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NONSUICIDAL SELF-INJURY IN ADOLESCENCE: ATTEMPTS TO IMPROVE AND DEVELOP TREATMENT

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Nonsuicidal Self-Injury in Adolescence: Attempts to Improve and Develop Treatment

Thesis for Doctoral Degree (Ph.D.)

By

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To youth suffering from self-injury

Popular science summary of the thesis

Nonsuicidal self-injury (NSSI) refers to deliberate injury to one's body that causes damage to the skin without suicidal ideation (e.g., through cutting, scraping, or banging). While NSSI is a behavior, there is also a mental disorder specifically for NSSI (i.e., NSSI disorder). NSSI and NSSI disorder are common among youth and often cause suffering and difficulties at school, home, and among friends. There is also a risk of developing other mental disorders and attempting suicide. Hence, preventing and treating NSSI is essential. Most people engage in NSSI with the expectation of escaping difficult emotions. According to theory, improving the ability to regulate emotions can reduce NSSI, and learning other less harmful ways to regulate emotions is thus a relevant treatment goal. Access to effective treatment for NSSI among adolescents is limited, often due to restricted resources. Delivering therapy over the internet can increase access to treatment, but we know little about how such treatment is experienced and if it is efficacious for NSSI among adolescents.

We recently developed an NSSI treatment entitled Internet-delivered Emotion Regulation Therapy for Adolescents (IERITA). The goal of this thesis was to develop and evaluate IERITA (Studies I-III), as well as to improve our understanding of how symptoms in childhood are associated with self-injury (Study IV).

In Study I, eleven adolescents with NSSI disorder and nine parents were interviewed about their experiences of IERITA. Both adolescents and parents appreciated the support from the online therapist and the flexibility to work with treatment whenever and wherever they wanted. However, the flexibility of the treatment was perceived as stressful for some. Parents treasured having their specific information in an online parent program, and the adolescents accepted that their parents were involved. Finding other ways to regulate emotions helped the adolescents to function better and refrain from NSSI. Nevertheless, for some adolescents, learning new emotion regulation skills and using them in daily life, was challenging. Based on what we learned from the interviews and feedback we received, we revised IERITA before conducting Study II.

In Study II, we evaluated the efficacy of IERITA in a randomized clinical trial. In total, 166 adolescents with NSSI disorder and past-month NSSI were randomized to either (1) IERITA as an addition to usual care or (2) usual care only (without IERITA). Adding IERITA to usual care was associated with few adverse events and reduced NSSI by 82% compared to 47% in usual care only. In addition, receiving IERITA contributed to greater reductions in emotion regulation difficulties, other destructive behaviors (e.g., anger bursts, taking drugs, drinking alcohol), and problems functioning in school, at home, and with friends, compared to regular care only. The advantage of IERITA was maintained at the three-month follow-up. In addition, improving one's ability to regulate emotions was

connected to reduced NSSI during IERITA. In sum, adding IERITA to usual care can be valuable when treating NSSI among adolescents.

In Study III, we followed up on Study II, using the same sample, and explored if any patient characteristics (e.g., age, suicidality, sleep difficulties) were relevant for the treatment outcome. We did not identify any subgroups that IERITA seemed to work better or worse for. However, parental invalidation (i.e., judging, denying, or diminishing their adolescents' emotions) was associated with a worse outcome regardless of whether adolescents received the add-on of IERITA. Hence, parents with high levels of invalidation may need support to understand and express that their adolescent's emotions are understandable. Finally, adolescents with NSSI disorder and varying mental health issues can potentially benefit from IERITA.

In Study IV, we investigated how Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms (impulsivity, inattention, and hyperactivity) in childhood were associated with NSSI and suicidal behavior. We used an existing data set with 391 twins at risk of neurodevelopmental disorders (e.g., ADHD, autism spectrum disorder) that were followed over three to six years. Childhood inattention was related to NSSI, while childhood impulsivity was related to suicidal behavior. Childhood hyperactivity was not associated with any of the self-injurious behaviors. In sum, impulsivity and inattention in childhood are valuable to pay attention to and reduce, also concerning risk for self-injury.

To conclude, IERITA can be an efficacious, appreciated, and flexible treatment for adolescents engaging in NSSI. However, some adolescents may need additional support if IERITA is perceived as distressing. Helping youth find other ways to regulate emotions by adding IERITA can bring meaningful effects for many with few adverse effects. It is crucial to investigate the usefulness of IERITA in additional studies to understand how IERITA can work in different settings, such as within health care services. IERITA can potentially increase access to effective treatment among a wide range of adolescents engaging in NSSI. To prevent adolescent self-injury, helping children with high levels of impulsivity and inattention to reduce these symptoms can be one part of the puzzle. When and how to best prevent self-injury (e.g., practice impulse control in emotional situations) are questions to consider. In the future, adolescents engaging in NSSI may be offered online treatment within regular care, and new methods to prevent self-injury can be evaluated and used.

Abstract

Nonsuicidal self-injury (NSSI) and NSSI disorder are common in adolescence and associated with adverse outcomes, including suicide attempts. Detecting vulnerable children and adolescents is essential to decrease the risk of initiation as well as repetition of self-injury. Most individuals engage in NSSI to regulate difficult emotions; to effectively treat NSSI, targeting emotion regulation can thus be of importance. Accessibility to effective treatment is a challenge for adolescents engaging in NSSI. Internet-delivered treatment can increase access to treatment, but little is known about how such treatment is experienced and if it is efficacious for adolescents with NSSI or NSSI disorder. This thesis aimed to develop and evaluate the efficacy of Internet-delivered Emotion Regulation Therapy for Adolescents (IERITA), as well as to improve our understanding of early correlates of self-injurious behaviors.

Study I was a qualitative study where eleven adolescents with NSSI disorder and nine parents were interviewed regarding their experience of IERITA. The results showed that receiving support from an online therapist was essential to the treatment. Parents appreciated having their separate intervention, and adolescents accepted this form of parental involvement. Self-responsibility and the flexibility of the treatment were appreciated but could be distressing. Implementing new emotion regulation skills was relevant but perceived as challenging for some. Nevertheless, improved emotion regulation ability was a mentioned effect of IERITA that improved functioning and could hinder NSSI. It was concluded that IERITA is acceptable and can be developed to facilitate learning and address potential distress inherent to the treatment format.

Based on the findings from Study I and feedback from clinicians and patient organizations, we revised IERITA before conducting Study II. Study II was a randomized clinical trial comparing IERITA adjunctive to Treatment as Usual (TAU) to TAU only. Adolescents ($N = 166$) between 13 to 17 years old with NSSI disorder and past month NSSI were included. The IERITA plus TAU group reduced the NSSI frequency by 82% on average from pre- to posttreatment, significantly larger than the 47% reduction in the TAU-only group (blinded clinician-rated). Statistically significant improvements favoring IERITA plus TAU were also observed on most secondary outcomes, including other destructive behavior, emotion regulation difficulties, and functional impairment. In addition, the advantages of IERITA were maintained at the three-month follow-up. In line with theory, improvements in emotion regulation difficulties mediated reductions in NSSI. In addition, adolescents reported few adverse events concerning IERITA. It was concluded that IERITA can potentially improve access to evidence-based treatment for adolescents engaging in NSSI.

In Study III, as a secondary analysis of Study II, we investigated for whom IERITA was more or less helpful. Age, emotion regulation difficulties, depressive symptoms, function

level, parental invalidation, prior NSSI frequency, sleep difficulties, and suicidality were measured before randomization and investigated as moderators and predictors of treatment effect (i.e., change in NSSI frequency). No significant moderation effects were found. High parental invalidation was predictive of a less favorable outcome regardless of treatment condition. It was concluded that there is preliminary support for the efficacy of IERITA for adolescents with NSSI disorder with varying patient characteristics. In addition, detecting and reducing parental invalidation is of importance in NSSI treatments for adolescents.

In Study IV, the focus shifted to childhood. We investigated the associations between Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms and NSSI as well as suicidal behaviors in children at risk of neurodevelopmental disorders ($N = 391$). The data came from an ongoing longitudinal cohort study of twins. At age 9 or 12, parents reported degree of ADHD symptoms and at age 15 clinicians assessed self-injury. Significant associations were found between childhood impulsivity and suicidal behavior, and inattention and NSSI. However, childhood hyperactivity was not significantly or meaningfully associated with either outcome. It was concluded that screening for and treating childhood impulsivity and inattention can be valuable to prevent self-injurious behaviors.

In sum, IERITA can be an efficacious, acceptable, and flexible treatment for adolescents engaging in NSSI. Nevertheless, additional support can be needed for those experiencing distress inherent to the online format. IERITA can increase access to evidence-based treatments for NSSI among a wide range of adolescents with NSSI disorder. Addressing difficulties in emotion regulation by adding IERITA to TAU can contribute to meaningful change for many with few adverse effects. Additional sufficiently powered trials are needed to understand the utility of IERITA across studies and samples. Inattention and impulsivity during childhood can, at least partly, help us understand self-injurious behaviors' development. Further studies are needed to establish the temporal order and understand the pathways of these associations. The contributions from the included studies can, by extension, innovate how we treat NSSI among adolescents and generate new hypotheses on preventing self-injury.

List of scientific papers

- I. **Simonsson, O.**, Engberg, H., Bjureberg, J., Ljótsson, B., Stensils, J., Sahlin, H., & Hellner, C. (2021). Experiences of an Online Treatment for Adolescents With Nonsuicidal Self-injury and Their Parents: Qualitative Study. *JMIR Formative Research*, 5(7), e17910.
- II. Bjureberg, J., **Ojala, O.**, Hesser., H., Häbel, H., Sahlin, H., Gratz, K. L., Tull, M. T., Claesdotter Knutsson, E., Hedman-Lagerlöf, E., Ljótsson, B., & Hellner, C. (2023). Effect of Internet-Delivered Emotion Regulation Individual Therapy for Adolescents With Nonsuicidal Self-Injury Disorder: A Randomized Clinical Trial. *JAMA Network Open*, 6(7), e2322069.
- III. **Ojala, O.**, Hesser, H., Gratz, K. L., Tull, M. T., Hedman-Lagerlöf, E., Sahlin, H., Ljótsson, B., Hellner, C., Bjureberg, J. (2023). Moderators and Predictors of Treatment Outcome Following Adjunctive Internet-Delivered Emotion Regulation Individual Therapy Relative to Treatment as Usual Alone for Adolescents with Nonsuicidal Self-Injury Disorder. *Unpublished manuscript*.
- IV. **Ojala, O.**, Kuja-Halkola, R., Bjureberg, J., Ohliss, A., Cederlöf, M., Norén Selinus, E., Lichtenstein, P., Larsson, H., Lundström, S., & Hellner, C. (2022). Associations of Impulsivity, Hyperactivity, and Inattention with Nonsuicidal Self-injury and Suicidal Behavior: Longitudinal Cohort Study Following Children at Risk for Neurodevelopmental Disorders into Mid-adolescence. *BMC Psychiatry*, 22(1), 679.

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List of abbreviations

ADHD	Attention-Deficit/Hyperactivity Disorder
A-TAC	Autism-Tics, ADHD, and other Comorbidities inventory
BPD	Borderline Personality Disorder
CATSS	Child and Adolescent Twin Study in Sweden
CBT	Cognitive Behavioral Therapy
CI	Confidence Interval
DBT	Dialectical Behavior Therapy
DBT-A	Dialectical Behavior Therapy for Adolescents
DSHI-Y	Deliberate Self Harm Inventory – Youth version
DSM-5	Diagnostic and Statistic manual of Mental disorders, fifth version
EAM	Experiential Avoidance Model
ERGT	Emotion Regulation Group Therapy
ERITA	Emotion Regulation Individual Therapy for Adolescents
IERITA	Internet-delivered Emotion Regulation Individual Therapy for Adolescents
IAPT	Improving Access to Psychological Therapies
IRR	Incidence Rate Ratio
K-SADS-PL	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version
NSSI	Nonsuicidal Self-Injury
OR	Odds Ratio
RCT	Randomized Clinical Trial
SD	Standard Deviation
SE	Standard Error
SSRI	Selective Serotonin Reuptake Inhibitors
TAU	Treatment as Usual

Introduction

Adolescence is a challenging time for many where a non-negligible group develops and suffers from nonsuicidal self-injury and the many adverse effects of it. Much has been done over the past years to increase our understanding of NSSI and to develop treatments for NSSI among adolescents. Still, the research field of self-injury is young, and several key questions remain. More knowledge is pressing as NSSI increases among our teenagers and is associated with suicide attempts, which is predictive of suicide – a leading cause of death among youth here in Sweden and other countries.

