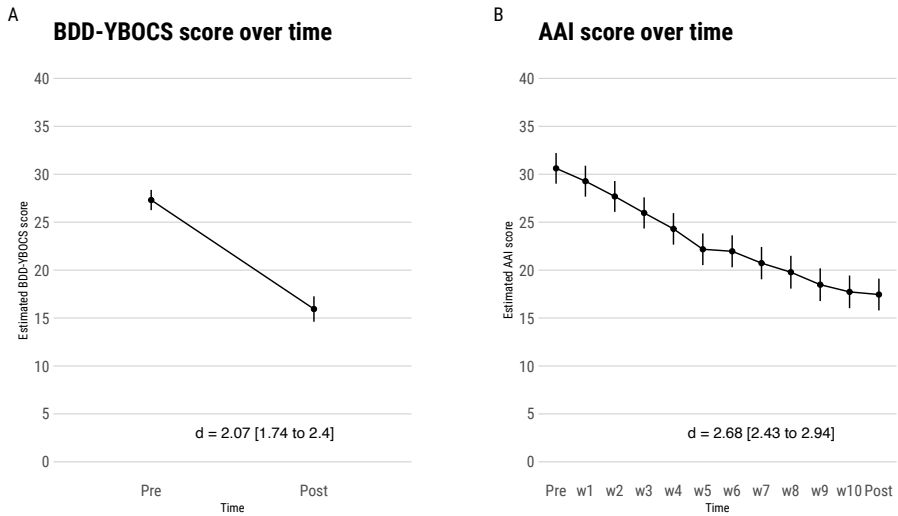
Participants in both OCD-NET and BDD-NET showed a significant decrease in OCD and BDD symptoms from pre-treatment to posttreatment (OCD-NET: mean reduction= -8.77 [95 % CI -9.48 to -8.05] $p < .001$, $d = 1.94$ [95 % CI 1.75 to 2.13]; BDD-NET: mean reduction= -11.37 [95 % CI -12.9 to -9.87] $p < .001$, $d = 2.07$ [95 % CI 1.74 to 2.40]). Forty-nine percent of the participants in OCD-NET and 69 % in BDD-NET were classified as treatment responders. Further, 21 % of the participants in OCD-NET and 48 % in BDD-NET were in remission (full or partial for BDD-NET). Participants in both treatment groups reported a high treatment satisfaction at posttreatment (OCD-NET= 87 %, BDD-NET= 79 %), and 87% of the participants in OCD-NET and 78% in BDD-NET were treatment completers. The implementation influenced treatment delivery and reduced waiting lists for other face-to-face treatment options at the clinic with 60-70%.

Figure 11. Y-BOCS and OCI-R scores from pre to posttreatment



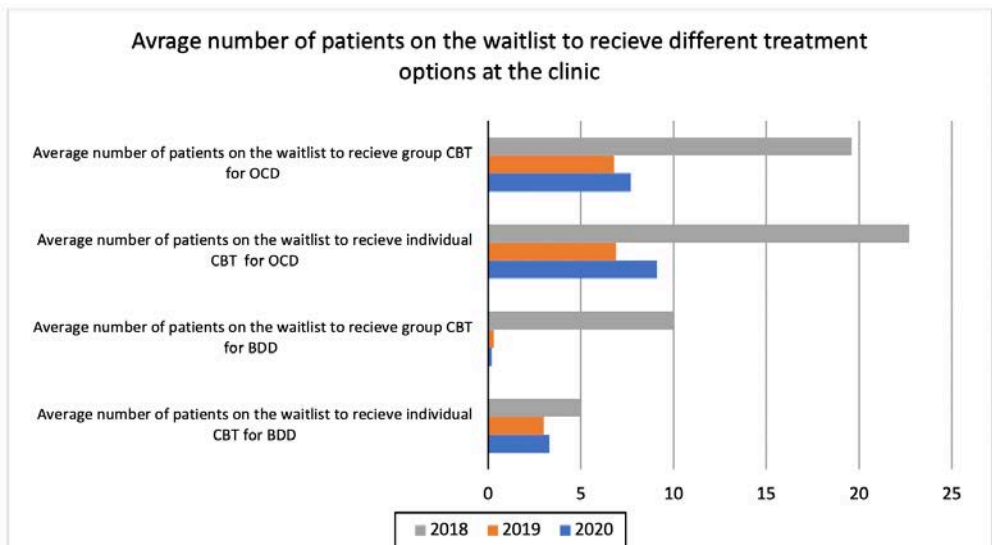
Abbreviations: d = Cohen's d within-group effect size; Y-BOCS, Yale-Brown Obsessive-Compulsive Scale; OCI-R, Obsessive Compulsive Inventory-Revised. Reproduced with permission from Internet Interventions.

