Mapping and comparing attitudes, practices and believes of physicians who treat ADHD in Serbia, Norway and Iceland

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Abstract

Introduction – Attention deficit hyperactivity disorder (ADHD) is a common psychiatric disorder among children, often presents throughout the lifespan. Main characteristics of the disorder are pronounced and disabling levels of inattention, hyperactivity and/or impulsivity. Although the exact causes of ADHD are unknown, it is assumed that interaction between genes and environment plays the most important role in the development of the disorder. Treatment of ADHD is often multimodal with the use of both medications and behavioural therapy. Prescription rates of ADHD medications vary substantially across the world, countries, regions, even cities, leaving the room for debate about under- or over-diagnosing and over-treatment. The aim of this study is to compare attitudes, prescribing practices and believes of physicians who treat ADHD in Serbia, Norway and Iceland.

Methods – The online questionnaire was developed to cover the diagnostic process, treatment, availability and reimbursement of specific ADHD medications and awareness and attitudes towards ADHD. The link to the questionnaire was sent to targeted specialists who treat ADHD in Serbia, Norway and Iceland.

Results - Seventy-nine questionnaires were completed and analysed. Fifty two percent of the respondents from Serbia reported using behavioural therapy as a standalone treatment, which is about four times more frequent than in Norwegian and Icelandic group. Furthermore, respondents from Serbia reported on average that the variety and reimbursement of medications available had negative impact on the number of patients treated, unlike the respondents from Norway and Iceland. The results are indicating on significantly lower awareness and higher psychiatry stigma levels in Serbia compared to Norway and Iceland.

Conclusion – The differences in utilization of pharmacological and non-pharmacological treatment options were observed between groups, which can indicate different approaches in the treatment of ADHD in these three countries. Furthermore, the misperception of ADHD as non-mental illness combined with lower awareness in Serbia compared to Norway and Iceland might result in lower referral rates in Serbia compared with Norway and Iceland. However, further research is needed in order to capture effect sizes of our findings in order to draw valid conclusions.

Sammendrag

Introduksjon - ADHD er en hyppig psykiatrisk lidelse blant barn, ofte tilstede gjennom hele livet. De viktigste symptomene av ADHD er upassende nivåer av uoppmerksomhet, hyperaktivitet og / eller impulsivitet. Selv om den eksakte årsaken til ADHD er ukjent, antas det at interaksjon mellom gener og miljø spiller en viktig rolle i utvikling av sykdommen. Behandlingen av ADHD er ofte multimodal ved bruk av både medisiner og atferdsterapi. Bruk av ADHD-medisiner varierer vesentlig over hele verden, land, regioner og til og med byer, og gir rom for debatt om under- eller overdiagnostisering og overbehandling. Målet med denne studien er å sammenligne holdninger, foreskrivende praksis og oppfatninger på de som behandler ADHD i Norge, Serbia og Island.

Metoder – Et nettbasert spørreskjema ble utviklet for å dekke diagnostisering prosess, behandling, tilgjengelighet og refusjon av spesifikke ADHD medisiner og atferd mot ADHD. Lenken til spørreskjema ble sendt til utvalgte spesialister som behandler ADHD i Norge, Serbia og Island.

Resultater – Sytti ni ferdige utfylte spørreskjemaer ble akseptert og analysert. Femti to prosent av respondentene fra Serbia rapporterte bruk av atferdsterapi som en frittstående behandling, som er omtrent fire ganger hyppigere enn i de norske og islandske gruppene. Respondenter fra Serbia rapporterte i gjennomsnitt at utvalget og refusjon av tilgjengelige ADHD medisiner reduserte antall behandlede pasienter, i motsetning til respondentene fra Norge og Island. Betydelig lavere bevissthetsnivå rundt ADHD og høyere nivå av psykiatri stigma er rapportert i serbisk gruppe sammenlignet med norsk og islandsk gruppe.

Konklusjon - Forskjellene i bruk av farmakologisk og ikke-farmakologisk behandling er observert mellom grupper, som kan indikere annerledes tilnærminger i behandling av ADHD i de tre landene. Misoppfatningen av ADHD som ikke psykiatrisk lidelse kombinert med lavere bevissthet rundt sykdom rapportert i serbisk gruppe sammenlignet med norsk og islandsk gruppe peker på mye lavere antall henvisninger av ADHD pasienter i Serbia. Imidlertid er det nødvendig med ytterligere forskning for å fange effektstørrelser av våre funn for å kunne trekke konklusjoner.

Preface

This master thesis was conducted at the department of Social Pharmacy at the Faculty of Mathematics and Natural Sciences, School of Pharmacy, University of Oslo in the period of October 2017 to April 2018.

To begin with, I would like to thank my supervisor Ingunn Björnsdóttir, associate professor at the School of pharmacy, University of Oslo, for guidance and help provided during my research.

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Djordje Zdravković

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Abbreviations

ADHD - Attention deficit hyperactivity disorder

BUP- Barne og Ungdom Psykiatri – Child and Adolescent psychiatry

CD - Conduct disorder

DA – Dopamine

DDD - Defined Daily Doses

DMN - Default Mode Network

DSM-5 - American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders

ICD -10 - The International Classification of Mental and Behavioural Disorders 10th revision.

ICD -11 - The International Classification of Mental and Behavioural Disorders 11th revision

MRI – Magnetic Resonance Imaging

NE – Norepinephrine

NICE – National Institute for Health and Care Excellence

NNF – Norsk Nevrologisk Forening – Norwegian Neurological Association

NPF – Norsk Psykiatri forening – Norwegian Psychiatric Association

ODD - Oppositional defiant disorder

PET – Positron Emitting Tomography

RZZO – Republicki Zavod za Zdravstveno Osiguranje -National Health Insurance Institution

SUD – Substance Use Disorder

WHO – World Health Organization

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1 Introduction

1.1 Definition of ADHD

Attention-deficit/hyperactivity disorder (ADHD) or Hyperkinetic disorder (HKD) is a neurodevelopmental disorder with long-term impacts on functioning, productivity and quality of life [1]. The disorder describes children, adolescents and adults with inattentiveness, overactivity and/or impulsivity [2].

The reason for existence of two different acronyms, ADHD and HKD, lies in the fact that there are two classification systems of mental disorders in use [3]. Although these two entities are very similar, they have small but distinct differences. The International Statistical Classification of Diseases (ICD), the 10th revision, issued by the World Health Organization in 1992 defines HKD [4]. Nevertheless, in the United States of America (USA), parallel classification for mental disorders exists, the Diagnostic and Statistical Manual of Mental Disorders (DSM); the latest fifth edition (DSM-5) issued in 2013, defines ADHD [5]. However, the next edition of the ICD, ICD – 11, which is to be published this year, recognizes the disorder in the same way as the DSM-5 [6]. Thus, in the rest of the text, it will be used the term ADHD to represent both conceptualizations, if not otherwise stated.

The cause of ADHD/HKD is not clearly established; many different factors were researched and suspected to be the cause of the disorder. The treatment is multidisciplinary; there is several different approaches, including medical, neuropsychological, educational and other disciplines [2].

1.2 History of ADHD

Under many different names, ADHD has been recognized and treated for longer than a century. Sir Alexander Crichton had described an example of the disorder in 1798 in his book "*On Attention and its Diseases*", which appears to be similar to ADHD [7]. The first concept introduced was a "*Brain Damage Syndrome*", which emphasized an organic brain damage. The illness had started a journey through many different explanations and names, such as post-encephalitic behaviour disorder (1922), proceeding to the brain-injured child (1947), the perceptually handicapped child (1963) and ending with minimal brain dysfunction (1966) [3].

In 1960s, there were intentions to abandon the brain damage concept and to create a more scientific and reliable classification, thus emphasis turned to its symptoms. Both the ICD-9 and DSM-II included the syndrome in their classification system as *hyperactive child syndrome*.

Table 1. ADHD evolution through ICD and DSM classification systems, adapted from [5, 6, 8]

DSM		ICD	
DSM II (1968)	Hyperkinetic reaction of childhood or adolescence	ICD-8 (1965)	Behaviour disorders in childhood
DSM III (1980)	ADD-Attention deficit disorder with hyperactivity and ADD without hyperactivity	ICD-9 (1977)	Hyperkinetic syndrome of childhood
DSM IV (1994)	3 subtypes ADHD-inattentive, ADHD hyperactive-impulsive, ADHD combined	ICD-10 (1992)	Hyperkinetic disorder
DSM -5 (2013)	3 subtypes ADHD but criteria have slightly changed compared to the DSM-IV	ICD-11 (2018)	Attention deficit hyperactivity disorder equal to DSM -5

Medications are an important part of ADHD treatment almost over the century. The first medical treatment for ADHD was described in 1937, when Charles Bradley was treating hyperactive behaviour in children with Benzedrine, racemic mixture of amphetamine [7]. Methylphenidate was first synthesized in 1944, by Leandro Panizzon, while soon after controlled trials showed a reduction of ADHD symptoms and the benefits were much greater than the side effects [9].

1.3 The causes of ADHD

The causes of ADHD are mostly unknown or idiopathic. In certain cases, ADHD can be a consequence of a brain structural abnormality, trauma or encephalitis [2]. There is no single factor that explains ADHD. Both inherited and external factors influence the outcome and development of the disorder, while their effects dependent on each other [10].

1.3.1 Genetics

It is widely known that ADHD runs in families. It is estimated that the heritability of ADHD is about 80% based on twin data studies [11]. Genetic factors may involve many genes, such as the dopamine receptor and transporter genes, but the gene-environment interaction is of greater importance in the aetiology [2, 12]. Based on studies that involved adopted children with ADHD, researchers have found that adoptive relatives were less likely to have ADHD, than the biological ones, which confirms a high hereditary rates of ADHD [13]. The strongest evidence exist for association between ADHD and a dopamine receptor D4 gene and a dopamine receptor D5 gene. However, there are evidence of involvement of other genes, such as dopamine transporter gene and catechol-O-methyl transferase [14].

1.3.2 Environmental factors

Environmental factors can occur prenatally, in the perinatal period, or postnatally. Some proposed ADHD environmental risk factors include prenatal substance exposures, heavy metal and chemical exposures, infections, nutritional factors and psychosocial factors [15]. The eventual confirmation of environmental factors in the aetiology of ADHD could lead to improved outcome of disorder [2].

Biological and psychosocial environments have been extensively studied as potential risk for ADHD. Several factors have been associated with the ADHD, but none has been proven to be a necessary and sufficient cause of the ADHD [11]. Prenatal exposure factors that have been extensively researched are tobacco, alcohol, antihypertensives and antidepressants. Nevertheless, none of the studies could not conclusively implicate them as ADHD risk factors [15].

Toxins, such as lead, mercury and manganese, have been suspected in the aetiology of ADHD. Hyperactivity, restlessness and lower intellectual functioning, caused by lead contamination are similar to the disease profile in ADHD. The developmental neurotoxicity of manganese has emerged as a significant public health concern in recent times [16].

The idea that certain food additives might cause ADHD came after a crossover trial in England, where was found that certain food colour-additives and preservatives were associated with more severe symptoms of ADHD in children [15]. Systematic studies, however, did not

show that the additive-restricted diet had any effect [11]. Additional evidence have emerged for low zinc and omega-3 fatty acid levels as a risk factors for ADHD [17].

Many studies have provided evidence for the importance of psychosocial adversity for ADHD. Nevertheless, they are not predictors that are specific to ADHD. They can be just described as unspecific triggers of any present predisposition [11]. Psychosocial causes, such as low social class, family conflicts and many others, must be observed with caution, because they can be consequences of the same genes that cause ADHD, just as likely to be the causes of the disorder [11].

1.4 Pathophysiology of ADHD

A few theoretical models tried to describe the neural bases of ADHD. They have focused on neurocognitive abnormalities which are leading the research of ADHD pathophysiology [18].

Executive dysfunction model

The executive dysfunction model holds that the executive function deficits are in the centre of ADHD [18]. Executive functions are cognitive processes, such as executive attention, planning, organization, response inhibition, working memory and others that bring behaviour under control [19]. It is known that fronto-striatal and subthalamic circuits are in associations with these functions [20]. These deficits are documented in children as well in adults with ADHD [21, 22]. Executive functions deficits that has the strongest association with ADHD are poor response inhibition, working memory and planning [23].

Motivational and reward-processing disruption model

Motivation and reward processing abnormalities are in the focus of another approach to describe the underlying cause of ADHD [22]. It was developed as a result from a dysfunction of the mesolimbic dopamine system [24]. This model thus predicts a disruption in dopaminergic signalling [18].

Many studies have shown differences in parts of brain that lie far away from the circuits that are described by these models [25]. The single-substrate models did not manage to explain ADHD sufficiently. Therefore, there is a tendency to expand standard frameworks to include other circuits [18].

Dual-pathway model

The combination of executive dysfunction and motivational/reward-processing models exists, so called dual-pathway model that is able to describe different subtypes of ADHD. Fronto–striato–thalamic dysfunction is responsible for inattention, while hyperactivity and impulsivity are attributed to mesolimbic dysfunction in this model [26].

Brain structure and function

It is proven that people with ADHD has some brain structure differences in comparison to healthy subjects, for example smaller total brain volumes, especially in the right hemisphere [18]. These differences are seen both in the grey and white matter, and as regional volumetric reductions [27, 28]. Regional volumetric differences between patients and controls were seen most pronounced in the right caudate nucleus, frontal and prefrontal regions and cerebellar regions [29]. Children with ADHD have delayed development of the cerebral cortex that follows the same regional development as in normal developing child, but it seems to be much slower [30]. Functional imaging studies of the brain have showed that there is significant association between ADHD and reduced activity in the anterior cingulate cortex, parts of prefrontal cortex, basal ganglia, thalamus, reduced activation of the cerebellum, ventral striatum and altered amygdala activity [18, 31].