When studying to become a clinical psychologist, I volunteered to support adults and adolescents with self-injurious thoughts and behaviors through chat and telephone. With this experience of remote support and the target group, I started to wonder how internet-delivered treatment could work for self-injurious thoughts and behaviors. When it was time to write my master thesis in 2017, I encountered the IERITA project. At the time, two of my supervisors were conducting the first pilot study on IERITA. Once involved in the project, I never left. I started my clinical career with a complete focus on child and adolescent psychiatry. I was eager to spend my time building skills to treat and help this patient group with support from excellent clinicians. Many devoted and skillful researchers and clinicians have made these studies possible. And not to forget, all the hard-working adolescents and parents committed to doing their best to change their current situation. It has been an honor working as a therapist and project coordinator in IERITA, supporting youth to overcome their difficulties and to live a life that is meaningful to them.

The anticipation with the work within this thesis is that it can expand the possibilities for how we can treat NSSI among adolescents. Also, to bring insight into how to detect vulnerable children and prevent self-injurious behaviors. I am, nevertheless, humble towards the fact that this is just the start of things. I hope this work can inspire and encourage research involving vulnerable groups because much more is needed within adolescent self-injury.

Olivia O

Lerum, autumn, 2023

1 Literature review

1.1 Nonsuicidal Self-injury

1.1.1 Definition and classification

Self-injury without the intent to die is nothing new, and many terms have been used to describe the behavior over time. Descriptions of this behavior were found already in the mid-19th-century clinical records. The need for defined terminology of the phenomena stems from a long history of trying to help individuals struggling with such behavior.¹

Over the years, several names of the behavior have been suggested, and usual terms seen in the literature are, for example, deliberate self-harm, self-mutilation, self-cutting, and parasuicide. Different terms with slightly different definitions can potentially cause confusion among researchers and clinicians.² Today, the term nonsuicidal self-injury (NSSI) is commonly used. NSSI is defined as “the deliberate, self-directed damage of body tissue without suicidal intent and for purposes not socially or culturally sanctioned” (para. 1).³ This excludes accidental injury and socially acceptable behaviors such as tattooing and piercing. Common behaviors include cutting, banging/hitting, scratching, carving, and scraping.⁴ The intent of self-injury is not always easy to assess. Therefore, a conservative assessment is advised: all “non-zero”, or vague evidence of suicidal intent should be assessed as suicidal self-injury, not NSSI.⁵

The concept of NSSI is debated⁶ and has been for a long time. The concerns put forward mainly concern two aspects. First, if it is meaningful to separate self-injury based on the intention; NSSI and suicidal behavior often co-occur, and assessing intention is difficult. Second, the classification of tissue damage particularly excludes cases of nonsuicidal self-poisoning. Although the term NSSI is debated and puts nonsuicidal self-poisoning in the diagnostic wilderness, NSSI is widely used in the literature and is acknowledged in the *Diagnostic and Statistical Manual of Mental Disorders, fifth version (DSM-5)*.⁷ Still, self-injurious behaviors as a broader concept is also commonly used and could entail both NSSI and suicidal behavior, as illustrated in Figure 1.

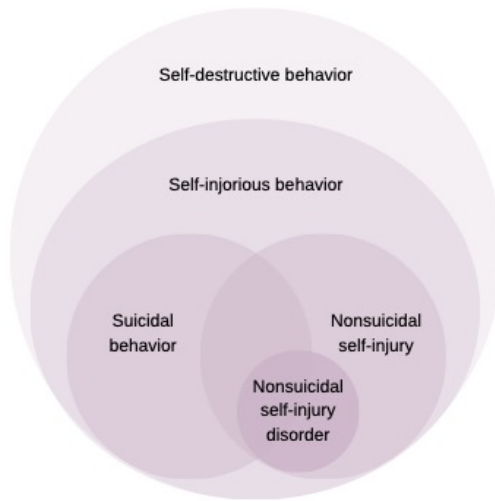


Figure 1. Illustration of the relations between self-destructive and self-injurious behaviors and the suggested NSSI disorder

NSSI could also be classified as a self-destructive behavior, as illustrated in Figure 1. Self-destructive behaviors, such as alcohol/substance abuse and disordered eating, can have deliberate self-harming intentions without tissue damage; if so, they can be classified as indirect self-injury.^{8,9} As illustrated in Figure 2, behaviors can vary on a spectrum of suicidal and self-harming intention,¹⁰ and tissue damage. Assessing these intentions and tissue damage can guide intervention for a given individual.

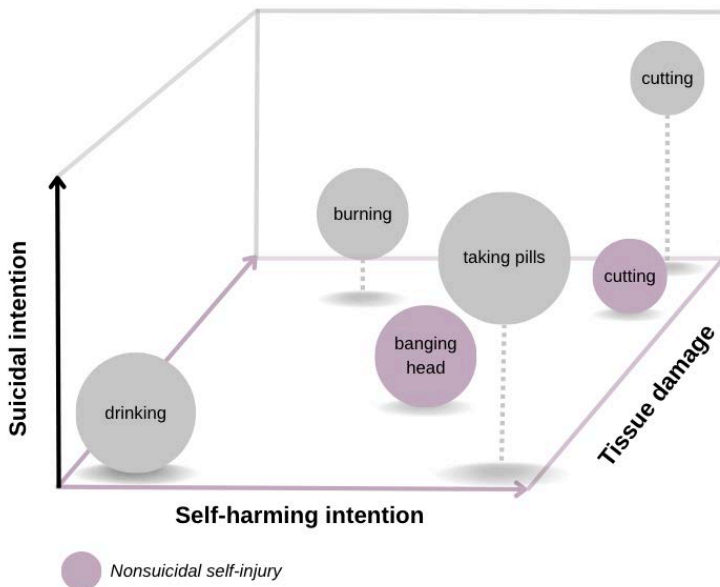


Figure 2. Illustration of how self-destructive behaviors can have different intentions and degree of tissue damage

Within psychiatric disorders, self-injury is one of nine criteria of borderline personality disorder (BPD). At least five criteria need to be presented to fulfill BPD. NSSI is commonly endorsed in those with BPD; around 80% of those fulfilling BPD have engaged in NSSI in the past year.^{11,12} However, not all adolescents engaging in NSSI fulfill the criteria for BPD; in previous studies, 21–52% of adolescents engaging in NSSI seem to fulfill the criteria for BPD.^{13–16} Hence, classifying NSSI solely within BPD seems insufficient. In some countries, a psychiatric disorder is needed for health care or insurance to fund interventions; such structure could increase the risk of misclassifying those with NSSI as having BPD or excluding those with NSSI without comorbidities from treatment.¹⁷ With this in mind, we will shift the focus from NSSI, the *behavior*, to the *disorder*.

1.1.2 Nonsuicidal self-injury disorder

One pressing question is how to capture those needing NSSI treatment and if a separate disorder can offer guidance. Several researchers have put forward the suggestion of a separate disorder for NSSI since the 1980s.^{2,18,19} In 2013, NSSI disorder was included in the latest diagnostic manual, DSM-5, as a disorder for further study. In short, the proposed criteria entail that NSSI (A) is present on five or more days the past year, (B) is expected to regulate emotions and/or interpersonal conflicts, (C) is preceded by inter- and intrapersonal difficulties and/or preoccupation of the behavior is present and hard to control, (D) is not socially sanctioned (e.g., piercing), (E) causes significant distress or impaired function, and (F) is not better explained by another disorder or condition.⁷

As a disorder for further study, more research is needed to validate the criteria and investigate the clinical utility. Although ten years have passed since NSSI disorder was introduced, few efforts have been made to validate the suggested disorder.²⁰ However, the studies that have been conducted indicate that NSSI disorder is distinct from other disorders and connected to adverse events beyond comorbidity.^{14,21,22} Nevertheless, concerns have been raised, for instance, that the frequency criterion is too low^{21–23} and that the distress/impairment criterion is difficult to assess.¹⁰ Validating and potentially establishing NSSI disorder can contribute to a consistent definition of clinically significant NSSI. Defining clinically significant NSSI can facilitate communication in research and practice, assessment of NSSI, and development and investigation of treatments for NSSI.^{20,24}

Since NSSI disorder is not yet acknowledged as an established disorder, less research has focused on NSSI disorder compared to NSSI (behavior). In the upcoming sections, literature concerning the *behavior* of NSSI, will be mentioned as “NSSI”. When literature concerns the *disorder*, it will be mentioned as “NSSI disorder”. In addition, in cases where there is no distinction regarding suicidal intention, “self-injury” will be used.

1.1.3 Developmental course and longitudinal outcome

Knowing the prevalence, age of onset, and developmental course is critical in detecting and treating NSSI. Generally, NSSI is most common during adolescence.²⁵ The probability of engaging in NSSI increases exponentially from age 9 to 10; the most common age for first NSSI engagement is around age 13 to 14.^{26,27} For many, NSSI or self-injury presented in adolescence decreases or ceases in adulthood.²⁸⁻³⁰ From what is known so far, those continuing with NSSI over adolescence or young adulthood seem to have more depressive symptoms and emotion regulation difficulties compared to those who ceased NSSI.^{31,32} The developmental course of NSSI can involve setbacks and relapses^{30,33} and switch to other self-destructive behavior;^{30,34} the course of NSSI is thus complex.

Although the majority ceases to engage in NSSI over time, there is reason to take NSSI in adolescence seriously. Sporadic and recurrent NSSI during adolescence is related to an increased risk of incidence of psychiatric disorders in later adolescence.³⁵ Furthermore, engaging in NSSI during adolescence is also connected to an elevated risk of adverse outcomes in adulthood, including substance abuse, symptoms of or diagnosed psychiatric disorder, using psychotropics, and poorer employment outcomes.^{28,36} The risks are even higher for those engaging in NSSI and suicidal self-injury.^{28,36} NSSI is predictive of future suicide attempts, which in turn is predictive of suicide death.^{37,38} Among those aged 15 – 19, suicide is the leading cause of death in Sweden and the leading or second cause of death in many countries in Europe and North America.³⁹ Hence, preventing and treating self-injury is an urgent call. It is encouraging that the risks can be reduced if NSSI ceases, although it may take time.^{30,40} Hence, early preventive and interventive strategies for NSSI are important.

1.1.4 Prevalence

How prevalent NSSI is depends on what time frame one considers, how one asks (i.e., checklist or open question), and in which population.^{41,42} It should be said that NSSI is a stigmatized behavior, and the decision to disclose NSSI is complex.⁴³ In the general population, the pooled lifetime prevalence has been estimated to be 5.5% among adults, 13.4% among young adults, and 17.2% among adolescents;⁴¹ in another more recent meta-analysis, the lifetime prevalence for adolescents was estimated to be 22.9%, and past-year prevalence 18.6%.⁴⁴ Less is known about clinical samples of adolescents; the knowledge is based on relatively small samples. It is reasonable to believe that 30–60% of adolescents within healthcare have ever or in the past year engaged in NSSI.^{14,45-47} Regarding NSSI disorder, the estimated prevalence is 3.1–7.6%^{48,49} for adolescents and 0.8% for adults.⁵⁰ Thus, if NSSI disorder becomes an established disorder, it could be a common psychiatric disorder among adolescents; in comparison, depressive or anxiety disorders have estimated prevalence rates of 2.6% and 6.5%, respectively⁵¹. In summary, independent of how it is measured, NSSI is present in adults and adolescents, with a

higher prevalence among adolescents. Childhood and adolescence could be optimal times to prevent and treat NSSI.