Figure 12. BDD-YBOCS and AAI scores from pre to posttreatment



Abbreviations: d= Cohen’s d within-group effect size; BDD-YBOCS, Yale-Brown Obsessive-Compulsive Scale for BDD; AAI, Appearance Anxiety Inventory. Reproduced with permission from Internet Interventions.

Figure 13. Waiting lists to receive different treatment options at the clinic



Reproduced with permission from Internet Interventions.

5.3 STUDY III

The CFA conducted on the OCTCDQ scale provided support for a two-factor structure, as opposed to a one-factor structure, with acceptable model of fit indices. Items pertaining to incompleteness and harm avoidance displayed high loadings (range: 0.70 and 0.94) on the two separate subscales of the OCTCDQ. Cronbach's alpha was high for both subscales (incompleteness: 0.92; harm avoidance 0.89). Moreover, the study revealed that incompleteness was positively associated with baseline symmetry/ordering symptoms ($B= 0.73$, $SE= 0.19$, $p < .001$), as well as with OCD severity ($B= 0.16$, $SE= 0.04$, $p < .001$) and comorbidity ($B= 0.17$, $SE= 0.07$, $p= 0.01$). In addition, the study found that individuals with higher levels of incompleteness experienced lower treatment effects with ICBT ($B= 0.13$, $SE= 0.04$, $p= 0.002$, [95% CI 0.05 to 0.21]), even after accounting for the influence of harm avoidance. The probability of treatment response and remission was substantially lower among individuals with a high degree of incompleteness (response, 39%; remission, 10%) than among those who scored lower on this subscale (response, 52%; remission, 34%).

Figure 14. Mean Y-BOCS score for the high and low incompleteness groups at pre and posttreatment

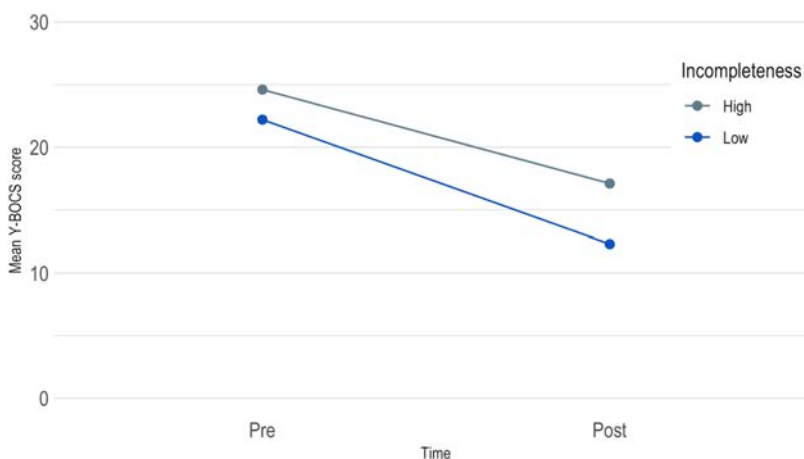


Figure caption: High incompleteness= OCTCDQ incompleteness subscale score of ≥ 18 ; Low incompleteness= OCTCDQ incompleteness subscale point of < 18 .

Figure 15. Proportion of remitters and responders in the high and low incompleteness groups