Structural & functional connectivity

There is a growing body of evidence showing that structural connectivity abnormalities in subjects with ADHD, such as decreased structural integrity across multiple white matter tracts [18]. A few networks were discovered that could be implicated in ADHD pathophysiology, such as the Default Mode Network (DMN) [32]. The DMN is activated while resting or wandering, or task-irrelevant activity, but suppressed during cognitive tasks in healthy subjects, thus the lack of suppressing of this network while doing some tasks could result in errors and attention difficulties [32, 33].

Neurotransmitters

This theoretical framework is based on catecholamine release impairment; suggesting that ADHD is associated with functional impairments in some of the brain's neurotransmitter systems, especially those involving dopamine and norepinephrine [34]. Neurocognitive functions, such as initiation of motor activity, sensitivity to rewards, goal-directed behaviour, executive functions, working memory and attention, are being influenced by catecholamines [18, 35]. The indirect body of evidence from studies has shown a significant role of dysfunction in catecholamine, particularly in the dopamine neurotransmission of ADHD [18]. The most powerful evidence of dopamine involvement in ADHD comes from the fact that stimulants, which improve symptoms of ADHD, are working by potentiating dopamine transmission [36].

1.5 Diagnostic systems and criteria

The most currently used criteria for the diagnosis of ADHD in both children and adults are provided in DSM-5 [5] and ICD-10 [4]. The DSM-5 classification is published by the American Psychiatric Association, and is widely used in northern America, while the ICD-10 is a published by the World Health Organization and is being used in Europe and other countries.

In Serbia, the ICD-10 diagnostic system is used exclusively, while in Iceland and Norway physicians use both classification systems, DSM-5 and ICD-10 [37-39].

Although, the DSM-5 and ICD-10 describe the same symptoms of inattentiveness, hyperactivity and impulsivity, ICD-10 requires presence of all three symptoms to make diagnose [40]. Other differences lie in quite strict exclusion criteria present in the ICD-10, while other coexisting psychiatric disorders are allowed under the DSM-5 [5]. The diagnosis of hyperkinetic disorder (ICD-10) is not made when criteria for certain other disorders, including anxiety disorders, mood disorders, schizophrenia and pervasive developmental disorder are met [4]. Therefore, HKD (ICD-10) can be observed as a severe form of combined ADHD type (DSM-5) [41].

Considering arrival of the ICD – 11 with the definition of Attention deficit hyperactivity disorder equal to that of the DSM-5, ICD-10 and HKD will be outdated [6].

1.6 Comorbidities

Conduct and oppositional defiant disorder

ADHD is often comorbid with conduct disorder and oppositional defiant disorder [42]. Oppositional defiant disorder characterizes a pattern of angry/irritable mood, argumentative/defiant behavior, or vindictiveness [5]. Conduct disorder represents more severe condition in a form a repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated [5]. All these problems can be seen in some children with ADHD, but they are not essential features of ADHD [41]. ODD symptomatology is more frequent in combined presentation of ADHD than inattentive type, while CD symptomatology co-occurs with 25% in combined type [5].There is evidence that children with ADHD comorbid behaviour problems tend to be more resistant to treatment [43].

Mood and anxiety disorders

Mood disorders, such as major depressive disorder, dysthymia and bipolar disorder, can be present in children with ADHD. Both mood disorders and anxiety disorders are observed in children with ADHD more than in general population [5]. It estimates that up to 50% children with ADHD can have mood disorders, and up to 30% anxiety disorders [42].

Substance use disorder

Substance use disorder are more frequent in adults with ADHD than in general population. Although independent effect of ADHD on substance misuse is evident, it can be also explained with comorbid CD [42].

Other comorbid disorders include among others: obsessive-compulsive disorder, tic disorders, and autism spectrum disorder [5].

1.7 Epidemiology of ADHD

Worldwide prevalence

Despite ADHD is a prevalent neurodevelopmental disorder, the prevalence information about its distribution by race, gender, age, and socio-economic status are still not well described. Complexity around the diagnostic process of ADHD might lead to differences in designing and setting of epidemiologic studies. There is no single reliable test for ADHD and the diagnosis is dependent mainly on parent and teachers' estimations [44], or patients' own reporting of symptoms in case of adult ADHD. ADHD prevalence is estimated to be around 5%, according to large systematic review of studies published in the period of 27 years [45].

Children and adolescents

ADHD has prevalence in the school age population at about 3-5 percent, but varies from 4 - 19 percent, the exact finding depends mainly on cut-off criteria applied and source of sample [46]. HKD, defined by ICD-10 criteria comes with a rate around 1 to 2 per cent of the school age population.

Adults

The rates of ADHD among adults decline with age in the general population. The prevalence of adult ADHD is estimated to be around 2 to 4% [47]. However, the questionable validity of DSM–V/ICD-10 diagnostic criteria for adult ADHD can lead to underestimated prevalence rates [48].

Male to female ratio

Male to female ratio differs from 9:1, in clinic-referred samples, to 2:1, in community-based samples. One explanation could be that boys are more likely to be referred to a psychiatric treatment than girls, due to predominant hyperactive type of ADHD, more prevalent aggression, and more frequent comorbidity [5]. However, the trend in more recent studies narrows the gap between the genders [49] and the new numbers on the prevalence ratio between males and females are 2:1 in children, and even 1.6:1 in adults [5]. Concerns have been raised that only girls with substantial impairments are referred to clinics [50].

1.8 Therapy of ADHD

1.8.1 Pharmacological treatment options

Stimulants

For decades, stimulants have been the most common medications used in the treatment of ADHD [51]. Stimulants include methylphenidate and amphetamine compounds: racemic amphetamine, dexamphetamine and lisdexamphetamine [52]. Both methylphenidate and amphetamine are structural similar to monoamine neurotransmitters dopamine and noradrenaline [53]. The first stimulant ever synthetized is amphetamine and it belongs to the class of β-phenylethylamines. At the time of amphetamine discovery, neurotransmitters were unknown, so the ratio behind was structural similarity to ephedrine, known biologically active substance [53].

Mechanism of action

The main effect of stimulants is increasing noradrenergic and dopaminergic neurotransmission in the brain, by increasing synaptic concentrations of dopamine and noradrenaline. However, the exact mechanism of action is not clearly understood, although believed that there is the blockage of norepinephrine and dopamine reuptake, which leads to greater concentrations of these two monoamines in the synaptic cleft [52]. In addition, amphetamine exerts effect of releasing dopamine from presynaptic storage vesicles and blocking dopamine uptake into cytoplasmic vesicles, thus leading to an increase in available dopamine in the presynaptic neuron [54].

Efficacy of stimulants

Stimulant medications are the medications of choice in ADHD treatment [55]. The effectiveness of stimulants is significantly greater than effectiveness of other medications [56]. ADHD symptoms such as, poor attention span, distractibility, impulsive behaviour and hyperactivity are being effectively reduced by stimulant medications [52]. They improve prefrontal cortex cognitive functions, both in healthy individuals and ADHD patients [52]. In addition, there is evidence that stimulants are associated with fewer errors on a driving simulator in teens and adults with ADHD [57].

Amphetamines are equally effective as methylphenidate in the treatment of ADHD [56]. However, there are some evidence showing slightly greater efficacy in the favour of amphetamine [51]. There is superior efficacy of amphetamine in ADHD treatment compared to non-stimulant atomoxetine is confirmed in several trials [58]. Amphetamine increases levels of serotonin, which although has no effect on ADHD, can be beneficial in comorbid depression and anxiety disorders [53].

Although effectiveness of both methylphenidate and amphetamine in patients with ADHD are presumed to be similar, effects of these two drugs can be significantly different [59]. While about two thirds of ADHD patients have significant improvement of symptoms as a response to a single stimulant, the percentage of responders may be up to 95%, if the other stimulant is introduced after the failure of the first [60, 61].

Choice of stimulant formulation

The elimination half-life of methylphenidate is about 3 hours, while for amphetamine is approximately 7 hours [62, 63]. Thus, usual dosing regimen for immediate release formulations of these drugs is two to three times a day [59]. It can be inconvenient, especially for children and adolescents. It can lead to several types of concerns, such as: storing and administering in school, diversion of drug and adherence problems [59]. To address such concerns, several modified-release formulations have been introduced. As a result, these formulations have changed the pharmacokinetic profile of the drugs and enabled effective once-daily dosing [64]. However, modified release formulations can be associated with certain levels of pharmacokinetic variability [64, 65]. Lisdexamphetamine, that represents only stimulant pro-drug, could be a solution for limitations of existing forms [66].

Adverse effects

Adverse effects such as anorexia, weight loss and insomnia are frequent [53]. Other adverse effects include nausea, headache, increased blood pressure, elevated pulse, abdominal pain, irritability and mood lability [52]. There could be tics worsening sometimes and among other rare adverse effects can be seizures, psychosis, hepatotoxicity and growth retardation [52].

Potential abuse

The stimulants abuse can be described either as excessive use of prescribed drug or misuse of the prescription by others, so called diversion [53]. On the other hand, there isn’t a lot of abuse

by patients with ADHD [67], in fact, it can be challenging for some physicians to keep the patients on the medications. Amphetamines were extensively abused, after the World War II, where they have been widely used to promote wakefulness. Huge quantities of medicine stocks got into the 'black market', and became available for abuse. This could have alarmed about potential dangers and abuse potential, and may have moved prescribers away from amphetamine to methylphenidate, as a safer drug [53]. While methylphenidate products dominate in Europe, amphetamine products have almost 50% share in the USA [68].

Atomoxetine

Atomoxetine is a non-stimulant medicine that is working through selective blockage of nor-epinephrine reuptake mechanism [69]. The supposed mechanism suggests that NE reuptake inhibition leads to increase levels of NE in neural synapses, which causes activation of synaptic α2 receptors [70]. Atomoxetine has also affinity for other brain receptors, but it is unknown whether this has some implications on ADHD [71, 72].

The efficacy of atomoxetine in the treatment of ADHD is proven trough many randomized clinical trials and a decade of presence on the market [73]. Atomoxetine has an effect delay of about four weeks, but it is described in some cases to work even after one week [74, 75]. Pharmacokinetics of atomoxetine allows one daily dosing regimen [76]. Newer studies have shown that effect increases with time, particularly after 12 weeks, when the full effect is present [77]. Many studies have shown inferiority of atomoxetine effect when comparing to stimulants, but that might be explained due to delayed onset of action [73].

Atomoxetine is not a scheduled substance and it lacks abuse potential and it can be particularly suitable in suspected comorbid substance abuse disorder [78].

Atomoxetine has shown acceptable safety profile across all patient ages, while the most frequent adverse effects are decreased appetite, nausea, dizziness, insomnia and fatigue. Suicidal ideation has been added later as a potential risk [70, 78].

Alpha-2 adrenergic agonists

There are two different compounds used in ADHD that belong to a class of α-2 adrenergic agonists, clonidine and guanfacine. Clonidine is an old antihypertensive agent that has been in use since 1966, while guanfacine is a relatively novel compound [79]. They both work through activation of α2 norepinephrine receptors, while guanfacine is highly selective for specific type of receptor- α-2A [55].

On the different markets, one may find both immediate release and extended release forms of both guanfacine and clonidine. Although, immediate release forms are not improved for the treatment of ADHD, off label use is not so uncommon throughout the world [55].

Both immediate release and extended release forms has been shown to improve symptoms of ADHD alone, or in combination with stimulants [80, 81]. Because of frequent dosing regimen, extended release forms are developed and preferred option [55]. Recommended dosage is once daily with or without stimulant medications. This group of medications has less effect on ADHD symptoms than stimulant medications, thus not considered as the first line treatment [55]. The α-2 agonists should be used in absence of effect of other medications, or in some cases of comorbidities [82, 83].

Adverse effects of α-2 agonists are usually mild. However, they have antihypertensive properties, thus cardiovascular monitoring is required, as also gradually discontinuation to prevent withdrawal hypertension [55]. Sedation can be present, especially in introducing faze of treatment, while guanfacine tends to be less sedating. Other common adverse effects include abdominal pain, sedation, headache, fatigue, headache, dry mouth, etc. [55].

Other medications in treatment of ADHD

Bupropion

Bupropion is used as off-label treatment of ADHD in many countries. Bupropion is developed as antidepressant, acting selective norepinephrine/dopamine reuptake inhibitor [84]. Because of mechanism of action, it is considered as an atypical antidepressant. While it was developed as antidepressant, it has another indication as smoking cessation treatment. It is believed that noncompetitive antagonism of acetylcholine-receptor is responsible for smoking cessation effect [85]. Evidence that supporting efficacy of bupropion in ADHD are inconsistent, while effect sizes are significantly smaller than seen in stimulant medications [55, 86]. Some studies has shown effectiveness of bupropion in comorbid substance abuse. It is not regarded as the first line therapy and according to guidelines used in the USA, it is listed as 4^{th} line in treatment of ADHD [87]. It can be seen as a reserve option, if both stimulant medications and atomoxetine are not effective or tolerable, or in comorbid SUD. It has onset of action in usually 14 days [55].

Special precaution is needed due to dose-related lowering threshold for seizure. Hence, bupropion is contraindicated in patients with history of seizures. It is usually well tolerated, while common adverse effects are headache, dry mouth, nausea and insomnia [88].

Modafinil

Modafinil is also a drug that is used off-label in treatment of ADHD. This novel drug, at present, has approved indication in narcolepsy. The mechanism of action is not clearly described, while showing some effects on histamine, norepinephrine, serotonin, dopamine and orexin transmission in the brain [84]. The response rates of modafinil seen in some trials on children with ADHD, are going up to 80% [89]. It alleviates symptoms of ADHD in children and adolescents regardless former exposure to stimulant medications [55]. The most common adverse effect of modafinil is headache, while insomnia and decreased appetite are often present [90].