Regarding gender differences in the prevalence of NSSI, the results have been inconsistent. In a comprehensive meta-analysis,⁵² it was concluded that females were more likely to report lifetime NSSI than males, with an odds ratio of 1.50 (95% CI = 1.35, 1.65). Furthermore, the gender difference was more prominent for clinical and younger samples. However, sample selection might influence the results as men are less likely to seek psychiatric treatment and, therefore, are underrepresented in clinical samples.^{52,53} NSSI disorder seems also to be more prevalent among females than males.⁴ Gender minority groups have been studied to a lesser extent. Recent studies have shown elevated prevalence of NSSI in gender minority groups compared to cisgender groups.^{54,55} The critical point here is to remember that NSSI and NSSI disorder seem to be present in all studied gender groups.

The prevalence of NSSI has increased over time. Studies exploring temporal trends until 2015, showed an increase in both lifetime and recurrent NSSI among adolescents, adults, and across genders.^{56,57} The greatest increase was found in girls and young women.^{56,58} Between 2014 and 2021, one study showed an increased prevalence of lifetime engagements in NSSI among adolescents.⁵⁹ Some possible reasons for the increases include, first, that younger generations could be more exposed to NSSI through media/internet, which could potentially impact contagion between individuals.^{60,61} Second, the stigmatization of NSSI could be decreasing,⁵⁶ resulting in more disclosures. In fact, there seems to be a general increase in mental health issues among the young, with uncertain causes.⁶² Yet, this is an important area for future research as it can inform health care services and society on what to target.

1.1.5 Etiology and maintenance

1.1.5.1 Risk factors

Our ability to predict NSSI is weak. However, this is not unique to NSSI but representative of self-injurious thoughts and behaviors.⁶³ We know more about correlates (i.e., factors associated with another factor) of NSSI than risk factors (i.e., correlates that precede the outcome). From where we stand today, we have limited knowledge of how single factors or combination of factors can constitute a risk for NSSI repetition and onset.⁶⁴⁻⁶⁶ In a meta-analysis published in 2015, the strongest predictors for repeating NSSI were a prior history of NSSI, cluster b personality disorders (e.g., BPD), and hopelessness.⁶⁵ Some of these risk factors may be shared with other behaviors; for instance, prior history of NSSI is also a risk factor for suicidal behaviors.⁶³ There is some evidence for heritability of NSSI of around 40–60%,⁶⁷ but no specific genes have been found associated with NSSI. The etiology and maintenance of NSSI are presumably influenced

by social, psychological, and biological factors and their interactions. Less attention has been given to biological factors. Recently, studies have shown some evidence regarding alterations in the stress system, specific brain regions involved in regulating emotions, and decreased pain sensitivity⁶⁸ concerning NSSI. Since NSSI most often initiates in adolescence, understanding early risk factors is vital to understand the development and prevent initiation.

1.1.5.2 *Maintaining factors*

A usual question in society is why some engage in NSSI. A common misconception is that it is just “attention-seeking,”⁶⁹ fostering unhelpful behaviors and stigmatization. From a functional approach (i.e., assuming that behaviors are driven by their instant antecedents and consequences), NSSI is maintained because it fulfills crucial functions for the individual short-term. The different functions/motivators of NSSI are usually separated into intrapersonal (e.g., reduce unpleasant thoughts or feelings) or social/interpersonal (e.g., escape difficult social situations or facilitate access to help).^{70,71} Functions could differ between individuals, but also over time, and NSSI could fulfill several functions simultaneously.^{71,72} Engaging in NSSI to regulate emotions is particularly common.⁷¹ However, social functions are likely underreported because intrapersonal functions could be seen as more socially acceptable.⁷³ Understanding why and how NSSI is maintained is essential knowledge for optimizing psychosocial treatments for NSSI.

1.1.5.3 *Theoretical models*

Several theoretical models have been put forward to describe the etiology and maintenance of NSSI based on the available empirical base at the time. In this thesis, the focus is on models with a functional approach, and such models are common in the literature. In 2006, Chapman, Gratz, and Brown proposed a model, the Experiential Avoidance Model (EAM)⁷⁴ of self-injury, that has been widely spread. This model proposes that NSSI is primarily a strategy for reducing or escaping unwanted emotional arousal. As illustrated in Figure 3, how one acts in a situation evoking emotional response can be understood from the interaction of several factors (e.g., emotion intensity, poor distress tolerance); these factors are results of previous experiences and learning. The presence of any or several of these factors can lead to experiential avoidance: choosing NSSI to avoid or escape from unwanted internal experiences. This temporary desired emotional relief makes NSSI more likely to occur in similar situations in the future. However, avoiding emotional experiences can have paradoxical effects; emotional avoidance can contribute to more frequent and more intense emotions, which can trigger NSSI. The vicious cycle of NSSI can be exacerbated over time as NSSI can be linked with fewer punishing consequences (such as decreased pain and fear) and knowledge through experience that NSSI can be a way to decrease emotional distress

quickly. Some promising psychosocial treatments for NSSI are built upon this model, which we will learn more about in later sections.

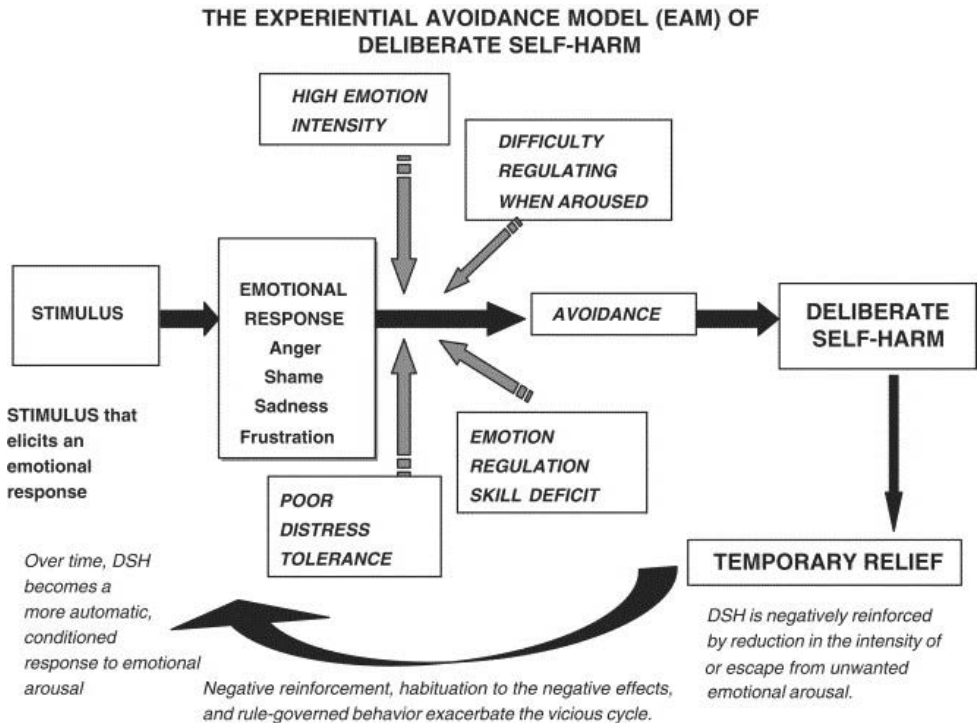


Figure 3. Graphical illustration of the steps in the Experiential Avoidance Model (EAM). In: Chapman, A.L., Gratz, K.L., & Brown, M.Z. (2006) Solving the puzzle of deliberate self-harm: The experiential avoidance model. *Behaviour Research and Therapy*, 44, 371-394. Reprinted with permission from Elsevier.

Other models have also had a great impact on the research field, for instance, the integrated model by Nock in 2009.⁶⁴ In extension to the EAM model, the integrated model proposes that distal risk factors, such as genetic predisposition, childhood abuse, and familial hostility, all create a disposition of having difficulties regulating one's internal experiences or environment. This vulnerability can, in a stressful situation, together with the presence of hypothesized vulnerability factors for NSSI (e.g., seeing or knowing others engage in NSSI, desire for self-punishment), lead to NSSI. In a more recent model, the Benefits and Barrier Model by Hooley and Franklin, published in 2018,⁷⁵ benefits of and barriers to NSSI are described to explain why some engage in NSSI while others do not. In their model, several benefits of NSSI are explained, such as affiliating to a group, self-punishment, means of communication, and emotional regulatory processes. In addition, several barriers are stated that discourage NSSI engagements, such as aversion to NSSI and pain, that can be targeted to hinder NSSI. In summary, although not all steps

of these models have been sufficiently empirically tested, they offer several hypotheses of preventing and treating NSSI worth considering further.

1.1.5.4 Emotion regulation

Many theoretical models include the notion that NSSI can regulate emotional experiences. In a broad sense, emotion regulation is the process of monitoring, evaluating, and modifying emotional reactions.⁷⁶ It is a multidimensional construct where several definitions exist. A commonly used definition, stated by Gratz and Roemer in 2004, conceptualizes emotion regulation as "(a) awareness and understanding of emotions, (b) acceptance of emotions, (c) ability to control impulsive behaviors and behave in accordance with desired goals when experiencing negative emotions, and (d) ability to use situationally appropriate emotion regulation strategies flexibly to modulate emotional responses as desired in order to meet individual goals and situational demands" (p.42).⁷⁷ Thus, many different abilities could be helpful in successful emotion regulation. Emotion dysregulation (i.e., difficulties with emotion regulation) is common across many psychiatric disorders, including depressive, anxiety, substance abuse disorders.^{78,79}

There are several ways to regulate emotions. Depending on the situation, individuals can use both adaptive and maladaptive strategies. The choice of using NSSI specifically to regulate emotions can be influenced by, for example, (1) pragmatic aspects as it could be rapid, effective, and easily implemented; (2) having seen or heard others using NSSI for this reason; and (3) other behaviors not having fulfilled the expected goal.⁶⁴ Potentially, NSSI has stronger neurobiological effects⁶⁸ than other maladaptive emotion regulation strategies. For instance, when the pain from tissue damage during NSSI relieves, this could increase positive affect and decrease negative affect and physiological arousal.⁷⁵ Studying the mechanism of emotion regulation during NSSI could be informative regarding how treatments can be optimized.

1.1.6 Clinical correlates

There is a wide range of clinical correlates to NSSI and NSSI disorder, including disorders such as depressive, anxiety, disruptive, substance use, and posttraumatic stress disorder.^{13,14,46} In this section, we will go into depth with some clinical correlates closely related to NSSI. They can offer ways to understand the developmental pathway of self-injurious behaviors.

1.1.6.1 Suicidal behavior

Suicidal behavior should always be considered in the light of NSSI. Suicidal behavior refers to directly self-injurious behaviors (e.g., suicide attempt or suicide) with some level of intent to end one's life.⁵ Although the motivator for suicidal behavior is to end one's life, emotion regulation difficulties are also associated with suicidal behavior.^{80,81}

This may not be surprising given the overlap between NSSI and suicidal behavior. The magnitude of overlap can vary, with 19–70% of adolescents with NSSI or NSSI disorder reporting at least one suicide attempt.^{13,45,46,82-84} How and why NSSI is linked to suicidal behavior is not fully understood, and several models can offer partial explanations. The three most preeminent theories will be described in short and more extensive summaries, including supporting evidence, can be found elsewhere.^{85,86} The *Third variable* theory suggests that NSSI and suicidal behavior are linked because they are associated with a third variable (e.g., depression). The *Gateway* theory proposes that self-injurious behaviors exist on a continuum where NSSI acts as a gateway to more severe self-injurious behavior, such as suicide attempts. The *Acquired capability* theory (stemming from Joiner's interpersonal theory of suicide⁸⁷) suggests that the fear of pain, injury, and death associated with a suicide attempt can decrease as individuals habituate toward pain and injury through engaging in NSSI. Based on these theories, treating NSSI, or shared risk factors for NSSI and suicidal behavior, can be potential ways of decreasing the risk of self-injurious behaviors.