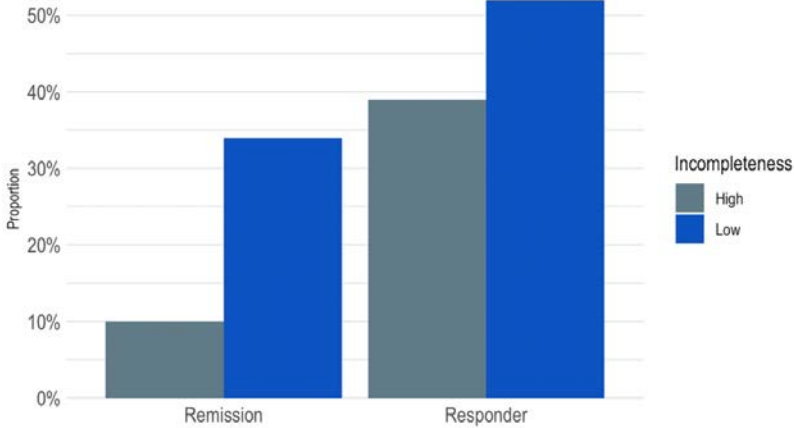


Figure caption: High incompleteness= OCTCDQ incompleteness subscale point of ≥ 18 ; Low incompleteness= OCTCDQ incompleteness subscale score of < 18 . Response= Y-BOCS $\geq 35\%$ and CGI-I ≤ 2 at post-treatment; Remission= Y-BOCS ≤ 12 and CGI-S ≤ 2 at post-treatment.¹⁵¹

6 DISCUSSION

6.1 IS ICBT NON-INFERIOR AND COST-EFFECTIVE COMPARED TO FACE-TO-FACE CBT FOR OCD?

Results from **Study I** showed that both ICBT treatments were cost-effective compared to face-to-face CBT, and this was also true when broadening the analysis to a full societal health economic perspective. All three treatments (face-to-face CBT, guided ICBT and unguided ICBT) were also effective in reducing OCD symptom severity at the primary endpoint (the 3-month follow-up). Nonetheless, the main non-inferiority results were inconclusive since the confidence intervals for both guided and unguided ICBT crossed the non-inferiority margin of 3 points at the 3-month follow-up. This means that no firm conclusions regarding the non-inferiority of ICBT compared to face-to-face could be drawn.

The 3-point non-inferiority margin used in this trial was more conservative compared to previous non-inferiority studies of OCD, where 4 and 5 point margins have been used.^{112,152,153} One issue with establishing a margin of non-inferiority is that no clear definition for how to do so exists, and the a priori decision is often based on clinical and statistical reasoning. Statistically, it is recommended that the margin should be defined based on previous evidence of the well-established treatment, by pooling the effect estimate (with a 95% confidence level) from RCTs of the well-established treatment, or by the limit of the confidence level that is closest to the null effect. Clinical reasoning is then used to determine the fraction that must be preserved by the new intervention to be considered non-inferior.¹⁵⁴ In **Study I**, we determined our non-inferiority margin based on clinical judgement, prior studies in OCD with a non-inferiority design and on our statistical power calculation using data from a previous study on ICBT for OCD with identical procedures.¹¹⁷ This a priori calculation concluded that our study would have enough power to detect a difference between the two treatments of 3 points on the Y-BOCS. In retrospect, our results would have been different if we e.g., had chosen a 5-point margin, where we would have concluded that therapist-guided ICBT was non-inferior to face-to-face CBT. In addition, a larger sample size may have enhanced the stability of outcome detection, lowering the chance of obtaining broad confidence intervals overlapping the non-inferiority margin. However, in terms of clinical interpretation, the 2.1 difference in the mean Y-BOCS scores between therapist-guided ICBT and face-to-face CBT is considered a minor distinction in symptom manifestation. As an example, a clinician seeing a patient with a Y-BOCS score of 18 points vs. a Y-BOCS score of 16 points would presumably not notice much of a difference in symptom presentation or functional impairment in that specific patient. Thus, I believe that our findings from **Study I** still can offer valuable insights into the role of ICBT in the context

of regular healthcare, where digital treatments certainly have an important role to play as efficacious, accessible and time efficient treatment alternatives.

Our full cost-effectiveness analysis of ICBT in comparison with face-to-face CBT is the first of its kind in an adult OCD population. This comparison holds significant importance for policymakers, as evaluating cost-effectiveness in relation to the standard treatment already established in healthcare is particularly compelling from a cost-benefit standpoint. Consistent with our findings, previous cost-effectiveness studies investigating ICBT for OCD have demonstrated its cost-effectiveness from various healthcare perspectives.^{134,135,137} Nonetheless, these studies have predominantly focused on comparing ICBT to control conditions, rather than evaluating it against the established standard treatment of choice, such as face-to-face CBT. The cost-effectiveness of ICBT compared to face-to-face CBT has been investigated in children and adolescents with OCD, using a stepped-care model where non-responders received additional face-to-face CBT. In line with our results, ICBT was found to be cost-effective from all healthcare perspectives when compared to face-to-face CBT.¹³⁶ Altogether, these findings show that ICBT can be considered a cost-effective treatment, mainly due to lower treatment costs compared to face-to-face CBT. In our **Study I**, cost-savings for ICBT compared to face-to-face CBT were also maintained long term (12-months follow-up), which indicate that the additional receipt of face-to-face CBT in non-responders to ICBT, did not alter the cost-effectiveness conclusion.