Antipsychotics

Atypical antipsychotics are used very often in psychiatry, but they do not have approved indication in ADHD, mostly due to limited evidence supporting the efficacy and safety in [91]. However, atypical antipsychotics have been used off-label in the treatment of ADHD in many years [92]. Off-Label proscribing is typical in cases of therapeutic failure of conventional therapy or unavailability of approved treatments [93].

Research conducted in the USA, reveals that atypical antipsychotics are used 66% off-label in paediatric patients. ADHD was found to be the most frequent primary diagnosis in this population [92]. While there is some evidence that atypical antipsychotics can be effective in treatment of ADHD comorbid with aggression or disruptive behaviour, they should be used with caution as a reserve option [94]. In case of failure of standard treatment, risperidone can be the most promising and the least harmful alternative [95]. Other studies have shown effectiveness of aripiprazole in ADHD, but further research is needed [96].

There has been a significant increase in concomitant use of atypical antipsychotics and stimulant medications in the treatment of ADHD [97]. More than 50% of children on stimulant therapy received concomitant antipsychotics in some point of treatment [98]. Stimulant medications and antipsychotics act through opposing mechanisms on dopamine, by increasing the dopamine in the synaptic cleft, and by blocking the effect of dopamine, respectively. Concomitant use of these medications created a dilemma, while explanations through different receptor subtypes, and different pathways exist [97].

There are significant and potentially life-treating adverse effects of antipsychotics and limited evidence of effectiveness make this group a last resort in the treatment of ADHD [99].

1.8.2 Non-pharmacological treatment

Although there is a large number of different non-pharmacological options available in the treatment of ADHD, few options has shown significant effects [3]. On the other hand, there is a substantial room for use of these techniques. The use of medications can be regarded as more effective in some cases, but substantial rates of adverse effects can lead to ethical dilemmas in younger children [100]. Efficacy and choice of techniques depends on the symptoms and age of the patient [101]. For younger patients focus is on training of parents and teachers, while with age focus is shifting to patients themselves. Parent training and classroom interventions are for preschool, schoolchildren, and young adolescents, while for older adolescents and adults treatment of choice would be CBT and social skills training. Behavioural parenting interventions, social skills training and cognitive behavioural therapy are recommended as treatment options in the UK [102].

Parent-training programs could be beneficial in the ADHD treatment in preschool children. They are recommended as a first-line treatment in preschool children in the UK [88]. Such programs are designed to educate parents to be ready and competent to deal with behavioural problems of their offspring [101].

Both **group parent training** and **classroom interventions** can improve symptom control in children with ADHD, as add-on therapy with stimulant medication. However, the evidence that supports behavioural therapy alone are not so conclusive; these approaches are limited to children with low to moderate symptom severity [101].

Variety of other non-pharmacological options for school children include:

- Child-centred academic interventions
- Cognitive behavioural therapy
- Social skills training
- Multimodal treatments

Cognitive behavioural therapy (CBT) and **social skills training** are options for adolescent without severe impairments and are recommended by the NICE guidelines. Other nonpharmacological options include:

- Classroom based interventions
- Academic interventions
- Multimodal approach [101]

Cognitive behavioural therapy could offer the most suitable approach to adult ADHD [101]. While it had strong foundations in other psychiatric conditions that are often comorbid with ADHD, there is not many good quality trials about efficacy in ADHD [103]. The NICE recommendations for first line treatment in adult ADHD differ from younger patients, and put the medications on the first place [88]. Non-pharmacological treatment is available for those who do not wish to take medications [101].

1.9 ADHD in Norway, Iceland and Serbia

Guidelines, medications available, reimbursement

Norway

In Norway, ADHD diagnosis and treatment relies on national guidelines [104]. General practitioners are the primary level of healthcare for both children and adults with ADHD and are responsible for screening and referring suspected ADHD patients to specialized healthcare institutions. Educational psychology services in schools are important source of information for paediatric patients.

The final diagnosis as well as medical treatment can be introduced only by physician specialist in child psychiatry, paediatrician, psychiatrist or neurologist. There is more than 2800 of these specialists in total (appendix 19). The official classification system used in Norway is the ICD-10, but it is allowed to use the DSM-5 as well [104].

Medications registered in Norway for ADHD treatment are presented in Table 2.

Table 2. Medications available for ADHD treatment in Norway, adapted from Norwegian medication registry - Felleskatalogen [105]

INN	Reimbursement conditions
methylphenidate immediate release	reimbursed for children (6-17 years old)[1]
methylphenidate sustained release	reimbursed for both children and adults
dexamphetamine	reimbursed for children (6-17 years old)[1,2]
lisdexamphetamine	reimbursed for children (6-17 years old)[1,2]
atomoxetine	reimbursed for children (6-17 years old)[1,2]
guanfacine	special approval for reimburement
1-need special approval for reimbursement in adults	
2-in case methylphenidate therapy failure	

Iceland

The ADHD diagnosis and treatment in Iceland relies on national guidelines and the NICE guidelines [39]. Both the DSM-5 and ICD-10 classification systems are in use. The diagnosis and treatment of ADHD in children are in hands of multidisciplinary teams of psychological and medical professionals specialized in ADHD. ADHD suspected paediatric patients are first referred to school specialist services for primary assessment and if necessary to secondary/tertiary services for further assessment. The Centre for Child Development and Behaviour is responsible for differential in-depth assessment conducted by a multidisciplinary team according to clinical guidelines, while the most severe cases are referred to The State Child Psychiatric Unit- BUGL [39].

Medications registered in Iceland for ADHD treatment are presented in a table 3:

Table 3. Medications available for ADHD treatment in Iceland, adapted from Icelandic Health Insurance [106]

INN	**Reimbursement conditions**
methylphenidate immediate release	reimbursed [1]
methylphenidate sustained release	reimbursed [1]
amphetamine	reimbursed [1,2]
dexamphetamine	reimbursed [1,2]
atomoxetine	reimbursed [1,2]
guanfacine	not reimbursed
modafinil	reimbursed [1,3]
1- presription from specialist	
2-in case methylphenidate therapy failure	
3-in case of therapy failure of both methylphenidate and atomoxetine	

In order to get reimbursement for ADHD medications specialist have to diagnose ADHD and apply for reimbursement that is valid for period of 18 months [106].

Serbia

There are no official guidelines for the diagnosis and treatment of ADHD in Serbia. The classification system in official use is the ICD-10. Paediatricians from primary care institutions, who are primary level of the child healthcare in Serbia, refer patients with ADHD suspicion to specialist health care institutions for further assessment and diagnosing of ADHD. The diagnosis is given only by a child psychiatrist or psychiatrist working with children and adolescents.

Only medication registered for the treatment of ADHD in Serbia is sustained release methylphenidate - Concerta® [107].

The National Health Insurance Fund regulates that only child psychiatrist or psychiatrist/neurologist, who is involved in treatment of children and youth or child neurologist or paediatrician with specialization in development neurology or psychiatry from six tertiary institutions, can prescribe methylphenidate [107]. According to the meeting of child and adolescent psychiatrist from 2017, there is 25 specialist who are entitled to prescribe Concerta®, which is reimbursed [108].

Main differences

Some of the key differences observed between countries are availability and reimbursement of ADHD treatment. That applies for both medications and non-pharmacological treatment options. While there is a number of different medications available in both Iceland and Norway, methylphenidate sustained release is only registered pharmacological option in Serbia. Hence, Serbian authorities do not recognize adult ADHD, thus Concerta® has only paediatric indication and reimbursement. Both Iceland and Norway have their national guidelines unlike Serbia. If we compare the sizes and levels of healthcare around ADHD, Serbia has the fewest physicians who are entitled to diagnose and to treat ADHD. Hence, the minimum level of care required for ADHD diagnosing/treatment in Serbia is tertiary.

Pharmacoepidemiology in Norway, Serbia and Iceland

A number of ADHD patients receiving medical treatment has increased 2-7 fold in Nordic countries from 2004 to 2014. Norway had an increase of 2.2 fold in this period. While the consumption of ADHD medications, DDD/1000 citizens /day, in Nordic countries had risen 3-13 fold. Both, Norway and Iceland had an increase of over 3 fold, while Iceland has a highest consumption of ADHD medications in Nordic countries (DDD/1000 inhabitants), almost 3 times higher than in Norway [109]. International narcotics control board issued a warning to the Icelandic government in 2011, raising concerns about high consumption of stimulants that is comparable high as in the USA [110].

The prevalence of ADHD and number of patients treated in Serbia is not known. A recent clinic-based study showed that the prevalence rate is about 7% and incidence rate of about 4% in children, adolescents and young adult age. Consumption of Concerta® has risen seven fold in the period from 2007 to 2013 [111]. Nevertheless, consumption of ADHD medications (Concerta®) in Serbia was 0.035 DDD/1000 inhabitants/day, which is nearly 200 times lower than in Norway and 600 times lower than in Iceland in the year of 2013 [109, 111]. Due to high utilization of non-pharmacological treatment options in Serbia [111], it is hard to estimate a real number of patients and prevalence of ADHD based exclusively on Concerta® sales data.

Concerns regarding the prevalence

There are a few different concerns about prevalence estimates of ADHD. There is higher estimates for Western societies, highest in the USA [112]. There is significant increase in rates of ADHD treated patients in the world over time, especially in the USA and some Western European countries [68, 112]. On the other hand, there are countries as France and Italy reporting incidence of ADHD medications use of 0.2% and 0.02 % by their paediatric population respective. Over-diagnosing or under-diagnosing of ADHD are controversial and debated, mainly because of increase in number of patients diagnosed, increase in ADHD medications consumption and changing diagnostic criteria [113, 114].

Prescribers' objectivity/subjectivity impacts mental health diagnosis and prescription rates, leading to different incidence of medications used. Differences can be observable on country level, regional level and even on a city level. Classifications mild, moderate, and severe

ADHD are rather academic than practical, leading to the uncertainty of indications, difficulties in setting cut-off criteria for prescriptions [114, 115].

Policies, regulations and accesses to mental health services affect prescription rates and consequently consumption of ADHD medications. As described, there are some mayor differences between Norway, Serbia and Iceland regarding available medications, reimbursement system and access to healthcare services.

A commercial influence is not to be underestimated. Pharmaceutical companies interact with policy makers, advisory boards and prescribers [116]. Majority of Work group advisers of DSM-5 for ADHD have disclosed links to pharmaceutical companies as a potential financial conflict of interest. However, transparency does not exclude possibility for bias regarding changes to ADHD criteria. Hence, pharmaceutical companies are raising awareness by reaching the public through mental health websites, non-government organizations, as well as through educational and professional networks. Public awareness is largely involved in increase of ADHD rates [117].

Social, cultural and economic influences on ADHD

The diagnosing process is circumstantial, depending on interpretations of those who observed the symptoms (teachers, parents and physicians), thus making the cultural influence on diagnosing and treatment of the disorder even greater [118].

Something that is normal parenting in one country can be seen as extreme in another. Different cultures have different expectations of normal conduct and activity levels. Hence, the same behaviours could be seen as impairing in one culture, but normal in another [118]. Furthermore, stigma can be accounted for difficulties in recognition, detection and treatment of ADHD, enforced with scheduled status of ADHD medications. Other cultures are more prone to seek medical assistance than others are. Knowledge and beliefs about the disorder can lead to differences in distribution of both diagnosing and treatment [119]. Perception of misuse of ADHD medication in adolescents, possible adverse effects and attitudes toward medications can lead to different prescription rates and different ratio between non-pharmacological /pharmacological treatment utilization [114].

However, the economy could be the major factor influencing the diagnosing and treatment of the disorder, since countries' economies are known predictors of medical spending.

The rates of ADHD medications used are in correlation to GDP per capita [120]. Higher needs than provisions of mental health services are present everywhere, but the gap is larger in poor economies and developing countries; thus, predicting lower rates of ADHD treatment [121].

1.10 Aim of the study

The aim of this study is to map and compare practices, attitudes and believes of those who prescribe ADHD medications in Serbia, Norway and Iceland. The study is focused on four different segments related to ADHD:

- Diagnosing,
- Treatment,
- Medications availability/Reimbursement and
- Attitudes and awareness.

2 Materials and methods

2.1 Materials

The data was obtained from 79 completed questionnaires from Serbian, Norwegian and Icelandic respondents. The number of responses collected was 81, but two questionnaires were excluded because respondents have stated that they did not have ADHD patients at all, that left us with 79 valid questionnaires that were analyzed. Since the purpose of this thesis was to compare countries between each other, all data has been divided into groups by country. Norwegian group had 37 respondents, Serbian group had 19 respondents and Icelandic group had 23 respondents.

2.2 Research design

This study is an online survey, which has quantitative descriptive design. The method of data collection in this study is developed questionnaire.

2.2.1 The questionnaire

The questionnaire was developed by the candidate in consultations with both supervisors (Appendix 22). The development of questionnaire was govern by the theory-driven approach based on the literature review on the topic [122]. It is based on previous studies about prescribing practices within psychiatry, as well as own and experts' experiences with this topic. The questionnaire has been reviewed by experts in order to check content validity, as well as wording and cognitive perception of questions. For such purposes, the questionnaire was sent to experts within medicine and psychiatry, but also within sociology. The experts involved in testing, were not included in research. The questionnaire is composed of combination of multiple choice, Likert like, and open-ended questions. The questionnaire was designed to cover the following areas:

1. ADHD diagnosis,
2. Treatment,
3. Availability and reimbursement of medications and
4. Attitudes and awareness

In order to avoid translation errors and bias, we have used English language under assumption that all physicians can be expected to understand it. The study used Surveymonkey portal as online platform for the questionnaire.