1.1.6.2 *Neurodevelopmental disorders*

Neurodevelopmental disorders are conditions that have an onset during childhood and are characterized by cognitive and motor functioning impairments.⁷ One of the most common neurodevelopmental disorders is Attention-Deficit/Hyperactivity Disorder (ADHD).⁸⁸ ADHD is the neurodevelopmental disorder that has been studied the most concerning self-injury. Although other neurodevelopmental disorders may be understudied regarding self-injury, there is reason to believe that ADHD is especially relevant to NSSI and suicidal behavior.

ADHD subdimensions. Emotion dysregulation, a central factor to NSSI and a correlate to suicidal behavior, is expected within ADHD.⁸⁹ This may partly explain why associations between ADHD and self-injury⁹⁰⁻⁹² have been found in systematic reviews. On a more detailed level, how the separate ADHD subdimensions (i.e., impulsivity, hyperactivity, and inattention) relate to self-injury is not fully understood. Symptoms of these subdimensions are common in children and not exclusive to ADHD.^{93,94} Impulsivity, or impulsivity and hyperactivity combined have, in many studies, shown associations with NSSI and suicidal behavior.⁹⁵⁻⁹⁸ However, the effect of hyperactivity has rarely been investigated separately, and the relative contribution of hyperactivity is uncertain. Turning to inattention, the few existing studies concerning self-injury have shown mixed results.^{95,96,99} A more detailed understanding of impulsivity, hyperactivity, inattention, and other risk factors or correlates (e.g., emotion dysregulation), can hopefully contribute to better preventive and intervention strategies for self-injury.

1.2 Treatment for nonsuicidal self-injury

At the end of the 20th century, the first randomized clinical trials investigating treatment targeting self-injury among youth were published. Within the past ten years, several researchers have reviewed¹⁰⁰⁻¹⁰⁴ or evaluated through meta-analyses¹⁰⁵⁻¹⁰⁷ the evidence of treatment for self-injury among youth. Some of these publications consider the evidence of treatment for NSSI specifically.¹⁰²⁻¹⁰⁴ The current knowledge is primarily based on small samples, including girls. In the upcoming sections, pharmacological and psychosocial treatment will be described separately.

1.2.1 Pharmacological treatment

The effect of pharmacological treatment is rarely investigated for NSSI specifically. Currently, no pharmacological treatment can be seen as established for treating NSSI.¹⁰⁸ In clinical guidelines, pharmacological treatment for self-injury is not recommended; it is only indicated for comorbidity.^{109,110} A proportion of adolescents with self-injury are treated with psychotropics, as thus can be an indicated treatment for comorbid disorders.⁵⁸ However, little is known about how these medications affect self-injury specifically, making it critical to investigate this further. For adolescents with a history of NSSI, pharmacological treatment with antidepressants may be associated with a risk that NSSI can persist or re-occur over the treatment period.^{45,111} How such results could generalize to other comorbid disorder or in combination with psychosocial treatment targeting NSSI remains unclear.

1.2.2 Psychosocial treatment

Several psychosocial treatments are promising for NSSI, including mentalization-based therapy, Cognitive Behavioral Therapy (CBT), and Dialectical Behavior Therapy for Adolescents (DBT-A).^{101-103,105} DBT-A is an evidence-based treatment for self-injury and NSSI evaluated in independent randomized clinical trials.¹⁰³ However, some researchers recommend further evaluations of DBT-A to become more confident of the generalizability of the results.¹⁰⁰ Although DBT-A can be effective in treating NSSI among adolescents, it is an extensive treatment where accessibility is limited.¹¹² Briefer treatments could be valuable complements, offered early in the development of NSSI. There are some novel and promising brief treatments for adolescent NSSI; for instance, the eight to twelve-session-long *Cutting Down Programme* based on CBT and DBT.¹¹³ However, additional studies are needed to establish the efficacy of brief treatments targeting NSSI among adolescents.

1.2.2.1 Emotion regulation individual therapy for adolescents

In 2006, Emotion Regulation Group Therapy (ERGT) was developed with the hope of being an economically and clinically feasible treatment for adults with Borderline Personality Disorder (BPD) and NSSI.¹¹⁴ ERGT is an acceptance-based behavioral therapy

founded on the theoretical framework of the Emotional Avoidance Model (EAM).⁷⁴ In ERGT, emotion regulation skills are practiced with the expectation that reducing emotion regulation difficulties will decrease NSSI. ERGT, as a brief add-on treatment, is effective in decreasing NSSI, improving emotion regulation ability, and other health outcomes among women with BPD.^{115,116} Subsequently, ERGT was adapted into an adolescent version, a treatment named Emotion Regulation Individual Therapy for Adolescents (ERITA).¹¹⁷ In contrast to ERGT, ERITA is an individual therapy where a parent is included and participates in a separate online parent course. In 2017, the first study on ERITA was published; in an uncontrolled pilot trial including adolescents with NSSI disorder ($N = 17$),¹¹⁷ the results showed significant improvements corresponding to a 42% reduction in NSSI episodes from pre- to posttreatment, with further improvement at the 6-month follow-up. The results were also promising regarding treatment adherence and credibility. Hence, these brief treatments focusing on emotion regulation seem promising in treating NSSI among adults and adolescents.

1.2.2.2 *Internet-delivered treatment*

Internet-delivered treatment (also known as online, computerized, digital, or web-based) has, over the past 20 years, shown to be effective for several mental health disorders for adults and adolescents.^{118,119} The most common form of internet-delivered treatment is reading self-help material online guided by an online therapist for a predetermined time frame. Some of the potential advantages of internet-delivered treatment include saving therapist time, large-scale access, allowing patients to work at their own pace where it suits them, saving traveling time, less drift from treatment manual (as material is structured), continuous monitoring of outcome, and easier access to the therapist.¹²⁰ Nevertheless, the online format presents several challenges, for instance, a risk of missing out on clinical information, technical issues, and responsibility to engage in the treatment according to plan.^{120,121} It is clear that this format offers advantages that could be of importance to patients and organizations, but not without challenges.

Internet-delivered treatment for self-injurious behaviors is less explored than other symptoms or disorders. One potential reason for this is that therapists have concerns on how to respond to elevated suicide risk through the online format.¹²² Hence, handling elevated suicide risk has to be carefully considered in the remote format (e.g., offering telephone or face-to-face contact if needed). However, more youth with self-injury could potentially access psychosocial treatment with this format; in fact, some might prefer the online format (or be reluctant or refuse traditional face-to-face contact)¹²³ and the access to care has shown to be unequal for adolescents with self-injury depending on geographical localization (at least in the United Kingdom).⁵⁸ In a review published in 2019 on internet- and mobile-delivered treatment for self-injury,¹²⁴ the knowledge base was scarce, especially for adolescent self-injury treatments; there

were two studies investigating supplementary mobile-delivered skills training for adolescents with self-injury and one pilot study on internet-delivered treatment for adolescents with NSSI disorder namely Internet-delivered ERITA (IERITA). The latter study on IERITA was conducted within our research group.

1.2.2.3 Internet-delivered emotion regulation individual therapy for adolescents

From the face-to-face manual of ERITA, an internet-delivered version was developed and tested in two pilot trials. In the first uncontrolled pilot trial published in 2018 ($N = 25$),¹²⁵ the results showed comparable results concerning utility, acceptability, and feasibility to the open pilot trial of face-to-face ERITA.¹¹⁷ In a recent randomized feasibility trial ($N = 30$)¹²⁶ in Denmark, the results showed that investigating IERITA as an addition to treatment as usual (TAU) compared to TAU only was feasible. Hence, IERITA seems to be an acceptable and feasible treatment for adolescents with NSSI and NSSI disorder. A large-scale randomized clinical trial is motivated to investigate efficacy compared to a control condition.

1.2.2.4 Experience of online treatment

The efficacy of any treatment is highly dependent on its acceptability. Letting adolescents with self-injury share their treatment experience and be involved in the development of treatments has been requested.¹⁰⁰ For internet-delivered treatment targeting self-injury, more knowledge on, for instance, the impact of technical issues and how the therapeutic alliance is experienced has been articulated.¹²⁴ Qualitative studies (such as interviewing participants and analyzing the transcriptions) contribute to in-depth knowledge of experience that could be valuable together with quantitative studies to develop treatment.

1.2.3 Mediation and moderation

One area for advancements within psychotherapy research in general¹²⁷ is understanding how and why a particular treatment works. When we detect a treatment effect, it leaves us wondering why we see this effect. Studying mediators (i.e., variables that may account for the effect between treatment and outcome¹²⁷) can be a starting point to answer the question. Emotion regulation difficulties have been shown to mediate change in NSSI in the small uncontrolled pilot trials of face-to-face ERITA¹¹⁷ and IERITA.¹²⁵ Investigating the mediating effect of emotion regulation in IERITA relative to other treatments without this theoretical foundation can provide evidence of specificity in treatment over and above nonspecific factors.

Another aspect we need to understand more about within NSSI¹⁰⁸ and self-injury¹⁰³ is treatment moderation: for whom and under what circumstances a specific treatment works.¹²⁸ Investigating nonspecific treatment predictors (i.e., variables associated with

treatment outcome regardless of treatment condition¹²⁸) is more common and can be evaluated in uncontrolled study designs. Studying treatment moderators and predictors can inform about the utility of treatment and be helpful in treatment decisions.

1.3 Summary

Nonsuicidal self-injury (NSSI) is prevalent among adolescents and is a risk factor for suicide attempts predictive of suicide, a common reason for death among youth in several countries. Accessible, evidence-based treatments for NSSI and NSSI disorder are highly needed. Delivering treatment online increases access to treatment, but the efficacy of internet-delivered treatment for NSSI is unknown. Emotion regulation is a common function of NSSI, and targeting emotion regulation in treatment can potentially reduce NSSI. A brief, Internet-delivered Emotion Regulation Individual Therapy for Adolescents (IERITA) seems promising regarding results from small pilot studies. Investigating the experience of IERITA more in-depth can increase our understanding of how IERITA works and can further be improved. A large-scale randomized clinical trial is essential to understand the efficacy of IERITA (compared to a control condition). Such a design also allows for more specific evaluations of whom the treatment works for and if the effect of IERITA is mediated via the theorized process of emotion regulation. At the same time, understanding the development of and preventing self-injury is also crucial. ADHD symptoms are common in childhood and related to both emotion regulation and self-injury with and without suicidal intention. Studying the effects of impulsivity, hyperactivity, and inattention in childhood on NSSI and suicidal behavior in adolescence can hopefully improve preventive and intervention strategies.

2 Research aims

The overarching aim of this thesis was to develop and evaluate Internet-delivered Emotion Regulation Individual Therapy for Adolescents (IERITA) with Nonsuicidal Self-Injury (NSSI) disorder and to improve our understanding of the early correlates of self-injurious behaviors.

Study I **Objective:** In participants from the pilot study of IERITA, we wanted to explore the experiences of IERITA among adolescents and their parents. We aimed to investigate how they experienced the online format, treatment content, the model with separated modules for adolescents and parents, and potential perceived changes in daily life.

Hypothesis: The study was exploratory, and no hypothesis was stated beforehand.

Study II **Objective:** To investigate the efficacy and the potential mediating effect of emotion regulation difficulties of IERITA adjunctive to Treatment as Usual (TAU) compared to TAU only.

Hypothesis: Those randomized to IERITA adjunctive to TAU would show larger decreases in NSSI frequency (primary outcome), emotion regulation difficulties, other destructive behaviors, psychiatric symptoms, and functional impairment (secondary outcomes) after treatment termination compared to those randomized to TAU only. Furthermore, we hypothesized that the decrease in NSSI would be mediated by a decrease in emotion regulation difficulties for those randomized to IERITA adjunctive to TAU.