Strengths of **Study I** were the use of a clinician rated gold standard measure for the primary outcome, where masked integrity checks revealed that assessors were truly blind to treatment allocation, as intended. An external party monitored the trial throughout the study period to ensure adherence to good clinical practice guidelines. Moreover, therapists delivering face-to-face treatment were evaluated for competence and adherence, and the same therapists treated participants in both the ICBT and face-to-face treatment conditions, thereby minimising the risk of therapeutic aspects affecting the results.

Study I also had some limitations. For instance, the unguided treatment condition had no therapist support, although participants were part of a research project and received bi-weekly telephone assessments and multiple assessments during the study period. These contacts may have influenced participants' engagement with the treatment compared to a treatment condition with no contact. Although the study aimed to include a diverse sample of participants, some comorbid diagnoses of OCD, such as autism, were excluded, which affects the generalisability of the results to the general OCD population, where comorbidity is common. Moreover, cost estimations were based on Swedish tariffs for healthcare visits; therefore, the results may not be generalisable to other countries or healthcare contexts. Finally, the non-inferiority of ICBT compared with

face-to-face CBT remains inconclusive, suggesting the need for further non-inferiority studies within the field of OCD. One possible avenue for future studies is to include larger sample sizes in order to be able to close the existing knowledge gap.

6.2 IS ICBT FOR OCD AND BDD EFFECTIVE WHEN IMPLEMENTED IN THE SWEDISH HEALTH CARE SYSTEM?

In **Study II**, both OCD-NET and BDD-NET led to significant reductions in OCD and BDD symptom severity at posttreatment, with large effect sizes. Treatment satisfaction was high in both treatment groups, and 87% of the participants in OCD-NET and 78% in BDD-NET were treatment completers, meaning that they had reached the core modules introducing ERP. The implementation also reduced the waiting lists for other OCD and BDD treatment options at the clinic by 60-70%.

Compared to other effectiveness studies on ICBT for OCD performed in clinical settings, the current study showed larger effect sizes, more in line with our previous studies on OCD-NET performed in research settings.^{113,115,117,147 146} One could argue that the implementation context in **Study II** closely resembled the research environment in which previous RCTs were conducted and it is worth considering that our findings may have varied if the study had been conducted in a different healthcare context, such as primary care. However, one evaluation of OCD-NET has been done in a health care context similar to primary care, within the IAPT services in England, where therapists also had limited or no experience in treating OCD.¹⁴⁶ Despite this, the obtained results from the IAPT study demonstrated effect sizes within a similar range as previously published RCT trials,^{115-117,147} and results were also consistent with our findings from **Study II**. Taken together, these results indicate that ICBT for OCD is effective and can be suitable for implementation in diverse healthcare contexts. No previous effectiveness studies on ICBT for BDD have been performed in clinical settings. It is crucial for future research to validate the results from the OCD treatment and further provide evidence for the effectiveness of ICBT for BDD in alternative implementation contexts in Sweden.

The study adherence was strong in both treatment groups, and the percentage of treatment completers was higher than in other routine care studies of ICBT for OCD.^{129,144,145} In OCD-NET and BDD-NET, participants have the opportunity to receive responses from their therapists within a 24 to 48 hour timeframe. It is plausible that the availability of frequent therapist contact contributed to the higher number of treatment completers in this study, compared to other digital ICBT programs with less frequent therapist support. Notably, the therapists in this study only spend 9.2 minutes (OCD-NET) and 7.19 minutes (BDD-NET) per participant per week to deliver treatment, indicating that the frequent therapist contact did not hinder an effective delivery of therapy.