2.2.2 Project approval

After drafting and selecting the questions that would be used, the questionnaire was submitted to NSD- Norwegian centre for research data on the 13th of October 2017, in order to get approval for our project. The approval has been granted on the 8th of November 2017. The Approval as well as informational sheet that we used to inform and invite potential respondents to participate in research are attached in Appendix 23 and 24, respectively.

2.3 Recruitment and population targeted in the study

Respondents were chosen by specialisation and the field of work. Only physicians who are directly involved in the diagnosis and treatment of ADHD were selected. We used a variety of approaches to deliver the questionnaires, sending the survey link by email direct to email addresses of respondents or using the physicians associations and/or hospitals as intermediaries.

2.3.1 Recruitment in Serbia

The right to prescribe Concerta®, as the only registered medication in Serbia for children and adolescents until the age of 18 years, poses just a small group of physicians specialized in child psychiatry or psychiatrists who are working in six tertiary institutions chosen by the Serbian government (see above). After this age, ADHD patients have to pay on their own for the treatment with Concerta®. We included adult psychiatrists in this research working in other institutions in order to uncover what kind of treatment get adult ADHD patients in Serbia, since there are no registered treatments for this population in Serbia. All Serbian physicians were contacted directly by email, using a mailing list of all registered child psychiatrist/psychiatrists as provided by the external supervisor.

2.3.2 Recruitment in Norway

The guidelines and prescribing rules in Norway give prescribing rights of ADHD medications to a broader group of physicians. Paediatricians, child and adolescent psychiatrists, neurologists and psychiatrists have right to independently prescribe ADHD medications to children, adolescents and adults. Although, we tried to reach prescribers through Norwegian Psychiatric Association (NPF), Child and Adolescent Psychiatric Association (BUP) and Norwegian Neurological Associations (NNF), there were almost no responses. Therefore, we have contacted a number of psychiatric hospitals that belong to all four Regional Health Authorities, and forwarded the questionnaire to the target population.

2.3.3 Recruitment in Iceland

In Iceland, we have approached Icelandic ADHD organization which helped us to establish good contact with the Icelandic Psychiatric Association, which was our further link to respondents on Iceland. At the same time, we contacted The Centre for Child Development and Behaviour in Iceland and managed to reach a few paediatric prescribers. However, we were denied to conduct our research with paediatric specialist of The State Child Psychiatric Unit-BUGL by ethical committee due to lack of information, despite that we had the approval issued by Norwegian centre for research data.

2.4 Survey timeline

The recruitment took place in period from the 10th of January to the 1th of February, while the questionnaire was available for answering in the period from the 10th of January to the 15th of February.

2.5 Statistical analyses

All data was downloaded from the Surveymonkey platform, coded and transferred into the statistical program IBM® SPSS® Statistics, Version 25 [123]. All Likert-scale questions were analysed by nonparametric tests. Differences between three groups were tested with Kruskal-Wallis test, presented with H and p values in the Results. Pairwise testing was used as post hoc analyses to show the differences between particular countries, presented with Bonferroni

corrected p value in the Results. Other test used in statistical analysis was chi-square test for categorical data, presented with χ^2 and p value in the Results.

3 Results

3.1 Study population

The total sample had 55.7% female and 44.30% male respondents. The Icelandic group had 39.1% to 60.9%, the Serbian group 68.4% to 31.6%, and Norwegian group 59.5% to 40.5% female to male ratio (Figure 1). The average age in the Serbian group was 46.53 (SD 10.03), Norwegian 46.6 (SD 10.03) and Icelandic 59.70 (SD 10.9) years.

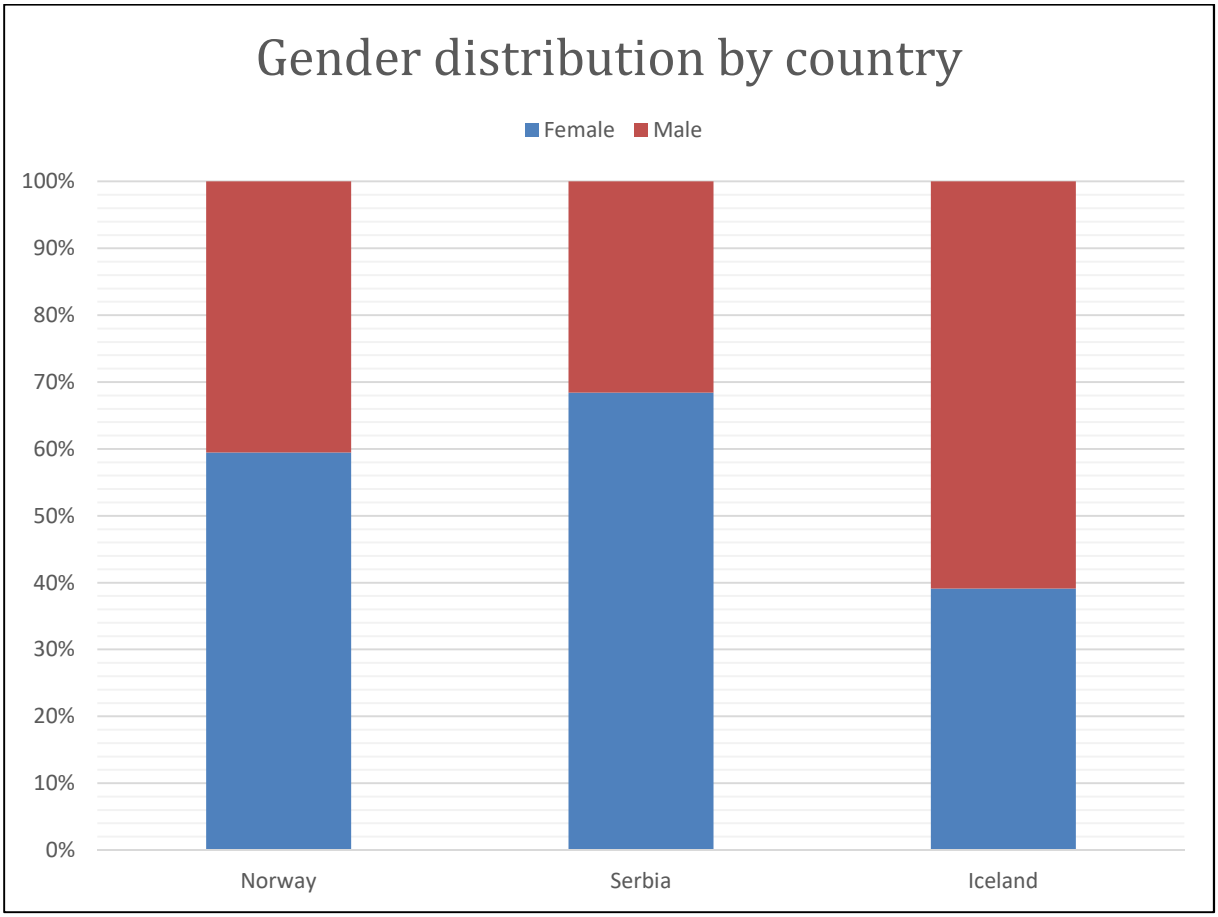

Figure 1. Female to male ratio by group. Data used to create this figure is available in Appendix 1.

The respondents were evenly distributed by experience in the treatment of ADHD between the groups. The majority of respondents had more than 10 years of experience. There was 59.46% of Norwegian, 57.9% of Serbian and 65.2% of Icelandic respondents with more than 10 years of experience (Figure 2).

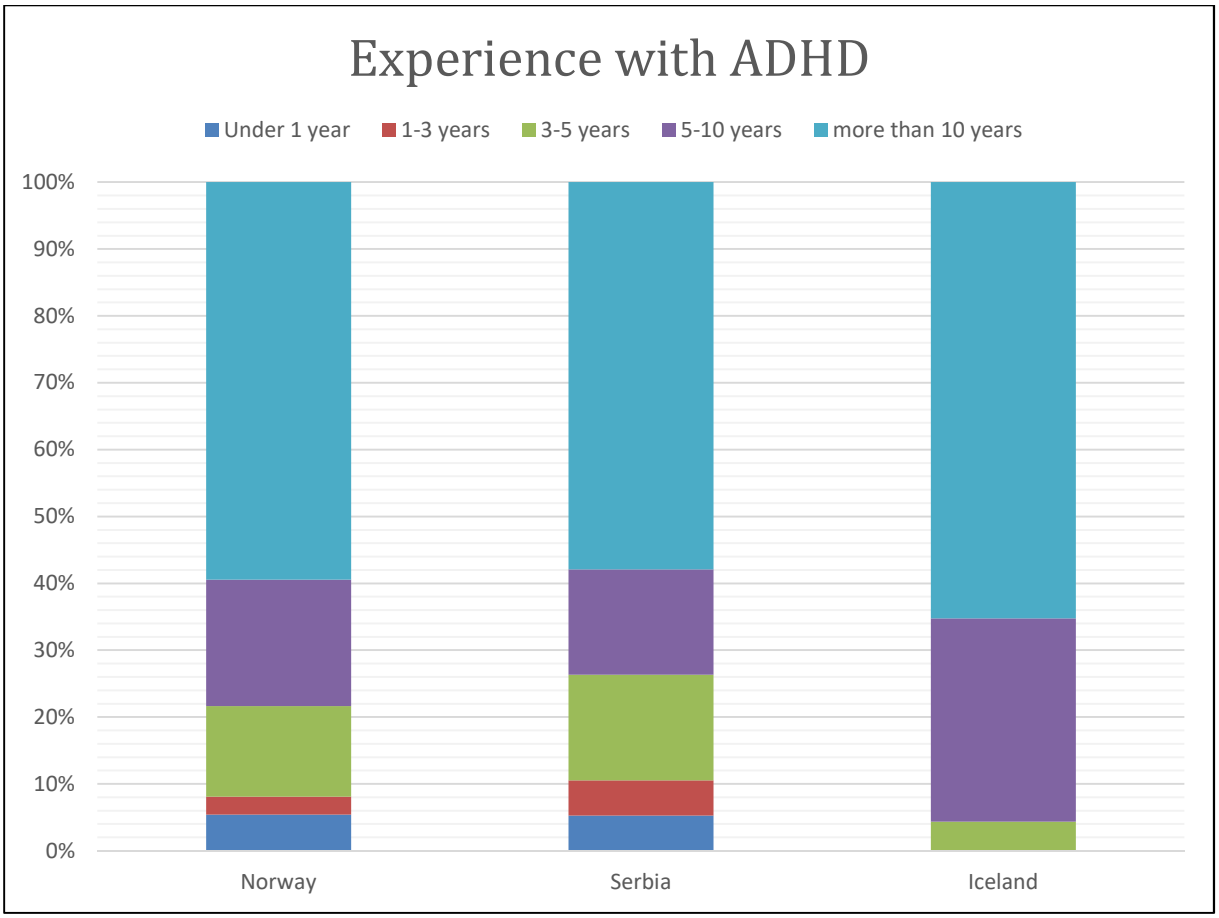

Figure 2. Experience in treatment of ADHD by group. Data used to create this figure is available in Appendix 2.

Overall distribution of respondents were 48.1% of those who treat children and adolescents, 44.30% of those who treat adult population and 7.6% of those who were involved in treatment of both children and adults. Norwegian and Serbian group had 64.8% and 57.9% of those prescribing to children and adolescents respectively, while Icelandic group had 82.6% of respondents who prescribe to adults only (Figure 3).

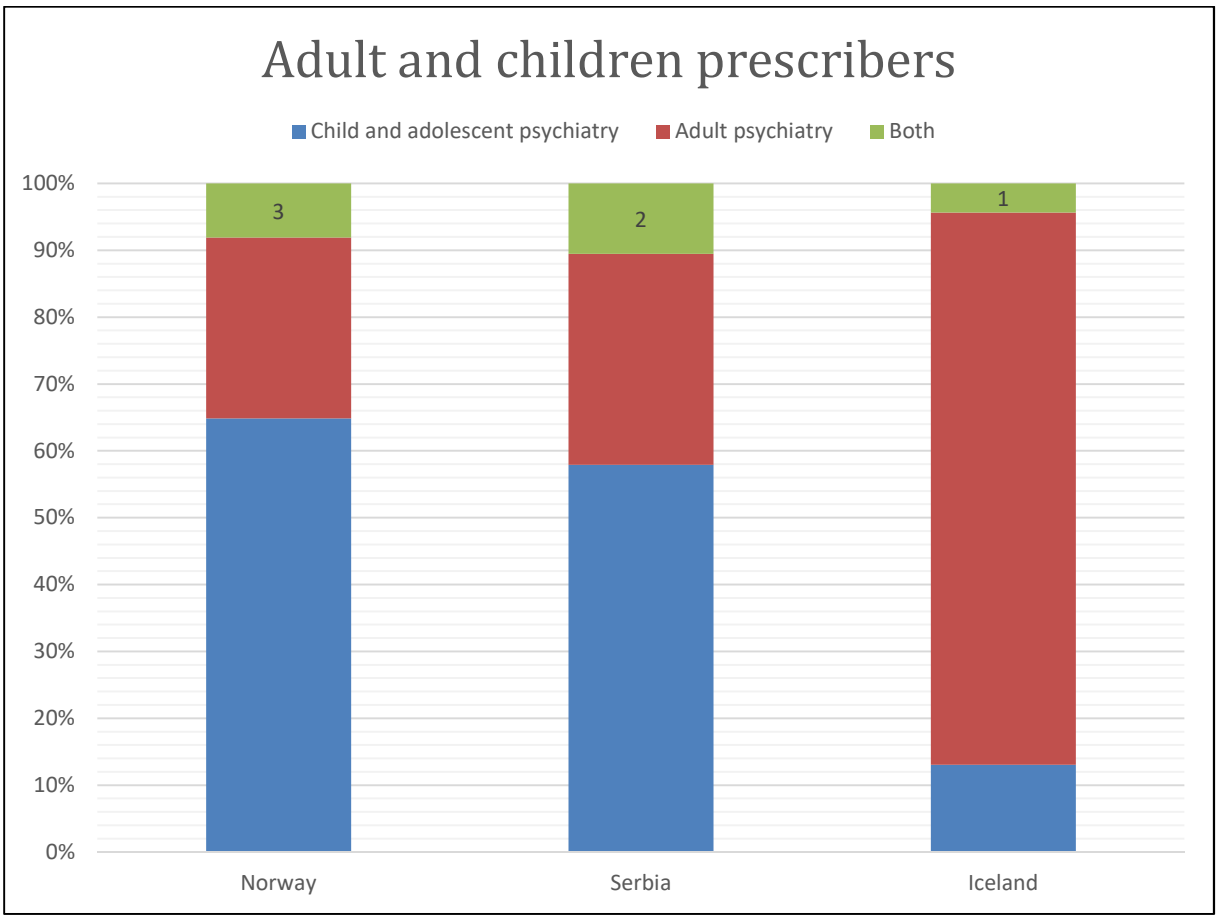

Figure 3. Distribution of adult and children prescribers by group. Data used to create this figure is available in Appendix 3.