Study III **Objective:** Following Study II, we wanted to understand for whom IERITA works better or worse. Eight variables were investigated as moderators and predictors based on theoretical and empirical justifications.

Hypothesis: Given the novelty of IERITA, potential moderators and predictors were exploratively investigated.

Study IV **Objective:** In a population-based twin cohort following children into mid-adolescence, we wanted to study the associations of childhood impulsivity, hyperactivity, and inattention with NSSI and suicidal behavior in children at risk for neurodevelopmental disorders (e.g., ADHD).

Hypothesis: Impulsivity would be associated with NSSI and suicidal behavior. Hyperactivity and inattention were investigated exploratively based on limited and conflicting previous knowledge.

3 The empirical studies

Most of the included studies in this thesis cover the development and evaluation of Internet-delivered Emotion Regulation Individual Therapy for Adolescents (IERITA; Studies I-III). The main methods and results will be summarized in this section. Please see the respective publication or manuscript for a more complete description of methods and results.

3.1 Treatment

Foundation of IERITA. IERITA was developed by a team of clinicians, researchers, web-based experts, and representatives of patient organizations for self-injury. The Child Internet Project in Stockholm, Sweden, hosted the web-based treatment platform used in Studies I-III. The interface of the platform was designed to be youth-friendly. Both adolescents, parents, and therapists log into the platform through a double-authentication process. The treatment modules resemble book chapters that the adolescent or parent can navigate by clicking through. The modules include audio files, videos, and interactive worksheets. Figure 4 shows examples of the interface of IERITA.



Figure 4. Screenshot from worksheets in Internet-delivered Emotion Regulation Individual Therapy for Adolescents (ERITA). In: Bjureberg, J., et al. (2018). Extending research on Emotion Regulation Individual Therapy for Adolescents (ERITA) with nonsuicidal self-injury disorder: open pilot trial and mediation analysis of a novel online version. *BMC Psychiatry*, 18(1), 1–13. Reproduced with permission.

Adolescent treatment. The adolescent treatment consists of 11 modules delivered over 12 weeks. A new module is opened every week with the option of taking a one-week break if needed. In the treatment, adolescents follow fictional characters to facilitate learning (social modeling). The treatment starts with psychoeducation about NSSI and how it is associated with emotional avoidance. The difference between short-term gains and long-term negative consequences of NSSI is clarified to increase motivation to engage in treatment. In the second module, *impulse control* skills are introduced to offer concrete skills to refrain from NSSI early in treatment. Throughout the treatment, the focus is put on increasing well-being through acting according to *valued directions*. The following modules aim to increase skills in *emotional awareness*: to learn to label emotions and use emotional information in adaptive ways. In the first half of the treatment, *mindfulness* skills are introduced. In the fifth module, participants practice *emotional acceptance*: to stay with discomfort without trying to change or modify the experience, to be able to do what is important in life. Once these skills have been taught, emphasis is put on *emotional approach*: identifying, labeling, and investigating what information the emotion is carrying and considering acting according to such information. *Emotional distraction* is taught as a first step before approaching the emotion if needed. As practice in emotional approach and distraction continue, *self-validation* is added to decrease self-judgment. The treatment finishes with a summary and information about how to handle obstacles and setbacks, to consolidate knowledge and foster maintained effects.

Mobile application. Adolescents receive access to a complementary mobile application where they can (1) practice skills training; (2) access their crisis plan; (3) register daily presence or absence of NSSI (or other self-destructive behaviors) impulses or acts, and the factors preceding the impulses, as well as protective factors, to learn more about one's behavioral pattern; and (4) be reminded of their homework assignment for the week. When a new module opens, more information and functionalities are added to the app. The start page in the mobile app is shown in Figure 5.

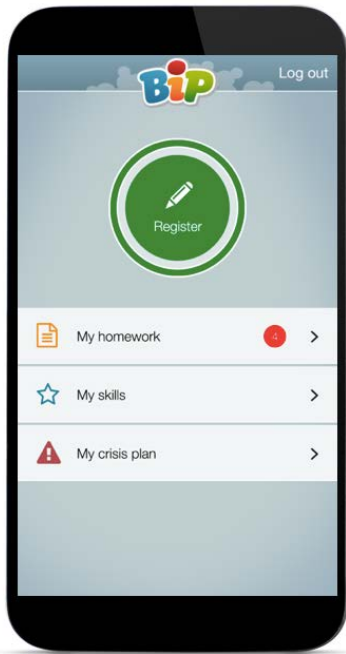


Figure 5. Illustration of the mobile app from Internet-delivered Emotion Regulation Individual Therapy for Adolescents (IERITA). In: Bjureberg, J., et al. (2018). Extending research on Emotion Regulation Individual Therapy for Adolescents (ERITA) with nonsuicidal self-injury disorder: open pilot trial and mediation analysis of a novel online version. *BMC Psychiatry*, 18(1), 1–13. Reproduced with permission.

Parent course. The parent course consists of six modules that the parent can choose to work through over six or twelve weeks. Parents will learn skills to understand and support their adolescent and handle their own emotional reactions. The parent also gets access to the adolescent treatment material every week to support the adolescent's skills training. The parent course starts with psychoeducation about NSSI and emotional reactivity (i.e., the tendency to experience high emotional intensity) to better understand the symptoms the adolescent is experiencing. In addition, parents are introduced to practice in *emotional awareness* to understand and handle their own emotional reactions. Parents are taught *validation* (i.e., recognizing, understanding, and accepting other's emotional experiences) to decrease invalidation of their adolescent's emotions. Furthermore, parents practice *self-validation* to decrease judgments of their emotional reactions. In the latter part of the course, *behavioral activation* is introduced to increase positive time together and time for likable or relaxing activities for the parent. The treatment finishes with a summary and information on how to handle obstacles and setbacks, to consolidate knowledge and foster maintained effects.

Therapist contact. The therapist contact is asynchronous; the therapist responds to the participant during weekdays office hours within two days. Both adolescents and parents have contact with an online therapist. The therapist gives feedback, explains content if needed, supports the generalization of skills, reminds the family of the treatment modules, and answers questions from adolescents and parents.

3.2 Study I

3.2.1 Methods

3.2.1.1 Study design, participants, and procedure

Adolescents and their parents who participated in the pilot study of IERITA¹²⁵ were invited to interviews after treatment termination. When selecting participants for interviews, the goal was to get as much variation as possible based on age, gender, and NSSI frequency pre- and posttreatment. In total, nine adolescents and eleven parents participated separately in interviews. The interviews were based on interview protocols with open-ended questions regarding the experience of IERITA. My colleague and I, at the time psychology master students, previously unknown to the participants, conducted and transcribed the interviews under supervision.

3.2.1.2 Data analysis

The analysis method was based on thematic analysis by Braun and Clarke,¹²⁹ a commonly used method for finding and analyzing patterns, codes, and themes within interview data. A data-driven approach was chosen, meaning that codes of interest were not decided before the analysis but rather emerging in the analysis process. We separated data from adolescents and parents to look at the convergence of the information from different sources and assess the consistency of findings (i.e., data source triangulation).

3.2.2 Main results

Three overarching themes were found. The theme “Support can come in different shapes” described how the participants received support. First, contact with the online therapist was an essential treatment feature. For some adolescents, communication was more effortless in the online format compared to face-to-face contact. Second, adolescents saw advantages in involving parents, such as having a common language. Third, the fictional characters one followed in the treatment and having access to a mobile app supported everyday skills training. The second theme “Self-responsibility can be empowering as well as distressing” described that the self-responsibility inherent to the online format could confer advantages and challenges. The high flexibility in time and place was appreciated, and being in charge of the treatment work created a sense of pride and empowerment. However, some were distressed because of the

treatment, leading to difficult emotions and thoughts, procrastination, and avoidance. The third theme “Acquiring new skills and treatment effects” described the outcomes during and after IERITA in daily life. The analysis did not point to any emotion regulation skill of specific importance. Instead, there was great variation between individuals and over time in helpful skills. The experienced changes included improved communication and acceptance of emotions and needs and improved knowledge and ability to implement emotion regulation strategies, which in turn, for some were mentioned as reasons for decreased or ceased NSSI.

3.3 Study II

3.3.1 Methods

3.3.1.1 Study design, participants, and procedure

Study II was a randomized clinical trial comparing IERITA adjunctive to Treatment as Usual (TAU) to TAU only at three different sites in Sweden (Stockholm, Västra Götaland, and Skåne). Adolescents 13 to 17 years old with NSSI disorder and engaging in NSSI the past month were included. Interested families were either clinician or self-referred and screened for eligibility via telephone and face-to-face. Participants answered self-reports both before, during, and after treatment (post and three-month follow-up). In addition, adolescents and parents participated in blinded assessments by telephone after treatment termination and at the three-month follow-up.

3.3.1.2 Outcome measures

The primary outcome measure was NSSI frequency, as measured with the Deliberate Self Harm Inventory – Youth version (DSHI-Y^{130,131}), both self-reported and clinician-rated. Secondary outcomes included emotion regulation difficulties, other self-destructive behaviors, functional impairment, and psychological distress. Adverse events, treatment adherence, credibility, and satisfaction were also monitored for the IERITA plus TAU group.

3.3.1.3 Interventions

Development of IERITA. Based on the findings of Study I and the received feedback from therapists and patient organization representatives, we revised IERITA before conducting Study II. First, more emphasis was put on increasing dedication and commitment to using emotion regulation skills that could displace NSSI early in the treatment. Second, several adaptations were made to facilitate learning and skills training, including, adding a quiz about emotions, audio-recorded treatment summaries, and adding treatment summaries (both text and audio) in the app. Third, the section about valued direction was expanded and moved to the end of treatment. The reason for moving the section about valued direction was to focus primarily on

displacing NSSI in the first modules. This priority order aligns with DBT-A,¹³² where decreasing life-threatening behaviors is the first priority. Increasing behaviors connected to well-being were introduced later when NSSI potentially had decreased. Fourth, questions about how the treatment was progressing and the need for additional support were added halfway through treatment. The anticipation with this revision was to normalize that treatment work can be challenging and detect the need for additional therapeutic support. Lastly, seeking situations that elicited emotional responses, both imaginary and in everyday life, to practice emotional approach was dropped. The experience was that it was challenging to identify appropriate situations for some participants. Instead, more focus was put on noting everyday risk situations (including emotions) for NSSI or other self-destructive behavior, generate suitable emotion regulation skills, and practice to access emotion regulation skills flexibly. Using emotion regulation skills flexibly is central in decreasing emotional avoidance and the risk of NSSI.⁷⁴

Therapists. The clinicians were psychologists or psychotherapists who worked part-time as therapists in the study. All therapists received education in the intervention, NSSI, and suicide assessment, as well as supervision during the trial.

Control condition. An ideal control condition should be potentially efficacious, safe, and desired.¹³³ At the time when we designed Study II, we landed in a TAU condition for the following reasons: (1) there were no evidence-based treatments targeting youth NSSI specifically at the time, and a TAU condition represented standard care, i.e., what is currently available to adolescents with NSSI, and; (2) given the potential suicidal risk and comorbidities, a strict waitlist control was not an option. As participants could have other treatment needs beyond NSSI, all participants were allowed to continue or initiate TAU. We also considered that discontinuing existing care could expose risks to the participants.¹³³ TAU was enhanced in the sense that weekly self-reports were monitored by study clinicians and the research team, and procedures according to safety protocols were followed if deterioration in health was detected.

3.3.1.4 *Statistical analysis*

The primary and secondary outcome measures were measured with mixed effects modeling. Mixed effects modeling (sometimes also referred to multilevel modeling, or growth models) was used based on the dependency between observations as participants were measured repeatedly, and missing values were assumed to be missing at random. To model change in the primary outcome, NSSI frequency, a zero-inflated negative binomial generalized mixed effects regression model was used. This model can be suitable when there are many zeros in the data and the non-negative counts (e.g., 1, 2, 3) follow a right-skewed distribution (e.g., many with low number of NSSI episodes and a long “tail” with few observations of many episodes).