Study II used broad inclusion and exclusion criteria for participation and was performed in a naturalistic setting, which can be considered strengths. Additionally, the clinician-rated Y-BOCS and BDD-YBOCS scales were used as primary outcome measures, as opposed to previous effectiveness studies that mainly used self-rated outcome measures.¹⁴⁴⁻¹⁴⁶ Further, our evaluation of OCD-NET and BDD-NET was conducted using the RE-AIM implementation framework, which encompassed not only the effectiveness aspect, but also the dimensions of reach, adoption, implementation and maintenance. By including a broader range of factors in the evaluation process, our findings make a unique contribution to the current body of literature on effectiveness trials for OCD and BDD.

Study II also had limitations, such as data loss and dropouts due to its naturalistic design and setting. Nevertheless, high rates of data loss and drop-outs are common in effectiveness studies in general, and previous investigations of ICBT for OCD in naturalistic settings have reported similar rates to those observed in the current study.¹⁴⁴⁻¹⁴⁶ The effects obtained from the self-rated outcome measures (with less data loss) were also in line with the effects from the clinician rated outcome measures. As effectiveness studies lack a control group, the obtained effects could be caused by factors other than the treatments, such as natural fluctuation of symptoms, passage of time, or therapeutic attention. However, spontaneous recovery is unusual in OCD²⁴ and BDD.⁶¹ Blinded assessments were not possible due to the naturalistic study design and no inter-rater reliability data checks were performed. However, the assessors involved in this study were clinicians with expertise in OCD-related disorders who had assessed participants in previous clinical trials of OCD-NET and BDD-NET, where reliability checks were performed.¹⁴⁷

6.3 IS INCOMPLETENESS A CLINICAL CHARACTERISTIC AND PREDICTOR OF TREATMENT OUTCOME WORTH FURTHER INVESTIGATION IN OCD?

Study III showed support for a 2-factor structure of the OCTCDQ scale, with high internal consistency. The study further found that higher levels of baseline incompleteness were associated with OCD severity and greater comorbidity, as well as strongly associated with symmetry/ordering symptoms, which is a highly replicated finding in previous research.¹⁴⁻²¹ Interestingly, symmetry/ordering is a factor that often stands out in studies investigating subcategories of OCD and results suggest that patients with these symptoms have certain cognitive deficits,¹⁵⁵⁻¹⁵⁸ a worse treatment response to medication,¹⁵⁹⁻¹⁶¹ CBT¹⁶² and neurosurgical interventions.^{163,164} Furthermore, patients with symmetry/ordering symptoms often struggle to articulate a specific feared consequence associated with their obsessions and instead report feelings of discomfort and an urge to reduce this feeling through compulsions,¹⁵⁵ which is more in

line with experiences of incompleteness. Taken together, results from research within the field of symmetry/ordering OCD have many similarities with findings from research conducted so far in the field of incompleteness OCD. Thus, it is possible that incompleteness serves as the motivational and emotional construct driving symmetry/ordering behaviours, and that patients with both incompleteness and symmetry/ordering exhibit a unique symptom profile that differs from other subcategories of OCD. This distinctive profile may follow a different psychopathological pathway, underscoring the importance of further investigating and assessing incompleteness in OCD.

In **Study III**, participants who displayed higher levels of baseline incompleteness demonstrated a poorer treatment outcome with ICBT. This is consistent with treatment studies investigating symmetry/ordering OCD,¹⁶² and something that Cervin et al. also found when investigating incompleteness in youths with OCD treated with CBT.¹⁶⁵ Exposure with ritual prevention is a fear-based intervention that emphasises the role of obsessions causing anxiety and compulsions performed as a way of reducing anxiety.¹⁶⁶ Treatment studies on CBT suggests that not all OCD patients benefit from traditional fear-based CBT treatments,^{167,168} and incompleteness OCD patients, who experience a feeling that something is not quite right rather than clear obsessions causing anxiety, may benefit less from this treatment approach.^{16,169,170} Recent research has suggested that psychological interventions that specifically target incompleteness are more effective in reducing symptoms than more general treatments for OCD¹⁶⁹ and considering the distinct symptom profile of incompleteness, it is important to further investigate adapted treatment formats for this patient population. Furthermore, given the association of incompleteness with disorders such as tics and skin-picking disorder,^{16,17,23} which are typically treated with habit reversal training, it is plausible that incompleteness is more closely linked to disorders where practicing inhibition to a behaviour is the key mechanism of change. These findings highlight the need to develop and implement tailored or entirely new treatment approaches for OCD that directly address incompleteness.