3.2 Diagnosing

Considering the referring of ADHD patients, 92% of respondents from Norway and 83% from Iceland stated that general practitioners from public health services were the most frequent source of referring. However, this was not the case in Serbia, where 47.4% of respondents identified paediatricians from public health services as the most frequent referring entity for ADHDs. Forty-eight percent of Icelandic and 38 % of Norwegian chose option "other" and specified psychologist and social workers as a source of referral.

The referring process of ADHD patients was classified as either adequate or slightly adequate by 73% of Norwegian, 43.5% of Icelandic and 42.1% of Serbian respondents. The referring process was very inadequate according to 21.7% of Icelandic, 15.8% of Serbian and 2.7% of Norwegian respondents (Figure 4). The differences between the groups were statistically significant ($H(2) = 7.9$, $p = 0.019$; Norway-Serbia $p=0.025$).

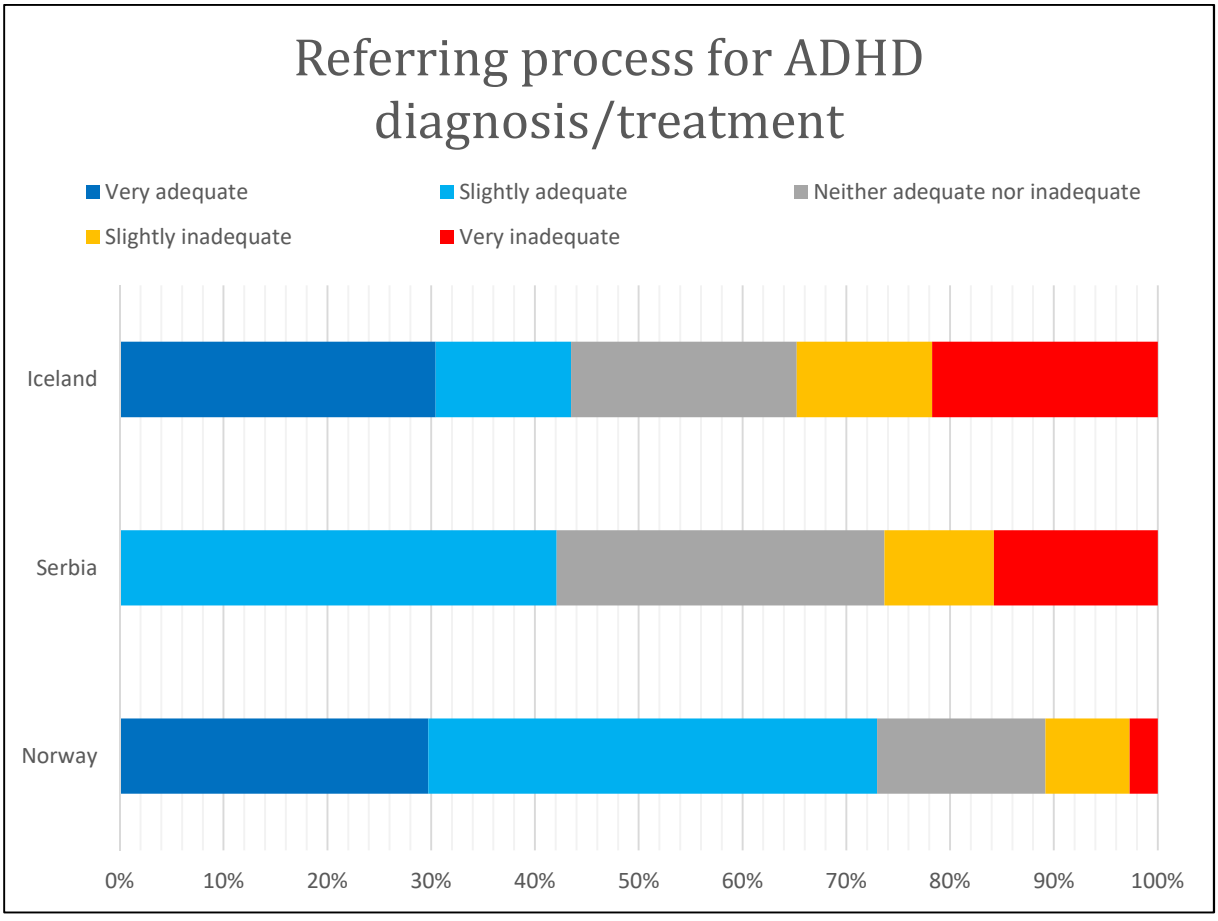

Figure 4. Satisfaction with referring process. Data used to create this figure is available in Appendix 4.

The waiting-time for patients from ADHD suspicion to diagnose differed between the groups, with the mean scores of 3.27 (SD 1.21), 3.65 (SD 2.12), and 4.47 (SD 1.93), stated by respondents from Norway, Iceland and Serbia respective, but without statistical significance ($H(2) = 4.37$, $p= 0.11$). More than 9 months in average from suspicion to diagnose of ADHD was chosen by 57.9% of Serbian, 39.1% of Icelandic and 8.8% of Norwegian respondents (Figure 5).

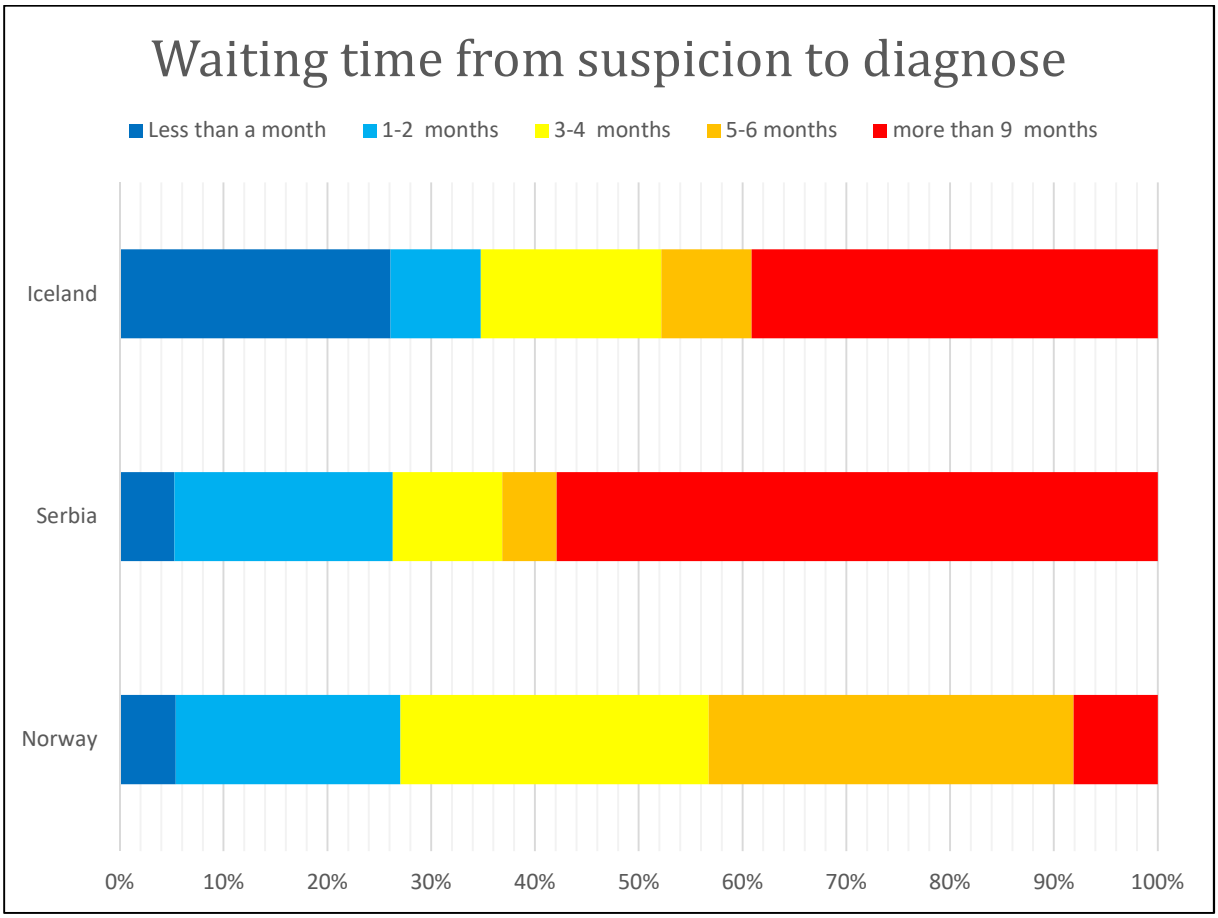

Figure 5. Waiting time from suspicion to diagnose. Data used to create this figure is available in Appendix 5.

Considering waiting for specific treatment once ADHD is diagnosed, 27.8% of respondents from Serbia stated that it takes more than 9 months, while only 4.3% of respondents from Iceland and 2.7% of respondent from Norway reported this time. According to 60.9% of respondents from Iceland, 70.3% of respondents from Norway and 33% of respondents from Serbia, it did not take longer than 2 months from ADHD diagnose to receiving of specific treatment. The mean scores of 2.22 (SD 1.25), 2.48 (SD 1.34) and 3.44 (SD 1.95) were for Norway, Iceland and Serbia respective. Differences were not statistically significant ($H(2)=5.34$ $p = 0.07$).

Transition to adult services was classified as either slightly or very inadequate by 84.2% of Icelandic, 42.1% of Serbian and 41.7% of Norwegian respondents. Differences between groups were statistically significant, (H(2)=7.38 p=0.025; Norway-Iceland p=0.02).

Considering the choice of classification system while diagnosing ADHD, the ICD – 10 used to be followed by 73.9% of Icelandic, 84.2% of Serbian and 89.2% of Norwegian respondents, while the rest of participants rather followed the DSM-5 classification system (Figure 6).

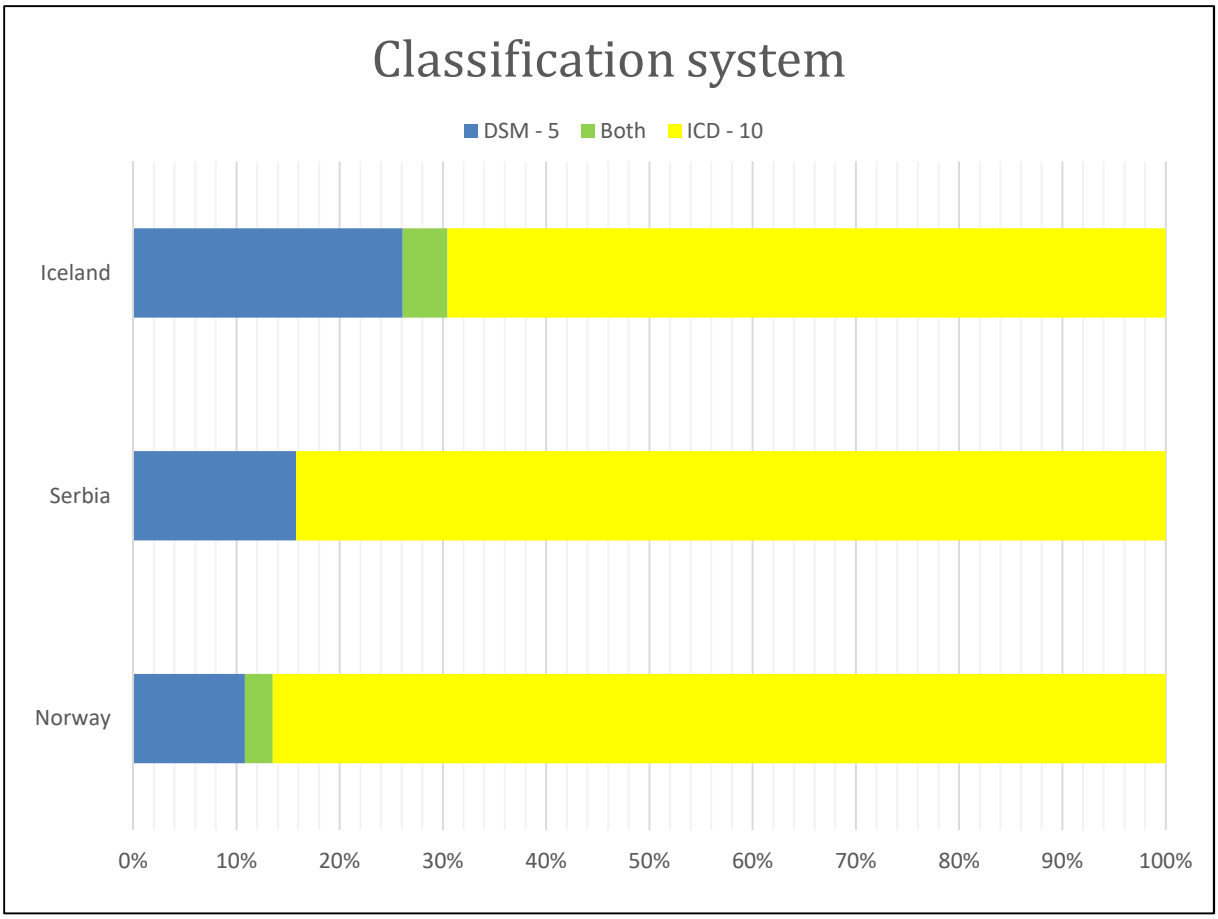

Figure 6. Preferred classification system. Data used to create this figure is available in Appendix 6.