The mediation analysis used a parallel process latent growth curve modeling approach for mediation.¹³⁴ Separate latent growth curves were performed for the hypothesized mediator (emotion regulation difficulties) and outcome (weekly NSSI frequency during and one-month posttreatment). Next, the two latent growth curves were combined to investigate if IERITA plus TAU, relative to TAU-only, influenced the growth (change) in emotion regulation difficulties that, in turn, affected the growth (change) in NSSI.

3.3.2 Main results

In total, 166 adolescents (93% girls, mean age = 15.0, SD = 1.2) participated in the trial; 84 families were randomized to IERITA plus TAU and 82 families to TAU only. Reduction in NSSI frequency was significantly larger in the IERITA plus TAU versus TAU-only for both self-reported NSSI (β [SE] = -0.08 [0.02]; $P < .001$; IRR = 0.29 [95% CI = 0.14-0.58]) and blinded clinician-rated NSSI (β [SE] = -1.09 [0.27]; $P < .001$; IRR = 0.34 [95% CI = 0.20-0.57]). From the month before to the one-month posttreatment, IERITA plus TAU had reduced NSSI frequency by 82%, whereas TAU-only had reduced by 47% (blinded clinician-rated). Furthermore, IERITA plus TAU improved significantly than TAU-only regarding emotion regulation difficulties, other self-destructive behaviors, and functional impairment. The significant superiority of IERITA plus TAU remained at the three-month follow-up. There was no significant group difference regarding psychiatric symptoms at one-month posttreatment or follow-up.

Participating in IERITA plus TAU, relative to TAU-only, was associated with greater reductions in emotion regulation difficulties, which led to greater reductions in NSSI frequency (indirect effect = -0.028 [95% bootstrap CI = -0.053 to -0.010]).

Adolescents completed on average 9.6 (SD = 2.2) of 11 modules, and parents completed 5.5 (SD = 1.0) of 6 modules. The treatment satisfaction rated by adolescents after IERITA was relatively high (mean = 25.2 out of 32, SD = 5.2). After completing the first module, adolescents rated IERITA as moderately credible (mean = 20.0 out of 27, SD = 4.1). The therapist time for IERITA (when therapists were reviewing treatment work, giving feedback, and answering questions) was on average 378.8 (SD = 163.1) minutes per family. Regarding adverse events, five participants (6%) in IERITA plus TAU and nine participants (11%) in TAU-only reported suicide attempts during the treatment period or at one-month posttreatment or three-month follow-up. In the IERITA plus TAU group 4 (5%) participants experienced adverse events connected to IERITA at one-month posttreatment. The events entailed increased sadness, increased stress, and increased self-destructive behaviors.

The type and frequency of TAU during the study did not differ significantly between the groups. In total, 118 participants (76%) received psychosocial treatment. The most common type and frequency was supportive therapy biweekly or monthly. Altogether, 67 participants (43%) received psychopharmacological treatment. Antidepressants,

specifically Selective Serotonin Reuptake Inhibitors (SSRI), was the most frequent medication.

3.4 Study III

3.4.1 Methods

3.4.1.1 Study design, participants, and procedure

Study III was a secondary analysis following Study II with the same setting, intervention, participants, and procedure.

3.4.1.2 Measures

The outcome was weekly self-reported NSSI frequency during and for four weeks after treatment termination measured with the DSHI-Y.^{130,131} The eight theoretically and empirically motivated variables to test as moderators and predictors were measured before randomization; the eight variables were age, emotion regulation difficulties, depressive symptoms, function level, parental invalidation, prior NSSI frequency, sleep difficulties, and suicidality.

3.4.1.3 Statistical analysis

A zero-inflated negative binomial generalized linear mixed effects regression model was used (same as in Study II). The client factor and its interactions with time were added to investigate prediction. Then, the client factor and its interactions with time and the treatment condition were added to investigate moderation.

3.4.2 Main results

No significant moderation effects were found. Parental invalidation significantly predicted the treatment effect (β [SE] = 0.027 [0.011]; $P = .014$). Thus, higher levels of parental invalidation before treatment started were predictive of less favorable outcomes regardless of treatment condition.

3.5 Study IV

3.5.1 Methods

3.5.1.1 Study design, participants, and procedure

Study IV was a longitudinal cohort study following twins at risk for neurodevelopmental disorders or common comorbidity from childhood into mid-adolescence. The data was collected from the Child and Adolescent Twin Study in Sweden (CATSS).¹³⁵ CATSS is an ongoing population-based cohort study investigating health (i.e., somatic, and mental) from childhood to adulthood. At age 9 or 12, a parent was interviewed via telephone regarding neurodevelopmental disorders symptoms. Families with children at risk for

neurodevelopmental disorder were invited to a face-to-face clinical assessment at age 15.

3.5.1.2 *Measurements*

The exposures in childhood were the degree of impulsivity, hyperactivity, and inattention as measured with the Autism–Tics, ADHD, and other Comorbidities inventory (A-TAC).^{136,137} The two outcomes in mid-adolescence were lifetime engagement of (1) NSSI and (2) suicidal behavior (yes or no) measured with the semi-structured clinical interview Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL),¹³⁸ the second version published in 2009.¹³⁹ We adjusted for age at childhood interview (9 or 12), birthyear, sex, and other neurodevelopmental disorder symptoms.

3.5.1.3 *Statistical analysis*

Odds ratios were calculated using logistic regression, applying generalized estimating equations, and cluster robust standard errors. Because observations between twins are clustered (non-independent), a method that does not make assumptions about independence between observations was needed. The outcomes were investigated in ten separate models. First, the three different exposures were investigated separately in univariable models with each outcome. Second, all exposures were included in the same model. Third, both exposures and potential confounders were included.

3.5.2 **Main results**

The sample (N = 391) included 225 (57.5%) boys and 166 (42.5%) girls. At age 15, 32 (8.2%) adolescents had ever engaged in NSSI, and 18 (4.6%) in suicidal behavior. The association between inattention and NSSI was statistically significant in all models (fully adjusted model: OR = 1.99, 95% CI = 1.36–2.91, $p < 0.001$). In addition, the association between impulsivity and suicidal behavior was statistically significant in all models (fully-adjusted model: OR = 2.08, 95% CI = 1.13–3.81, $p = 0.018$). The other associations (i.e., hyperactivity and NSSI or suicidal behavior, inattention and suicidal behavior, impulsivity and NSSI) were statistically non-significant in all models.

3.6 **Ethical considerations**

Ethical considerations are of great concern in all the steps of a scientific project and should weigh the risks against potential gains. Certain care should be taken regarding youth and those with potentially life-threatening behaviors. The studies in this thesis have received ethical approval, and several ethical considerations have been made.

First, the design of the treatment studies was carefully chosen to maximize safety. In Study II, being randomized to the one group that did not include internet-delivered

treatment could disappoint families. However, the control group received IERITA after the three-month follow-up. Nevertheless, families were informed of the study design via telephone and face-to-face to minimize the potential disappointment. In Studies I-III, all participating adolescents were allowed, encouraged, and recommended regular care based on their needs; this was a precaution taken given the experimental nature of the intervention and the risk of not getting other interventions based on their care needs. All participants were registered in regular care during the treatment phase to facilitate rapid access to regular care. All adolescents were monitored weekly during the intervention period and at follow-up. Therapists and members of the research group monitored the answers on weekdays. In case of detected deterioration, the family was contacted according to a set procedure. Members of the research group, psychologists and a senior child and adolescent psychiatrist, were contactable on demand and participated in weekly treatment conferences. Altogether, these additional components (e.g., weekly monitoring and regular treatment conferences) contributed to enhanced care, compared to regular care only, for all participants.

Self-reports containing sensitive questions (e.g., suicidal behavior, NSSI) seem to have no iatrogenic effects on a group level,^{140,141} but could still be burdensome for some. The number of questions was kept to a minimum by choosing short, validated scales. Regular self-reports were discussed with the adolescent at the assessment meeting to detect potential adverse effects. In case of missed self-reports, we contacted the family according to a structured routine. This procedure aimed to detect any adverse effects of the questions or deterioration. When interviewing adolescents in Study I, we considered that talking about previous or current problems with somebody unknown could have a negative impact. We tried to minimize this by letting the adolescent decide on the format and place for the interview. The interview was guided by what adolescents wanted to talk about, and interviewers asked adolescents during and after the interview how it felt.

We considered that an experimental online treatment might not be suitable for the most severely affected. Adolescents with conditions in need of acute treatment (i.e., anorexia nervosa, psychosis, immediate suicide risk) were excluded from the treatment studies to focus on more extensive treatment at first hand. Experienced and trained clinicians tried to detect such severe conditions in both the telephone and face-to-face pre-assessment, to refer or recommend families to suitable care.

Participant safety and confidentiality in the online format were critical regarding the sensitivity of the data gathered. The platform was on a secure server where both therapists and participants logged in through a two-factor authentication process (i.e.,

both password and code) for both therapist and participants. Participants and therapists were automatically logged out in case of inactivity. The mobile app offered to adolescents was discreet with a neutral mobile app icon (e.g., not mentioning mental health) to protect adolescents' privacy. All participants were encouraged to engage with the treatment material in settings where they could be alone and undisturbed.

The choice of involving parents yields some ethical considerations concerning the autonomy of the adolescent. Some adolescents may not have wanted to participate in the treatment studies as at least one parent had to be informed and involved. If such concerns were communicated, therapists would discuss this with the adolescent and assist in communicating with the parent(s) if requested. From a safety and feasibility perspective, we assessed that there were potentially important positive effects of involving the parent(s). It could benefit the adolescent that the parent practiced skills to support the adolescent.^{103,104} Still, the integrity of the adolescent was important. It was necessary that adolescents had individual contact with the therapist online and during face-to-face assessment. Not the least to offer opportunities to disclose sensitive information. Also, when conducting the interviews in Study I, the interviews were conducted in separate rooms.

In comparison to the other studies, Study IV did not include a treatment-seeking group. Nevertheless, those potentially at risk of neurodevelopmental disorders were offered a professional assessment to better understand strengths and difficulties. Study IV included experienced clinicians who were observant of the status and aware of the sensitivity of the questions. They were prepared to give advice, recommend, or refer families if requested or needed.

In summary, although it can be challenging to handle risks when studying this target group, several steps can be taken to increase safety. Involving adolescents engaging in NSSI in studies evaluating treatments developed for them is vital for the results to be generalizable to the target group. Limited knowledge of effective treatments could have adverse effects through missing out on potentially effective treatments.

4 Discussion

4.1 Main findings

Internet-delivered Emotion Regulation Individual Therapy for Adolescents (IERITA) targeting Nonsuicidal Self-Injury (NSSI) was experienced as a treatment with high support levels where parents can be involved successfully. The flexibility inherent to the format was appreciated by many but challenging for some. Having access to emotion regulation skills was helpful to hinder NSSI, and several skills were beneficial to reduce emotion regulation difficulties. IERITA adjunctive to Treatment as Usual (TAU) was significantly more efficacious than TAU-only in reducing NSSI frequency, emotion regulation difficulties, other destructive behavior, and functional impairment. For the IERITA plus TAU group, reductions in emotional regulation difficulties were associated with reductions in NSSI. No significant moderators were found, but a high level of parental invalidation was predictive of less favorable outcomes irrespective of treatment condition. For children at risk of neurodevelopmental disorders, impulsivity was associated with suicidal behavior, while inattention was associated with NSSI.

4.2 Is IERITA an efficacious treatment for adolescents with NSSI disorder?

At this point, Study II offers the best opportunity to answer this question. What are the main findings that speak for the efficacy of IERITA? First, significantly larger reductions in self- and clinician-rated NSSI were found for IERITA plus TAU compared to TAU-only in a relatively large sample. The high module completion indicates the acceptability and relevance of IERITA. The moderate credibility and relatively high satisfaction suggest that IERITA can be appreciated by many interested in internet-delivered treatment. The external validity of the findings is strengthened by conducting the study within regular care and in a sample with a relatively high level of psychiatric comorbidity.