Study III had several limitations. The non-experimental design and the single measurement point for incompleteness mean that the associations observed in this study could potentially be linked to another hidden factor, rather than incompleteness itself. Therefore, future research should utilise study designs that permit the direct manipulation of incompleteness to explore its effects on OCD symptoms. In addition, the relatively large amount of data loss in this study could impact the reliability of the results. However, a post-hoc analysis demonstrated that higher levels of incompleteness did not predict increased data attrition. The structured treatment format of ICBT may present a limitation to the generalisability of our findings to other

CBT modalities. It is plausible that conventional CBT, which enables greater flexibility in treatment customisation, may have a lower impact on treatment outcome for patients with incompleteness and further research is warranted to investigate this.

7 CONCLUSIONS

Therapist-guided ICBT is a cost-effective treatment alternative to face-to-face CBT. Unguided ICBT is also cost-effective, but less efficacious compared to face-to-face CBT, but could be a treatment alternative when providing remote clinician support is not feasible. ICBT for OCD and BDD are effective, acceptable and safe treatments that can be successfully implemented in the Swedish health care system. The implementation of ICBT had a positive impact on treatment delivery and reduced waiting lists to other treatment options, coupled with no waiting time for starting ICBT. This suggests that clinics incorporating ICBT into their regular practice, can scale up treatment delivery, and by that increase the number of people receiving treatment in a timely manner. The underlying emotional construct of incompleteness seems to be an important clinical characteristic worth further investigation in OCD. Higher levels of incompleteness also appear to predict a more modest treatment effect with ICBT. The findings from the studies included in this thesis expand upon previous evaluations of ICBT for OCD and BDD, highlighting the applicability and effectiveness of these treatments. The studies have further contributed to extending help to a broader range of patients suffering from OCD and BDD.

8 POINTS OF PERSPECTIVE

The studies in this thesis have contributed to new knowledge in the field of ICBT for OCD and BDD. However, while certain questions have been answered, new questions have also emerged. In this section, the findings from **Study I, II, and III** are discussed in the broader context of psychiatric healthcare, and potential future research directions are suggested.

8.1 INTERNET DELIVERED TREATMENTS AND THEIR ROLE WITHIN HEALTH CARE

Digital healthcare is experiencing rapid expansion, with health interventions and online psychological treatments now being delivered through computers, apps, and tablets. This mode of treatment delivery is enabling a larger proportion of the population to access healthcare services. The COVID-19 pandemic also accelerated the adoption of digital health care services, further advancing online treatment delivery. As changes in healthcare delivery continue to occur at a fast pace, it becomes essential to scientifically investigate these new treatment modalities regarding their efficacy and cost-effectiveness, as well as potential negative effects associated with them.

Today, a substantial body of research indicates that certain guided internet-delivered treatments for both somatic and psychiatric disorders are comparably effective compared to face-to-face treatment options.¹⁰⁶ However, limited knowledge is available regarding the role of ICBT within the broader healthcare system. When should ICBT be offered? To which patients? And in which specific format? Answers to these questions are of particular importance to policymakers who seek to ensure that research investments provide maximum value in real health care settings. The three studies of this thesis sought to address several important questions regarding the potential role of ICBT as a treatment alternative for OCD and BDD within the framework of regular healthcare. The findings of **Study I** indicate that both guided and unguided ICBT are cost-effective treatment options suitable for both self-referred and clinically referred patients with OCD. **Study II** demonstrated that ICBT for OCD and BDD could be delivered safely with sustained treatment effects in a regular healthcare setting, while also substantially reducing waiting times for other face-to-face treatment options. **Study III** indicated that underlying emotional constructs such as incompleteness may predict a worse treatment outcome with ICBT. All these findings are encouraging and suggest that ICBT has an important role to play, for a broad range of patients, within regular healthcare. Nevertheless, future research should aim at investigating how the ICBT treatments for OCD and BDD would work in a less specialised healthcare contexts in Sweden, such as primary care, where time is often limited and the knowledge regarding OCD and BDD is lower than in specialised units. Additionally, future research

should investigate whether a stepped care model that first provides ICBT followed by face-to-face CBT to non-responders is effective and cost-effective for patients with OCD and BDD. This approach has been evaluated with positive results in children and adolescents with OCD,¹⁷¹ and the model has now been incorporated as part of routine care in several regions in Sweden.