3.3 Treatment

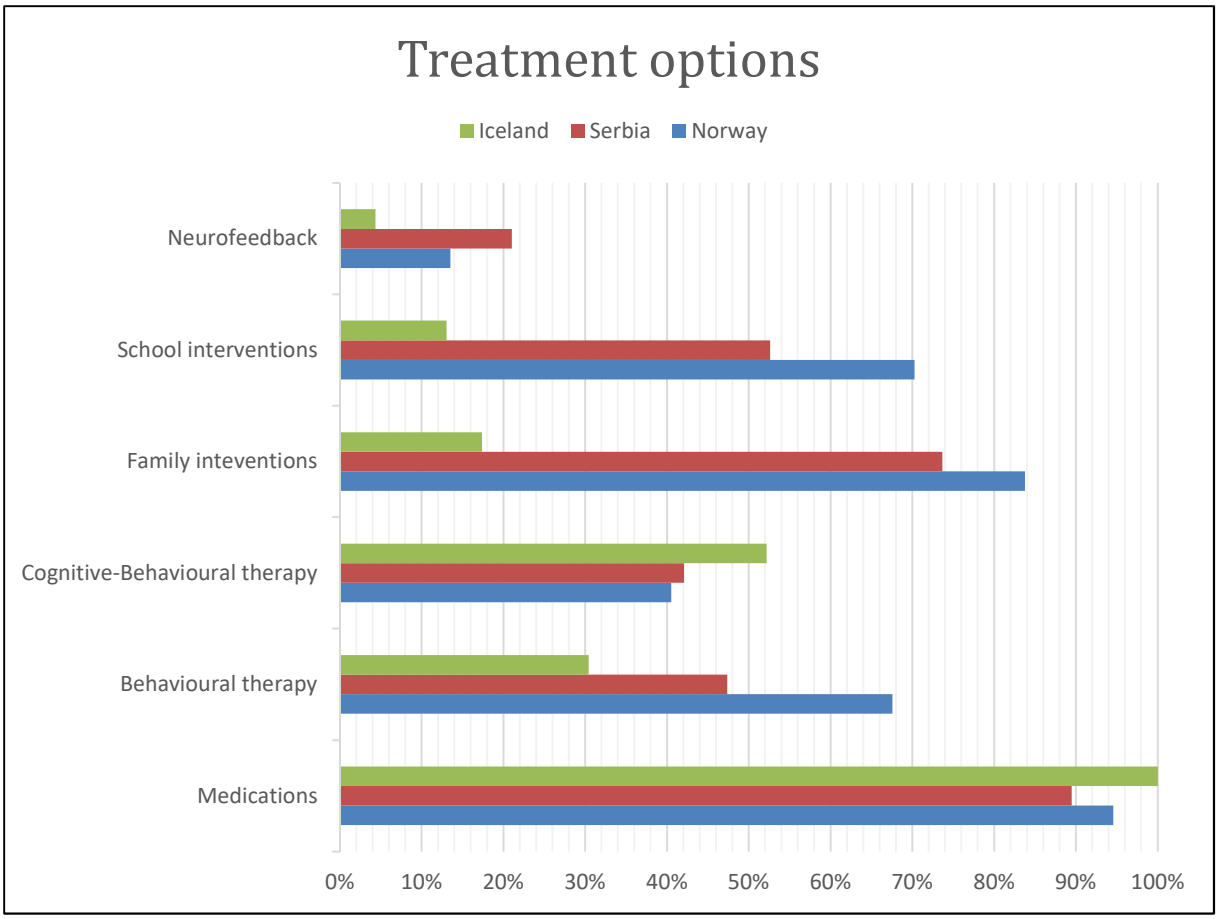

Figure 7. Consideration of different treatment options. Data used to create this figure is available in Appendix 7.

Considering medications, there were no statistical significant differences between these three countries; 100% of Icelandic, 95 % of Norwegian and 89 % of Serbian respondents stated that they consider using medications in the treatment of ADHD (Figure 7). However, there was significant difference regarding the use of behavioural therapy ($\chi^2(2) = 8.04$, $p=0.018$), family interventions ($\chi^2(2) = 27.99$, $p<0.001$), school interventions ($\chi^2(2) = 18.69$, $p<0.001$) and neurofeedback ($\chi^2(2) = 8.78$, $p=0.012$) between the groups.

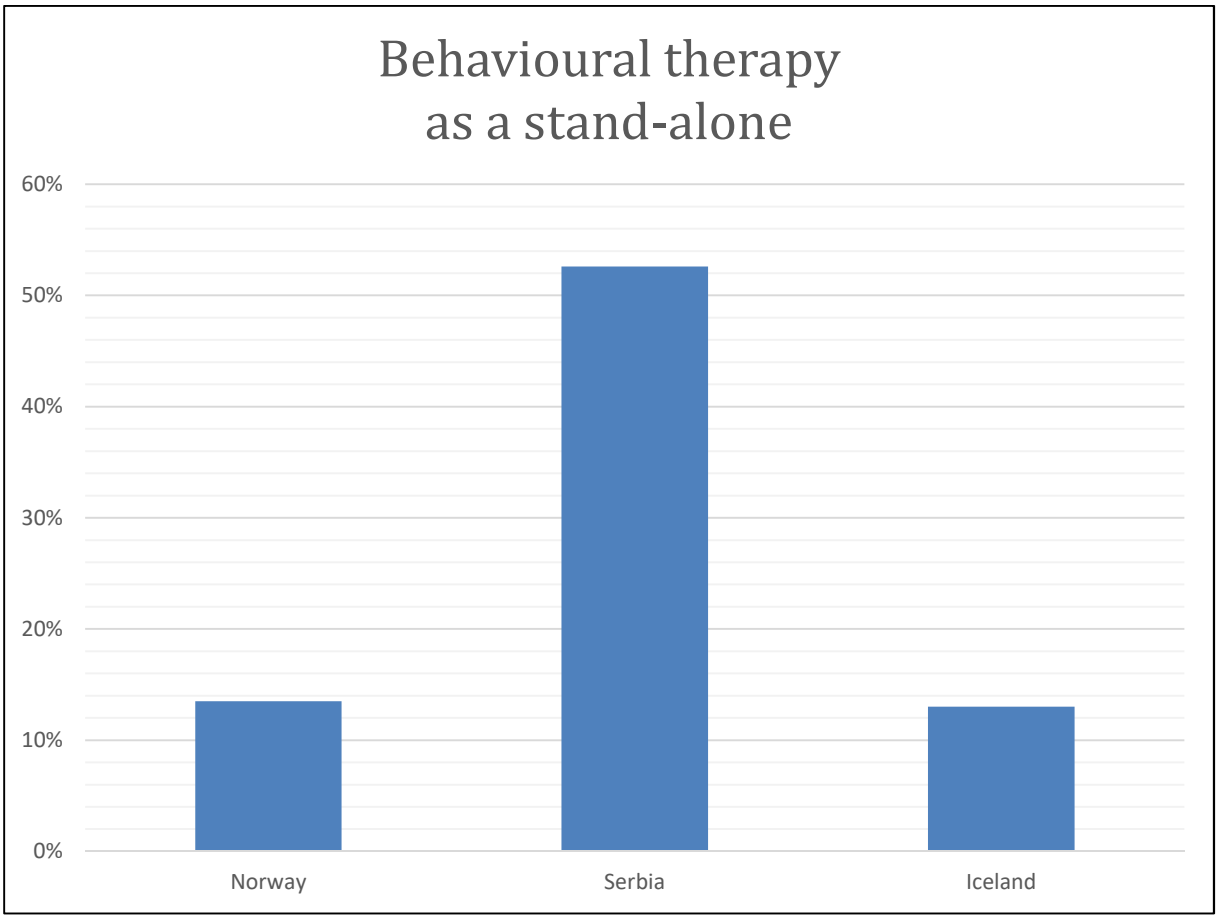

Figure 8. Use of behavioural therapy as a stand-alone treatment. Data used to create this figure is available in Appendix 8.

Fifty-three percent of respondents from Serbia reported prescribing behavioural therapy as a standalone treatment. While percentage in Norway and Iceland were 14.2% and 13.6% (Figure 8). This difference was statistically significant ($\chi^2(2)=12.36$, $p = 0.002$).

The highest number of respondents who used to prescribe medications as a standalone treatment were in Iceland, 67%, followed by Serbia with 47% and Norway with 16% (Figure 9). Difference were statistically significant ($\chi^2(2)=15.54$ with $p < 0.001$).

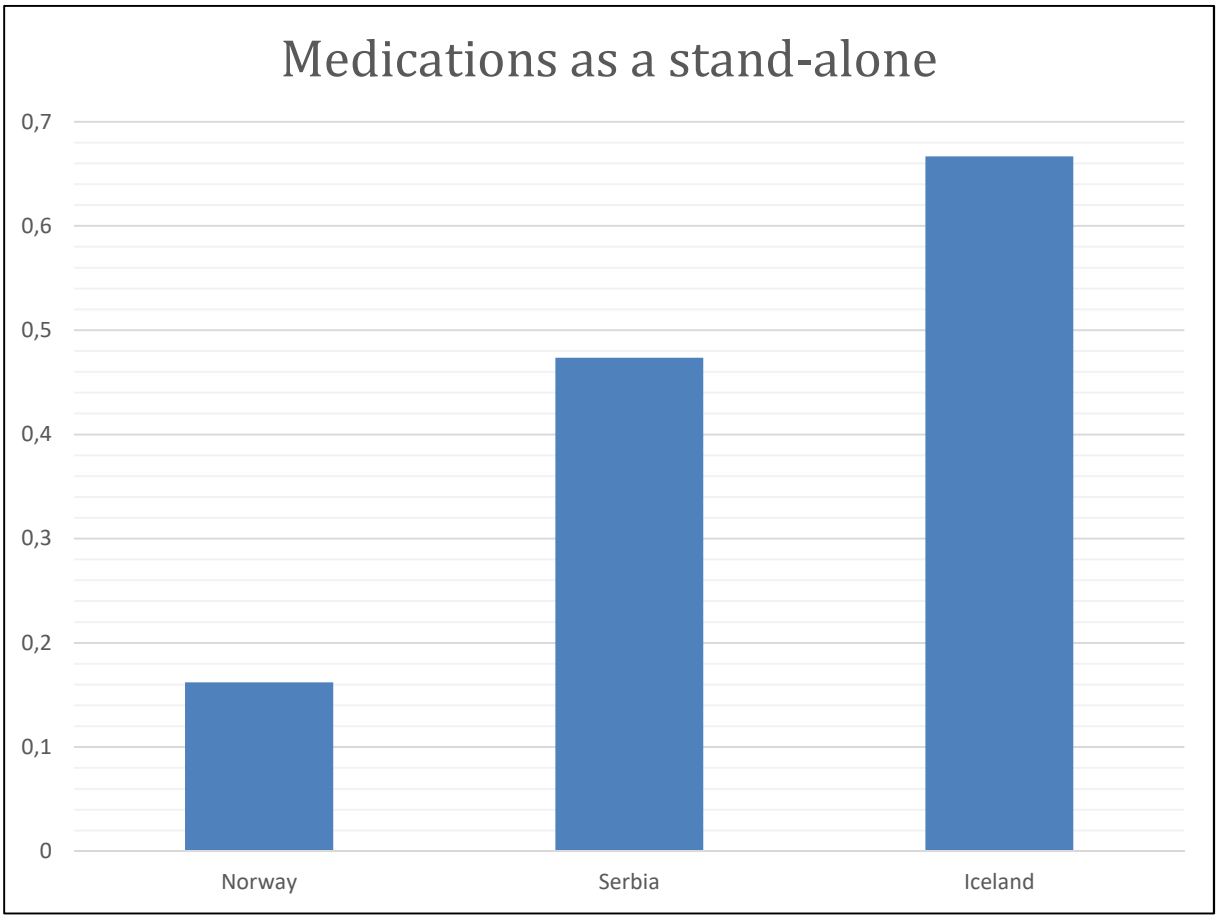

Figure 9. Use of medications as a stand-alone treatment. Data used to create this figure is available in Appendix 8.

Methylphenidate was used as first line by majority of physicians in all three countries; 97% of Norwegian respondents, 70% of Icelandic respondents and 63% of Serbian respondents reported using methylphenidate as a first choice medication. Additionally, 26% of Icelandic respondents reported using atomoxetine as the first line; while in Serbia 18.7% and 12,5% have reported use of dexamphetamine and antipsychotics as the first line medication (Figure 10).