A subsequent question is *how* efficacious IERITA plus TAU is in relation to other psychosocial treatments targeting adolescent NSSI. Comparing results with previous treatment studies targeting NSSI among adolescents is challenging because of differences in: (1) how change in NSSI frequency is evaluated (e.g., proportion of individuals with NSSI 0, 1 to 3, 4–6, ≥ 7 ¹⁴² or 50% reduction in NSSI¹¹³ with varied time-spans); (2) target groups (e.g., being at high risk of suicide, some degree of BPD criteria); (3) treatment length and intensity; (4) primary outcome (e.g., suicide attempts, NSSI thoughts, suicidal ideation). To contextualize the findings from Study II, results from a selection of previous treatment studies is summarized in Table 1. These studies are also randomized clinical trials with similar treatment lengths that evaluate self-injury frequency in a comparable timeframe. Still, as the target groups and sample sizes differ, I am hesitant to make direct comparisons between studies. Nevertheless, I believe some

general patterns are worth commenting: overall, the magnitude of reduction in NSSI and average NSSI frequency after treatment for IERITA adjunctive to TAU are comparable to other psychosocial treatments with relatively similar treatment length. Moreover, the effects of IERITA adjunctive to TAU were accomplished with less therapist time on average, compared to several other treatments in Table 1 (where therapist time or session length was reported).

A considerable shortcoming within this research field is the lack of a threshold for clinically significant NSSI. To define treatment responders, using the absence of NSSI has been suggested by some.^{106,142} A significantly higher proportion of adolescents with no NSSI one-month posttreatment was observed in the IERITA plus TAU group ($n = 43$, 56% [8% missing]) compared to the TAU-only group ($n = 26$, 34% [6% missing]). However, this difference was non-significant at three-month follow-up ($n = 33$, 47% in IERITA plus TAU [15% missing], $n = 33$, 44% in TAU-only [9% missing]). From the studies presented in Table 1, only the study by Santamarina-Perez et al.¹⁴³ reported on NSSI absence. In this study, eleven adolescents (79% [21% missing]) receiving DBT-A reported no NSSI 13 to 16 weeks after treatment start. However, current or recent NSSI was not an inclusion criterion (as in Study II); thus, the proportion could, at least partly, be explained by the fact that some adolescents did not currently engage in NSSI when starting treatment. These observed values should be interpreted with caution given that missing values could greatly impact on the results (especially in small samples). If using the proportion of NSSI absence after treatment as a response rate, around 50% of responders to cognitive behavioral therapy is shared across several psychiatric disorders.¹⁴⁴

The average high-maintained reduction resulting in no or few episodes of NSSI indicates that IERITA adjunctive to TAU can have a clinically meaningful effect for many. Nevertheless, some may still need more or other treatment, and the effect remains unknown beyond three months after treatment. At this point, any additional reductions in NSSI compared to what is currently offered (that TAU could represent) are, in my opinion, meaningful.

Table 1. Nonsuicidal self-injury and self-injury outcomes after brief psychosocial treatment from a selection of randomized clinical trials targeting adolescent self-injury, experimental group only

Study	Sample	Treatment type	N	Treatment length and dose	Outcomes: frequency of NSSI or SI ^a
Bjureberg et al., 2023 (Study II)	Age 13-17, NSSI disorder, ≥ 1 NSSI episode in the past month	IERITA + TAU	82	12 weeks 11 weekly treatment modules for adolescents and 6 for parents. Average weekly therapist time 32 to 34 minutes. TAU according to treatment need (typically supportive therapy biweekly)	NSSI observed median week 13-16 = 0 (IQR = 0-4, 8% missing). NSSI estimation week 13-16 = 1.2 (95% CI 0.9-1.4) ^b 82% estimated reduction in NSSI episodes from the month before to the month after treatment SI (presented to emergency departments) observed mean week 12-24 = 0.2 (range 0-2) 68% reduction from the 12 weeks before to the 12 weeks after treatment
Griffiths et al., 2019¹⁴⁵	Age 12-18, ≥ 1 SI episode in the past 6 months	MBT-AI + TAU	26	12 weekly group sessions (75 min) TAU according to treatment need ^c	NSSI observed median week 13-16 = 1 (IQR = 0-3) 90% reduction in NSSI episodes from the month before to the month after treatment
Kaess et al., 2019¹⁴³	Age 12-17, ≥ 5 NSSI episodes the past 6 months, ≥ 1 NSSI episode in the past month	Cutting down programme; CBT	37	8-16 weeks 8-12 sessions and parental sessions on as-needed basis (no info on sessions length)	SI observed mean week 10-15 = 1.2 (SD = 2.0) Not possible to estimate reduction from before the treatment
Mehlum et al., 2014¹⁴⁶	Age 12-18, ≥ 2 previous SI, ≥ 1 SI past 16 weeks, 2 BPD criteria (or 3 if 2 were assessed as threshold)	DBT-A	39	19 weeks Weekly individual sessions (60 min) and multifamily sessions (120 min) with telephone and family sessions on an as-needed basis	NSSI estimated mean week 13-16 = 1.3 (95% CI 0.7-1.9) Not possible to estimate reduction from before the treatment
Santamarina-Perez et al., 2020¹⁴³	Age 12-17, NSSI disorder or suicide attempt the past 12 months, and high risk of suicide	DBT-A	18	16 weeks Biweekly individual sessions (60 min), weekly group sessions for adolescents (60 min), and separate for family (60 min) with telephone coaching on demand	Not possible to estimate reduction from before the treatment

Note. Only within-group results of the experimental condition are presented. BPD = borderline personality disorder, CBT = cognitive behavior therapy, CI = confidence interval, DBT-A = dialectical behavior therapy for adolescents, IERITA = internet-delivered emotion regulation individual therapy, IQR = interquartile range, MBT - AI = mentalization based therapy introductory group manual for an adolescent population, NSSI = nonsuicidal self-injury, NSSI disorder = nonsuicidal self-injury disorder, RCT = randomized clinical trial, SI = self-injury, TAU = treatment as usual

^aResults presented here selected for comparison purposes to the results of Study II

^bExponentiated marginal predictions, blinded clinician-assessed

^cNo information on the most common type and frequency of treatment as usual

It is encouraging that IERITA in adjunctive to TAU can also be efficacious for other symptoms. Significantly larger reductions for the IERITA plus TAU group compared to the TAU-only group were found for other destructive behaviors (such as drinking alcohol, taking drugs, anger bursts, binge eating), emotion regulation difficulties, and functional impairment. On the other hand, contrary to our hypothesis, there was no significant difference between the groups on psychiatric symptoms (i.e., depression, anxiety, and stress). IERITA emphasizes *behavioral* emotion regulation strategies: accepting internal experiences and controlling behaviors in emotional situations. Potentially, *cognitive* emotion regulation strategies (e.g., cognitive reappraisal, not included in IERITA) are specifically beneficial to reduce depressive and anxiety symptoms among youth,¹⁴⁷ how these findings apply to adolescents engaging in NSSI is something to investigate further. For adolescents with clinical levels of depression, anxiety, and stress, it is reasonable to include evidence-based interventions for these symptoms (e.g., behavioral activation, exposure, relaxation techniques) in parallel TAU. Consequently, it is crucial to evaluate if such TAU in combination with IERITA is advantageous for this subgroup.

If IERITA should be considered an efficacious treatment, the benefits should outweigh the adverse effects. A few ($n = 4$, 5%) participants in Study II reported adverse events related to IERITA at treatment termination. Reports included increased distress, sadness, and symptoms that the treatment addresses (self-destructive behaviors) and are likely to be reported by some receiving internet-delivered psychotherapy.¹²¹ Nevertheless, such adverse events are necessary to detect early to intervene, for instance, through enhancing therapist contact. A few individuals reported suicide attempts during the five-month-long study period (i.e., 5 [6%] in IERITA plus TAU and 9 [11%] in TAU-only). Based on these reports, there is no reason to believe that adding IERITA to TAU results in a higher number of suicide attempts, at least. As NSSI and suicidal behavior overlap,^{13,45,46,82-84} and only adolescents with immediate suicide risk were excluded, suicide attempts can be expected. However, based on previous findings,^{113,142,143} suicide attempts could have followed the same decreasing trend as NSSI in Study II. This hypothesis can be supported by the fact that NSSI, the strongest risk factor for suicide attempts,^{37,38} was reduced. Because suicide attempts are rarer than NSSI, larger samples are needed to investigate changes over time and between groups. In conclusion, adding IERITA to TAU can be more beneficial than harmful for adolescents with NSSI disorder on a group level.

4.3 Can emotion regulation be a mechanism of change in IERITA?

In Study II, mediation was investigated with a high resolution (weekly measures) of the theorized treatment mechanism and outcome. The results indicate that the effect of IERITA adjunctive to TAU, at least partly, goes through reducing emotion regulation difficulties. Hence, to optimize the effect of IERITA, the focus should be on decreasing

emotion regulation difficulties. There is still more to understand regarding *how* the change in emotion regulation difficulties the change NSSI frequency in IERITA (moving from mediator to mechanism). Results from Study I indicate that no specific skills taught in IERITA were superior in improving emotion regulation on a group level. Thus, which emotion regulation skill is most efficient for preventing NSSI can depend largely on individual and contextual factors.

There are still some crucial steps to establish emotion regulation as an empirically proven treatment mechanism. These steps include, for instance, investigating competing mediators; considering family functioning¹⁴⁸ or mentalization and attachment avoidance¹⁴⁹ as competing mediators are relevant as they have mediated outcomes in other treatments targeting adolescent self-injury. Investigating competing mediators can increase knowledge of shared or specific processes through which treatments for NSSI work. Secondly, demonstration of change in the mediator preceding change in the outcome and consistency across studies and samples are important. Emotion regulation difficulties have mediated treatment outcomes in other treatment studies targeting NSSI. It applies to adolescents receiving DBT-A,¹⁵⁰ and adults receiving Emotion Regulation Group Therapy (ERGT).¹⁵¹ In addition, the dose-response relationship found in Study II (the more reduction in emotion regulation difficulties, the more reduction in NSSI) strengthens the notion that emotion regulation can be a potential mechanism of change in IERITA.

4.4 What can we learn from the participant experience of IERITA?

The knowledge gained from Study I was beneficial for developing IERITA for Study II and has some implications worth discussing. First, investigating the supplementary app in a larger scale can increase the understanding of the added value of the app. Mobile apps can potentially be effective as a stand-alone intervention or in addition to face-to-face treatments.¹⁵² The mobile app was perceived as crucial for some adolescents. Adding mobile apps to complement face-to-face treatment can potentially increase the reach of digital aids to more extensive treatments. The flexibility in how to communicate with the therapist (online or telephone) or engage with the material (web-based material or mobile app) was appreciated in IERITA. Meeting treatment preferences can positively affect treatment adherence and outcome;¹⁵³ offering a toolbox of components to use in IERITA can thus hopefully facilitate optimal outcomes.

Our results from Study I indicate that therapist support is essential to both adolescents and parents. Also, many adolescents with other disorders have experienced that the online format can facilitate communication with the therapist.¹⁵⁴ If more or other formats (e.g., face-to-face/video meeting halfway through) of therapist contact could increase the efficacy of IERITA, should be considered further. Based on findings from Study I, how to combine skills and use them in challenging situations and how to structure treatment

work, are relevant topics for additional meetings. What therapist behaviors are most desirable should be investigated and can be informative in educating therapists and assessing therapist adherence.

Parents appreciated being involved in the treatment, and adolescents accepted their participation and could see the advantages of it. In addition, involving parents in a separate parent course was not associated with any apparent adverse effects. Nevertheless, some families may need additional family/parent interactive parts, as wished for by some parents in Study I. In fact, low family functioning can be a risk factor for NSSI.⁶⁵ Detecting and targeting low family functioning or high parental invalidation, as seen in Study III, is needed across conditions.