Despite the promising results of ICBT, relatively little is known about the predictors of treatment outcome with ICBT.^{172,173} This information is especially important for clinical decision making, in order to know which patients benefit from the treatment or to find early signs of treatment failure. **Study III** revealed that higher levels of baseline incompleteness were associated with less reduction in OCD symptoms after receiving therapist-guided ICBT. These results indicate that incompleteness may serve as a potential predictor of treatment outcome in ICBT, warranting further investigation. From a methodological standpoint, the use of machine learning techniques to predict treatment outcomes is gradually emerging in the field of psychiatry, with applications observed in prediction studies of ICBT for social anxiety disorder, BDD and pediatric OCD.^{174–176} These techniques hold the potential to significantly enhance our capacity to generate more precise predictions concerning treatment outcomes in the future. This information is crucial in order to determine which patients are most likely to benefit from specific treatment alternatives. It can also help prevent treatment failure and minimise costs associated with ineffective treatment delivery.

8.1.1 Enhancement of internet delivered treatments

There are various alternatives that could be explored to enhance the effectiveness of digital treatments, such as combining them in a hybrid format with live contacts or telephone support. This combination has e.g., been investigated in OCD, using self-guided ICBT programs with additional weekly therapist sessions. Results showed that higher attendance to therapist sessions during treatment was associated with better treatment outcome.¹⁷³ To further optimise treatment efficacy, certain aspects of a treatment, such as psychoeducational elements, could be delivered online, while additional face-to-face sessions or online video calls could be incorporated during the more active ERP phase of the treatment.

In **Study I**, an unguided ICBT treatment was used, where participants were contacted bi-weekly during treatment for a structured assessment of symptoms, but where no issues regarding the treatment content were discussed. Although less effective than the therapist-guided ICBT treatment, the unguided ICBT treatment showed a large within-group effect size ($d = 1.35$) at the 3-month follow-up. These results are encouraging, and future studies should develop and test unguided treatment formats of ICBT for OCD that are specifically designed for self-guiding purposes. This because the unguided treatment employed in **Study I** was essentially the therapist-guided treatment with the

psychologist contact removed, lacking other adaptations for the self-guided format. An app-based CBT treatment, supplemented with online and telephone coach support, has been examined in the context of BDD with positive results.¹¹⁹ Future unguided treatments for OCD and BDD could possibly incorporate automated prompt messages and have app devices connected to the treatment, where patients can be reminded and record ERP exercises directly in their mobile phones.

8.2 STRATEGIES FOR SUCCESSFUL IMPLEMENTATION

The average time of 17 years for scientific results to be implemented into healthcare practice¹⁴⁰ is far too long. Implementation science is critical in this regard, as it evaluates different aspects of the implementation process to identify the best ways to adopt a treatment or intervention into a specific "real-world" context.¹⁷⁷ The identification of time lags in implementation is also of significant policy interest, given the substantial amount of resources invested in healthcare research. Interestingly, comparatively little research has focused on identifying key aspects contributing to time lags in implementation, and more research is necessary in this field, including the use of standardised measures to facilitate comparisons between studies.¹⁴⁰

In **Study II**, we did not use any specific measures to examine the time aspect or time-lags in the implementation process. However, a probable factor for our relatively fast implementation could be the close collaboration between the research unit and the clinical unit where the implementation took place. This collaboration meant that the clinic staff were familiar with working with research and with measuring outcomes in a structured way.

Not all implementation situations are similar to that of **Study II**, and in the future, it would be valuable to investigate the implementation of ICBT for OCD and BDD in another implementation context. Additionally, it would be important to assess the implementation process from the perspective of staff and organisations and evaluate the long-term maintenance effects of the treatments.

The organisation of healthcare needs to be diverse and operate at different levels of care, however, it is noteworthy that the close collaboration observed between our research unit and the specialised healthcare unit for OCD and related disorders in **Study II**, can be regarded as an exemplary model for how healthcare could be organised in order to facilitate faster implementation. This collaborative approach establishes a robust connection between the research unit and the practical healthcare environment, facilitating transfer of knowledge between the two entities. This example demonstrates the potential for future healthcare organisations to adopt similar collaborative strategies, leading to faster implementation of research findings and ultimately benefiting patients and the field of healthcare as a whole. Another area of future development involves

creating universal platforms that facilitate the distribution of ICBT. In order to effectively expand the reach of ICBT, both within individual countries and across international borders, it becomes crucial to establish a comprehensive infrastructure that supports the distribution of digital interventions.