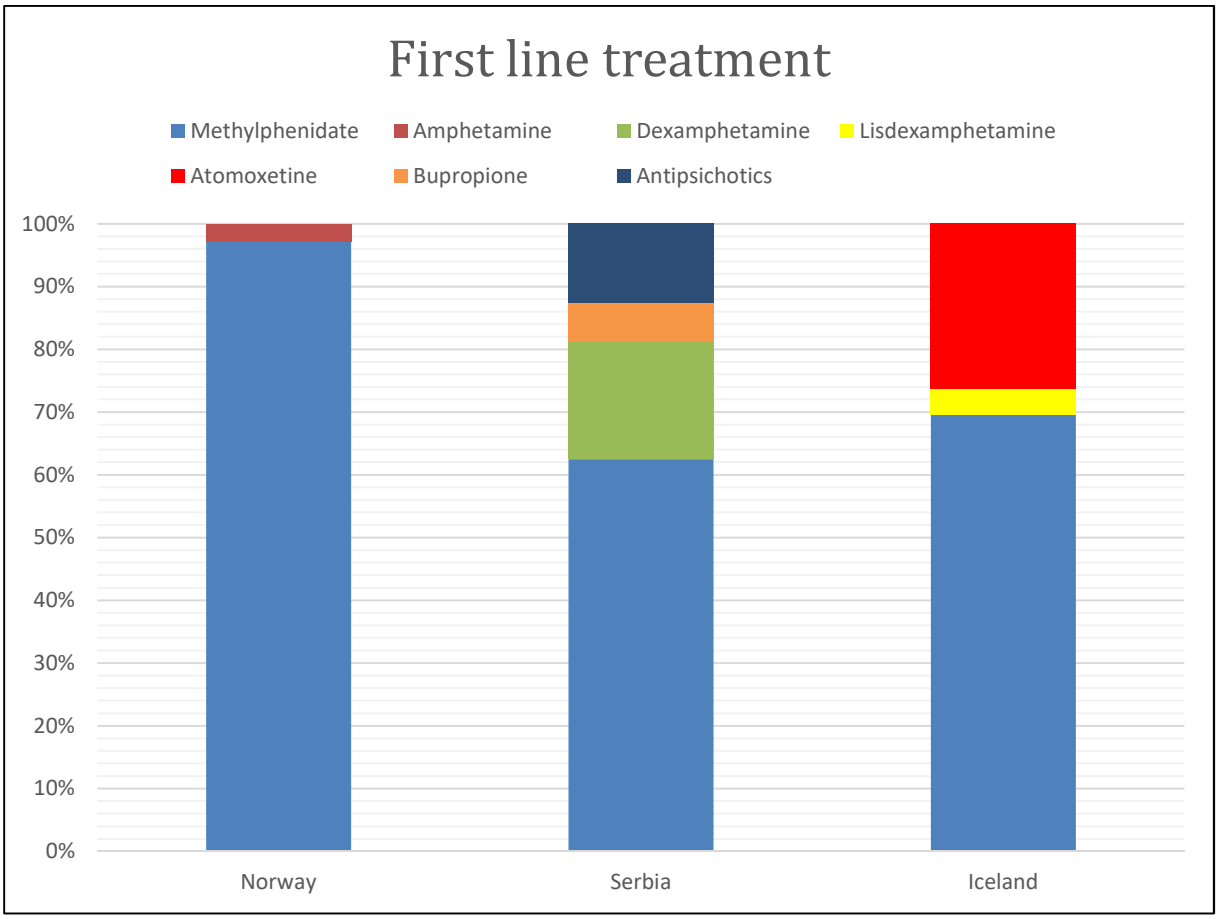

Figure 10. First line treatment. Data used to create this figure is available in Appendix 9.

As for the second line treatment, 50.0% of Norwegian respondents reported lisdexamphetamine, while 36% were using atomoxetine. Icelandic respondents reported using atomoxetine in 35% and dexamphetamine in 22% of answers, while antipsychotics were preferred treatment in Serbia according to 36.4% of the respondents. As for the third line treatment, 44.4% of Norwegian respondents reported atomoxetine, while 30.4% of Icelandic respondents reported using bupropion and 21.7% atomoxetine as a third line treatment. The third line in Serbia were antipsychotics according to 13% respondents. Antipsychotics were reported only by respondents from Serbia in these three lines of treatment. Used antipsychotics were risperidone and aripiprazole. Other medications that were reported by respondents were modafinil, anxiolytics, mood stabilizers and antidepressants.

The respondents were satisfied with behavioural therapy as a standalone treatment according to 44.4% of Serbian respondents, 31.2% of Norwegian respondents and 20% of Icelandic respondents, but differences between groups were not statistically significant ($H(2)=0.997$ $p=0.60$).

The share of satisfied respondents with MPH sustained release formulations was highest on Iceland, where 95.2% of respondents stated that they were either vary or slightly satisfied, followed by 88.9% of Norwegian respondents and 75% of Serbian respondents (Figure 11). However, the differences were not statistically significant (H (2) = 2.50 p = 0.29). Considering amphetamine of choice, 70.4% of Norwegian, 53.8% Icelandic and 44.4% respondents from Serbia were either vary or slightly satisfied. Differences between groups were not statistically significant (H(2)= 2.71 p=0.26).

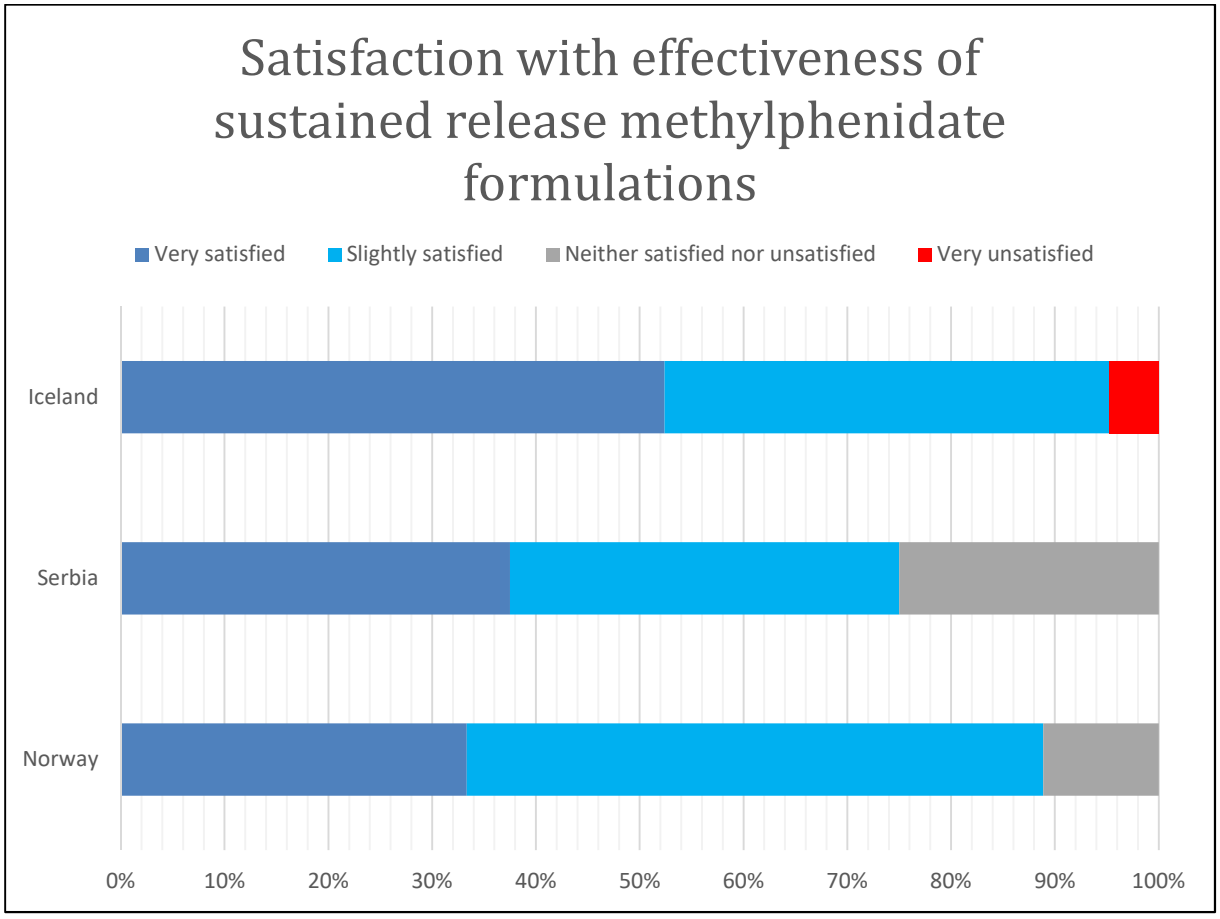

Figure 11. Satisfaction with effectiveness with sustained release methylphenidate formulations. Data used to create this figure is available in Appendix 10.

However, satisfaction with immediate release methylphenidate was in average lower than that seen with sustained release formulations. In total, 66.7% of Norwegian, 45% of Icelandic and 50% of Serbian respondents were either very or slightly satisfied, while differences between groups were not statistically significant (H (2) = 2.18 p=0.34). Vary or slightly satisfied with atomoxetine were 45.95% of Norwegian and 47.6% of Icelandic

respondents, followed by 15.8% of respondents from Serbia. Differences between groups were not statistically significant (H(2)= 0.21 p=0.9).

Respondents from all three countries were the most satisfied with effectiveness of sustained release methylphenidate, and least satisfied with atomoxetine (Figure 12). Differences between medications were statistically significant ($\chi^2(3)=37.90$ $p<0.001$, sustained release methylphenidate-atomoxetine $p<0.001$).

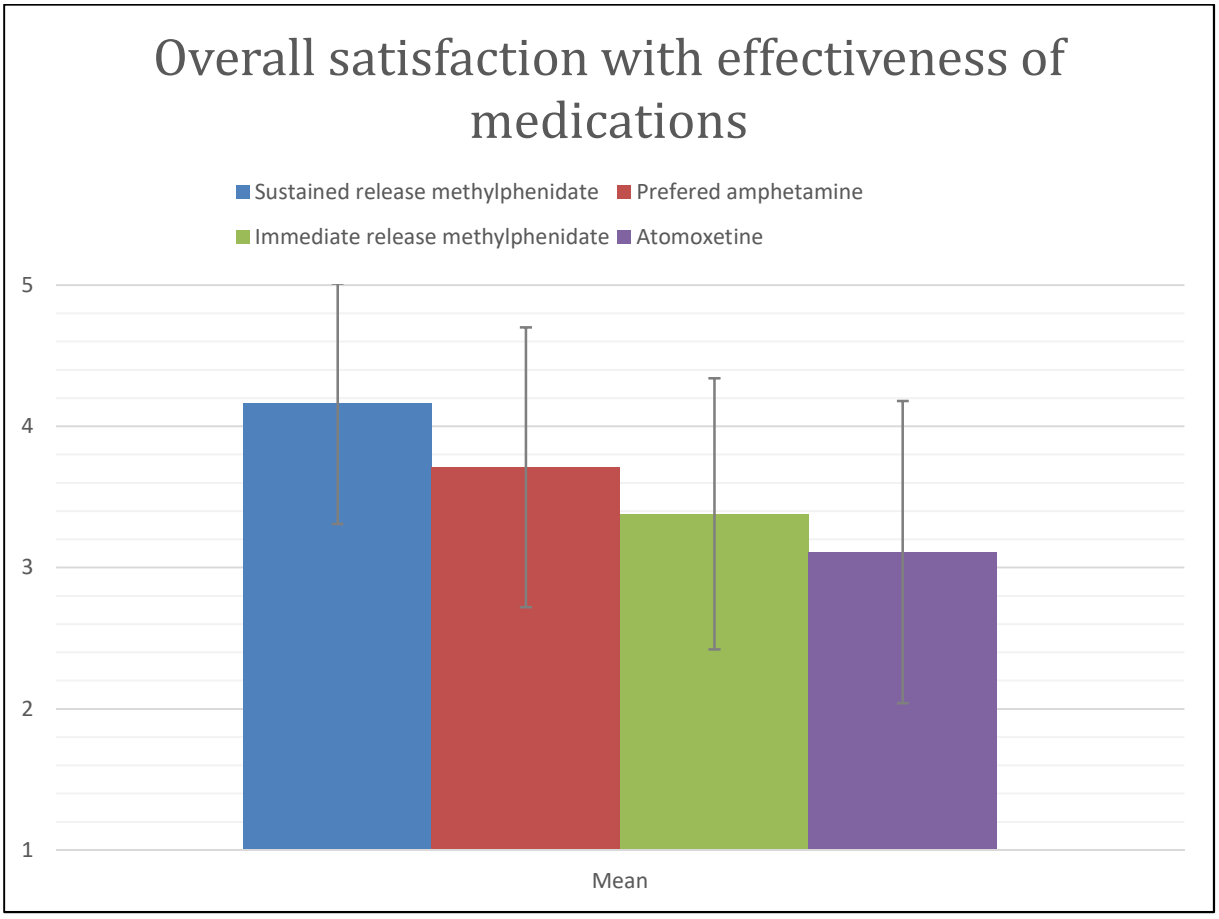

Figure 12. Satisfaction with effectiveness of different medications. Data used to create this figure is available in Appendix 11.

Considering self-reported confidence level in identifying adverse effects of stimulants, most confident respondents were from Iceland with 95.7% of them choosing either very or slightly confident, followed by Norway with 89.2% of respondents, and Serbia with 57.9% of respondents (Figure 13). Differences between groups were statistically significant (H (2) = 10.23 p=0.006).