4.5 For whom can IERITA be more or less helpful?

IERITA was developed to create a treatment suitable for widespread use among youth with and without comorbidity. The results of Study III provided preliminary support for a broad utility as no strong or significant moderators were found. However, other variables that were not measured could still be of importance. It is also unknown if the results would differ if the outcome were operationalized differently, such as NSSI absence. Reductions on a group level are not likely to apply to every adolescent. A next relevant step can be investigating unaltered or decreasing NSSI trajectories and who is more likely to face such trajectories. Another possible future direction is to study the predictive effect of factors *during* treatment (e.g., credibility or initial response). Such evaluations can inform potential treatment modification (i.e., additional support) or decisions to switch to another treatment format. Larger samples are needed to investigate questions regarding differences in treatment response with greater certainty.

4.6 Can impulsivity and inattention in childhood be of importance to NSSI and suicidal behavior in adolescence?

The results from Study IV indicate that impulsivity and inattention are something to target across genders, possibly not only within ADHD. Impulsivity and inattention can be transient,¹⁵⁵ but still increase the risk of adverse outcomes at a later point. The findings from Study IV should be seen as one step of the way, where a central subsequent question is: Through what pathways do impulsivity and inattention increase the risk of NSSI and suicidal behavior? Longitudinal studies where exposure, mediator, and outcome are measured more than twice can help understand the associations in more detail and establish the temporal order. Potential mediators (factors to explain the association) to investigate further are, for instance, emotion dysregulation,¹⁵⁶ suicidal ideation,^{156,157} painful and proactive events,^{156,158} and negative self-image and self-criticism⁷⁵. Such future studies are needed to develop effective early prevention strategies and understand the optimal time to intervene.

Given the connections between ADHD, emotion regulation, and self-injury,^{80,81,89-92} is it possible that targeting impulsivity and inattention in emotional situations is important to decrease the risk of self-injury? From the stance of the Experiential Avoidance Model,⁷⁴ youth with a high degree of impulsivity may need help to shift focus from short-term benefits to emotion regulation strategies with long-term benefits; youth with a high degree of inattention may need assistance to direct attention to select and retain situationally appropriate emotion regulation strategies. Emotion regulation treatment is promising not only for NSSI, but also in reducing impulsivity and inattention.⁸⁹ Thus, the hope is that IERITA, to some degree, could also reduce impulsivity and inattention symptoms. Some adolescents interested in IERITA will show elevated levels of impulsivity or inattention; for instance, in Study II, 18% had been diagnosed with ADHD.

4.7 General limitations

Designing a study of high quality is the aim of any researcher. Nonetheless, conducting research on potentially suicidal youth confers challenges that need to be handled with great care.¹³³ In Study II, the lack of balance between the groups (e.g., the group that received IERITA had additional material and an additional therapist contact in another format) limits internal validity concerning the specific effects of IERITA. In Study III, the statistical power was potentially constrained; however, it is common practice to base power calculations on the research question concerning efficacy on the primary outcome and evaluate moderators exploratively for novel treatments.¹⁵⁹ In Study IV, the sample size was pre-determined, and the estimated statistical power was low for effects of smaller magnitude. The expected effect is not always easy to determine when conducting power calculations, often because of limited previous research.

Some threats to the validity and reliability of measuring NSSI should be brought to attention. First, assessing NSSI can be challenging in some cases; for instance, separating NSSI from skin-picking and assessing the presence of tissue damage. In some cases, what defines one NSSI episode can be difficult to assess; if somebody stops self-injuring for a few minutes and then starts again, is this reported as one or two episodes? To overcome such challenges, interrater reliability evaluations and expert panel recommendations can be beneficial. Second, measurements of NSSI and suicidal behavior typically consist of self-reports, which entail certain risks of bias. The choice to disclose NSSI could be hindered by shame, fear of stigma and rejection.⁴³ However, when seeking treatment for NSSI (Studies I-III), willingness to disclose NSSI can increase.⁴³ Third, there is a risk of recall bias when reporting the occurrence of NSSI in retrospect. Hopefully, using weekly measures (Studies II-III) can decrease the risk of recall bias. Outcomes measured frequently can offer greater statistical power but should be balanced against the risk of missing values. In Studies II-III, the proportion of missing values was low for most weeks but relatively large for a few weeks. Missing values can threaten the validity of findings; thus, using efficient methods to deal with missing values

is essential. Likelihood-based models (used in Studies II–III) or multiple imputation are recommended methods under the assumption of missing at random.¹⁶⁰

The generalizability of the findings in Studies II–III can be threatened by low gender diversity (almost only girls). The underrepresentation of boys is a general limitation within this field of research¹⁰⁰ and regular care.⁵² In addition, NSSI is common among gender minorities⁵⁴ and thus desirable to have gender minorities represented in treatment studies. Including adolescents fulfilling NSSI disorder in Studies I–III entails a defined group of individuals (in comparison to having only a frequency criteria of NSSI). Nevertheless, NSSI disorder is not established, and the efficacy of IERITA adjunctive to TAU for subthreshold NSSI disorder remains unknown. Study IV included a defined but still heterogenic group: children at risk of neurodevelopmental disorders for different reasons. The generalizability is unclear as the study was underpowered to investigate differences based on reasons for being at risk of neurodevelopmental disorders.

5 Conclusions

The overarching aim of this thesis was to develop and evaluate Internet-delivered Emotion Regulation Individual Therapy for Adolescents (IERITA) with Nonsuicidal Self-Injury (NSSI) disorder and to improve our understanding of the early correlates of self-injurious behaviors.

IERITA can be an acceptable, flexible, and credible treatment where therapist support is essential, and parents can successfully be involved. Nevertheless, additional support can be needed for those experiencing distress inherent to the online format. IERITA adjunctive to Treatment as Usual (TAU), is significantly more efficacious in reducing NSSI, emotion regulation difficulties, other self-destructive behaviors, and functional impairment compared to TAU only for adolescents with NSSI disorder. Additional trials are needed to understand the utility of IERITA across studies and samples. The mediation analysis strengthens the notion that emotion regulation can be a potential change mechanism in IERITA. For many, IERITA adjunctive to TAU can contribute to large, maintained reductions in NSSI with only a few or no NSSI episodes after treatment. Although the benefits of IERITA may outweigh the risks on a group level, adverse effects, including suicidal behavior, should be carefully monitored. IERITA can increase access to evidence-based NSSI treatment among a wide range of youth. These contributions could, by extension, innovate how we treat NSSI among adolescents.

For children at risk of neurodevelopmental disorders, detecting and treating impulsivity and inattention can be valuable to prevent self-injurious behaviors. Establishing the temporal precedence and investigating through potential pathways (e.g., emotion dysregulation) between impulsivity/inattention and NSSI/suicidal behavior are valuable further directions for optimal prevention and intervention.

6 Points of perspective

What does the future hold for the research field of adolescent Nonsuicidal Self-Injury (NSSI)? I hope the answer is “a lot” and I expect that we learn more in the following areas specifically during the upcoming years: (1) understanding the different presentations of NSSI (i.e., frequency, severity, persistence) in more detail and the impact of these; (2) how to validly categorize clinically significant NSSI; (3) the temporal associations between NSSI and biological, neurobiological, psychological, and social factors, not only through self-report; (4) treatment utility through well-designed treatment studies targeting NSSI (e.g., sufficient statistical power, balanced comparators, several clinically relevant outcomes measured, lengthy controlled follow-up). With that said, we will now focus on future directions and clinical implications of the studies in this thesis explicitly.

6.1 Replication

Replication studies are needed to become more confident of the actual effect of Internet-delivered Emotion Regulation Individual Therapy for Adolescents (IERITA). IERITA is currently being evaluated in a large-scale randomized clinical trial in Denmark (Clinical trial identifier: NCT05179655). The strengths of this study include a large sample (300 adolescents) that will be recruited from within mental health services (clinical sample – increases external validity). Almost six years after starting Study II, other treatment studies involving internet-delivered treatment for adolescent NSSI are being conducted.¹⁶¹ This development creates opportunities to compare different kinds of treatments matched on the degree of therapist contact and treatment material in the future. Since designing Study II, investigator-delivered supportive therapy has been studied as a structured control condition for self-injury among adolescents.¹⁴² Supportive therapy can represent what many receive in regular health care services, as indicated by results from Study II. These progresses within the field are helpful in establishing the efficacy of treatments and can guide decisions regarding design questions in future studies.

6.2 Stepped care

Can IERITA be a potential first-line treatment for adolescents with NSSI disorder where more or other treatment can be initiated for those in need? If IERITA is cost-effective (as is currently being evaluated), more adolescents can be treated. Consequently, more resources can be put into families with more extensive treatment needs.

Testing IERITA in a stepped-care model for NSSI could be valuable to optimize outcomes. Getting inspiration from the stepped-care model in regular care for adult depression and anxiety in the United Kingdom, Improving Access to Psychological Therapies (IAPT),¹⁶² can be helpful; hence, a first step in a stepped-care model for NSSI

can entail a thorough assessment of symptom severity and functional impairment to decide on treatment intensity. For adolescent NSSI, adding a structured *therapeutic* assessment can be advantageous as it can increase subsequent treatment engagement and global functioning.^{100,163,164} During treatment, continuous monitoring and supervision are essential to guide decisions on moving to a more high-intensive alternative.¹⁶² What the more high-intensity alternatives for adolescent NSSI can comprise is an empirical question. Examples of high-intensity steps can include extending treatment length or increasing contact,^{103,104} switching to face-to-face or video sessions after IERITA (as has been beneficial for youth with obsessive-compulsive disorder¹⁶⁵), or other treatments, such as DBT-A – an extensive evidence-based treatment for self-injury.¹⁰³ Stepped-care models have, to my best knowledge, not been tested for NSSI among adolescents or adults. However, a stepped care model for adolescents at high risk of suicide is currently under investigation,¹⁶⁶ including internet-delivered treatment. A comprehensive treatment structure to treat NSSI among adolescents could benefit patients (e.g., getting the best possible treatment based on current needs) and organizations (e.g., guidance for clinicians on what steps to take if insufficient treatment effect is needed).

6.3 Implementation

The ambition is that IERITA, given evidence of its efficacy, can constitute a low-threshold treatment for a wide range of adolescents with NSSI. To find adolescents that can benefit from IERITA, health care professionals need to screen for NSSI routinely. In addition, health care professionals need to be educated about NSSI and how to respond in helpful, non-stigmatizing ways.⁴³ One of the main benefits of internet-delivered treatment is scalability. What key steps must be taken to achieve this for IERITA? First, IERITA must be implemented on a platform that can be used within health care services, preferably nationally. To successfully implement IERITA, inspiration from the experiences of the IAPT program¹⁶² can be helpful; for instance, creating a platform with sufficiently trained IERITA therapists, central administration, and a high degree of regular supervision. In addition, safety, assessment, and evaluation procedures used in the research studies need to be applied to suit the health care structure.

Evaluating the implementation of IERITA should be prioritized, given that there is only one published large-scale randomized clinical trial. Several testable questions may arise in the implementation process, including but not limited to: Who is it reasonable to offer IERITA to – could the eligibility from the studies be modified? How many of those offered IERITA accept and adhere to treatment? What are the reasons for non-participation or low adherence? How does IERITA work in combination with different types of TAU? How can IERITA be optimized to improve treatment outcomes? What is the therapists' experience from working with IERITA – what are the challenges?

6.4 Prevention

Screening children and adolescents for impulsivity and inattention, regardless of primary reason for contact, is easily done within mental health services. If high levels of impulsivity or inattention are detected, offering interventions targeting impulse control and attentional ability can be valuable. In addition, children, or adolescents with high levels of impulsivity and inattention should be monitored concerning self-injury and associated correlates (e.g., suicidal ideation, emotion dysregulation).

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