8.3 MECHANISMS IN MENTAL ILLNESS, FUTURE ASSESSMENT AND TREATMENT DEVELOPMENT

In the field of psychiatry, traditional methods have focused on surface-level symptoms, relying on questionnaires, observations, and behavioural assessments. However, advancements in neuroimaging and genetic analysis have allowed researchers to look into the living brain and investigate psychiatric disorders in entirely new ways. This has led to the emergence of more dimensional approaches to understand mental disorders, such as the Research Domain Criteria (RDoC) framework, which aims to understand mental health and illness in terms of the varying degrees of dysfunction in fundamental psychological and biological systems.¹⁷⁸ Despite being introduced over a decade ago, the widespread utilisation of RDoC remains limited. Critics of RDoC argue that the framework is conceptually flawed when it comes to the most severe mental illnesses, as it combines variations along dimensional axes of normal functioning, which departs from the disease model of major mental illnesses.¹⁷⁹ Additionally, methodological and conceptual concerns pertain to an overemphasis on biological units and measures, a lack of considerations for measurement error and challenges of differentiating between biological predispositions and their behavioural manifestations.¹⁸⁰

Despite its flaws and limited widespread utilisation, RDoC and similar concepts still presents a promising new approach to the investigation of psychiatric illness. From my perspective, the future of psychiatry and the advancement of treatment development lie in the exploration of underlying mechanisms and neurobiological origins of mental illnesses, rather than solely relying on categorising disorders based on symptom manifestation. A deeper understanding of the underlying mechanisms involved in specific mental health problems will hopefully help develop new and more effective treatment approaches that target these specific mechanisms. In **Study III**, we investigated the underlying emotional construct of incompleteness and instead of merely assessing symptoms, we employed a questionnaire designed to capture the emotional component of a behaviour. Hopefully, by obtaining a deeper understanding of the emotional constructs that drive OCD behaviour, we may gain insight into the heterogeneity of OCD. In the future, we may even conclude that the underlying mechanisms involved in specific OCD subtypes, such as incompleteness, overlap more with other disorders than with OCD itself.

In a broader context, finding common mechanistic deficits in various psychiatric disorders, could cluster current psychiatric disorders into entirely new domains. In the

future, diagnostic classification systems may not even be used, and instead, we may focus on dysfunctions in neurobiological networks as the level of analysis and assessment. Future advancements in psychological treatments have the potential to focus on addressing these specific mechanistic deficits, while ensuring accessibility and delivering effective treatment interventions.

8.4 REFLECTIONS

As I conclude this thesis, I would like to reflect on some of the things I have learned throughout these years of research. Undoubtedly, this journey has been transformative, to the extent that I believe this PhD has even shaped my own character. I am now a far more methodical, well-organised, and patient individual compared to who I was before.

When I started this, I had no idea that patience would prove to be such a critical aspect of scientific research. Endless hours of writing and rewriting, revising and reapplying and waiting for submissions and ethical applications to be approved. Frustration, when a text you invested numerous of hours into writing suddenly is met with feedback suggesting that it should be removed, what is patience if not that. However, through these experiences, I have learned that patience is an essential quality in research. It is the ability to persist and continue through challenges, to dedicate numerous hours to refining one's work, and to remain persistent in the face of setbacks that ultimately result in advancements. I'm still in the process of obtaining this patience, but somewhere along the path.

As the main title of this thesis suggests, this PhD has also marked a transformation from efficacy to implementation, which also applies to me personally. I started with the standard know-how in a familiar environment such as the therapy room, where efficacy was assessed on a daily basis by working with patients and receiving instant feedback. This bridged over to a more gradual progressing research practice, where new ideas took time to mature and manifest, not necessarily in the straightforward, efficient way I was used to. A take home message from all this is that while science can be creative and inspiring, it is also a slow-paced and delayed-rewarding effort, sometimes leading one to question the purpose of endless forms and applications. Nonetheless, it has taught me the importance of nurturing my scientific creativity and staying focused on the path to new discoveries, while parallelly navigating the requirements of research institutions.

In conclusion, these years have not only improved my research understanding but have also enhanced my personal growth and development. A thirst for new knowledge still remains, and as I move forward, I hope that the lessons learned during this period will continue to guide me in my professional and personal efforts in the future.

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