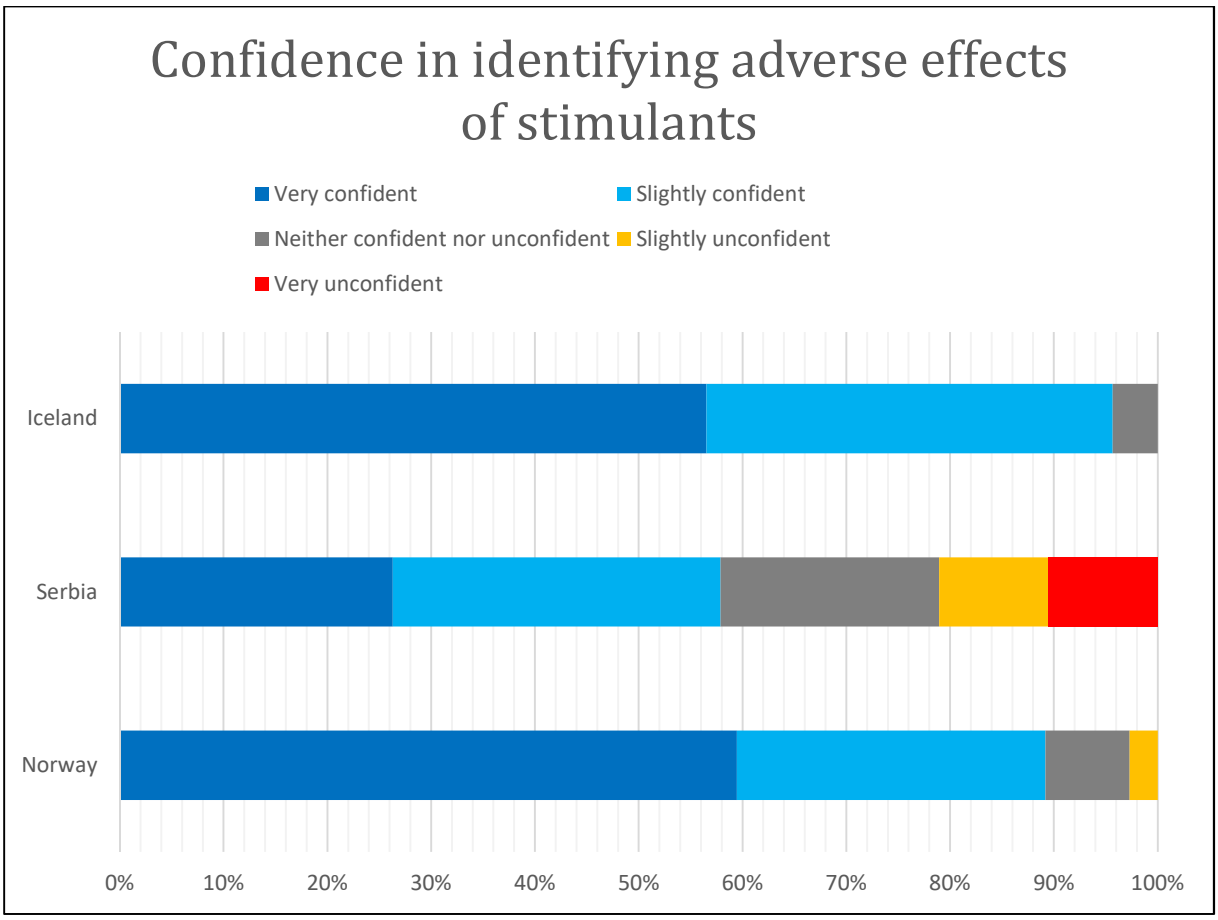

Figure 13. Confidence in identifying adverse effects of stimulants. Data used to create this figure is available in Appendix 12.

However, when it comes to level of confidence in managing adverse effects of stimulants, results were very similar for all three countries. Sixty-nine percent of Icelandic respondents, 63.2% of Serbian respondents and 78.4% of Norwegian respondents were either confident or slightly confident in manging adverse effects of stimulants. The differences were without statistical significance ($H(2)=4.66$ $p=0.10$).

3.4 Availability/reimbursement of medications

On the scale from one to ten, where one was the lowest and ten was the highest score on the scale, the variety of medications available for children and adolescents was scored 7.29 (SD 1.81), 6.83 (SD 1.64) and 4.06 (SD 2.4) by Norwegian, Icelandic and Serbian respondents respectively. The reimbursement conditions of medications available for children and adolescents was scored 8.39 (SD 1.31), 6.64 (SD 1.75) and 5.19 (SD 2.46) by Norwegian, Icelandic and Serbian respondents respectively (Figure 14). Differences between groups were statistically significant ($H(2)=17.60$ $P<0.001$ for variety of medications available for children and adolescents, Serbia-Norway $p<0.001$, Serbia-Iceland $p=0.024$; $H(2)=20.47$ $P<0.001$ for reimbursement of available medications for children and adolescents, Serbia-Norway $p<0.001$ Iceland-Serbia $p=0.039$).

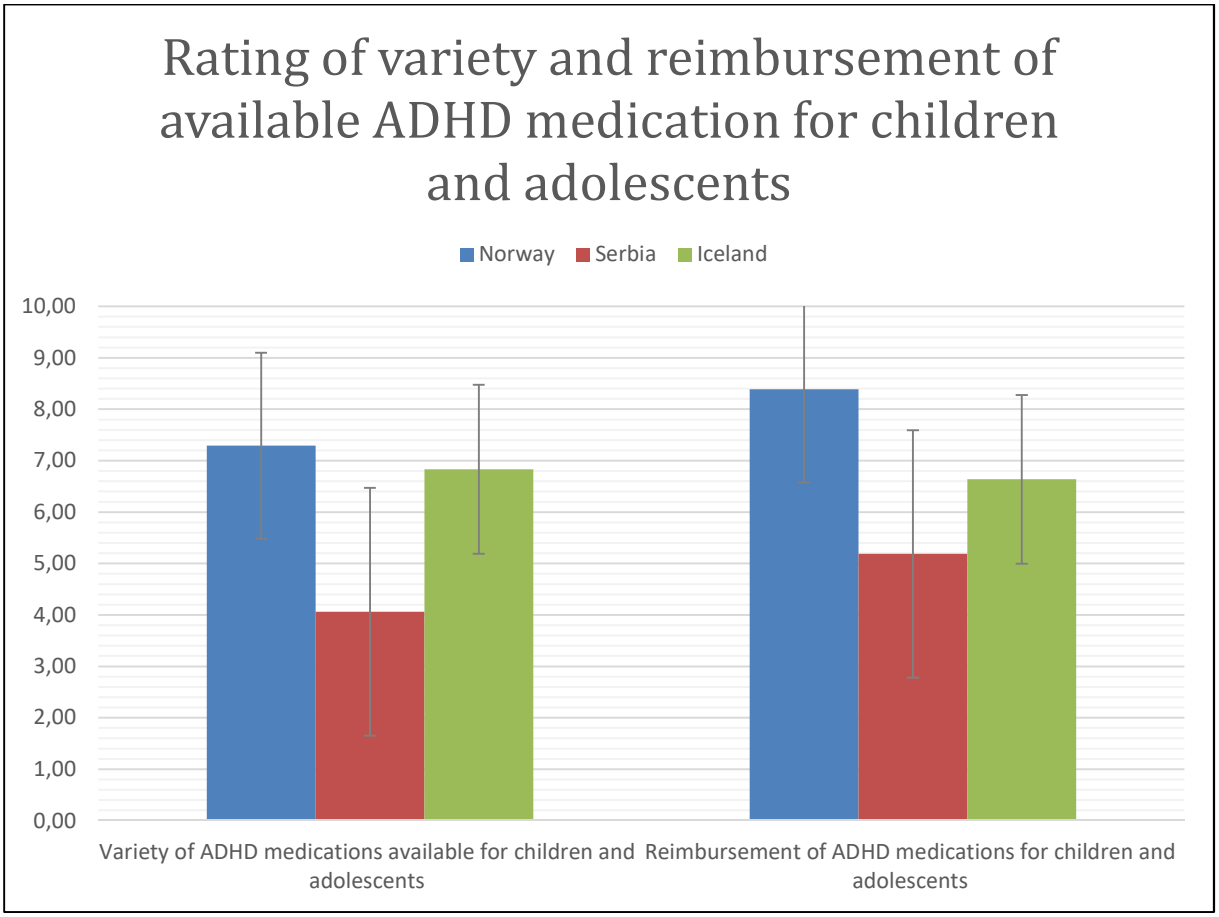

Figure 14. Rating of variety and reimbursement of available ADHD medications for children and adolescents, on the scale from one to ten, where one was the lowest and ten was the highest score on the scale. Data used to create this figure is available in Appendix 13.

On the scale from one to ten, where one was the lowest and ten was the highest score on the scale, the variety of medications available for adults was scored 6.06 (SD 2.39), 6.40 (SD 1.57) and 3.18 (SD 2.43) by Norwegian, Icelandic and Serbian respondents respectively. The reimbursement conditions of medications available for adults was scored 6.10 (SD 2.34), 6.95 (SD 1.60) and 3.25 (SD 2.15) by Norwegian, Icelandic and Serbian respondents respectively (Figure 15). The differences between groups were statistically significant ($H(2)= 17.28$ $p<0.001$ for variety of medications available for adults, Serbia-Norway $p=0.001$, Serbia-Iceland $p<0.001$; for reimbursement of medications available for adults $H(2)=20.66$ $p<0.001$, Serbia-Norway $p=0.001$, Serbia-Iceland $p<0.001$).

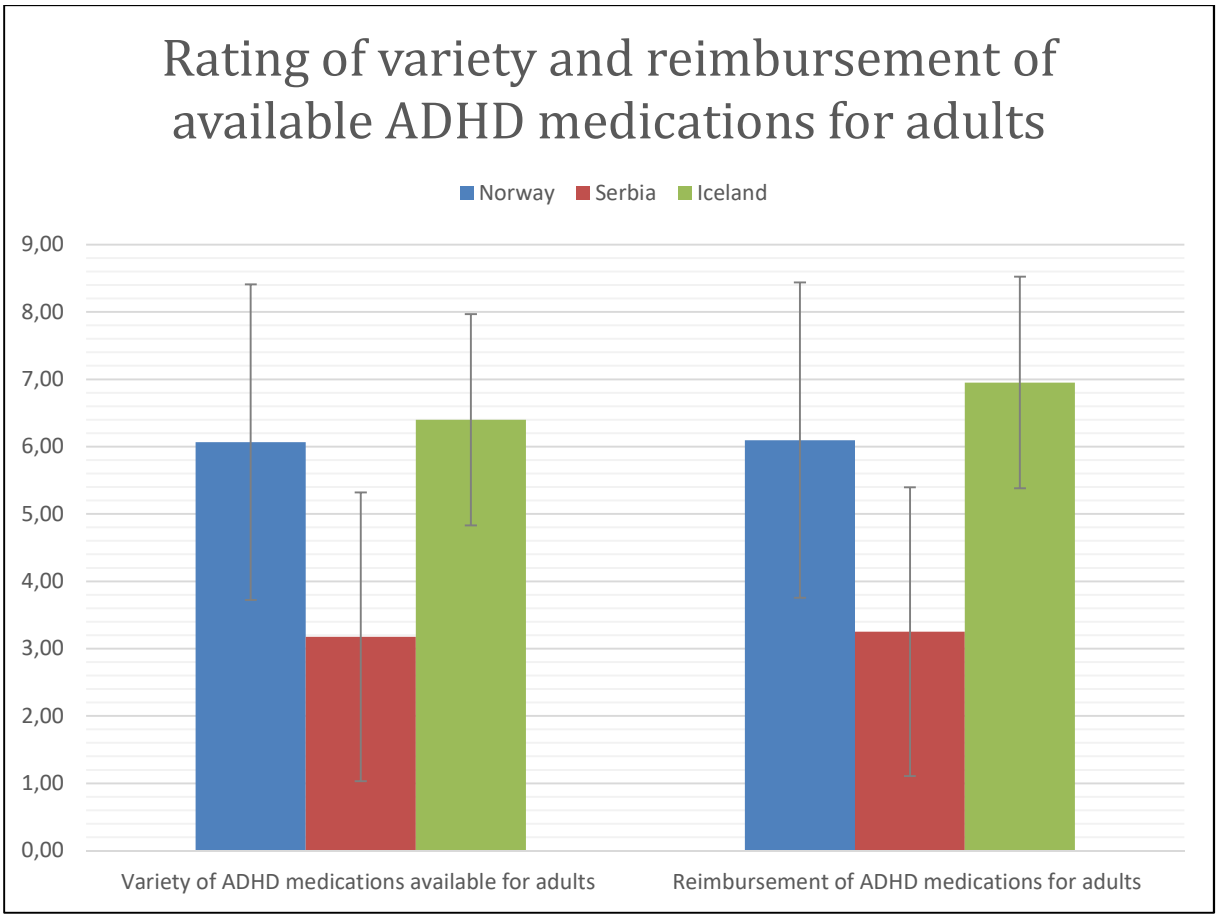

Figure 15. Rating of variety and reimbursement of available ADHD medications for adults, on the scale from one to ten, where one was the lowest and ten was the highest score on the scale. Data used to create this figure is available in Appendix 13.

Considering the influence of variety of medications available for ADHD treatment in children and adolescents, respondents from Serbia had in average decreasing score of -0.59 (SD 1.21), while respondents from Norway and Iceland increasing scores of 0.69 (SD 0.82) and 0.27 (SD 0.80) respectively. Differences were statistically significant ($H(2)=16.08$ $p<0.001$, Serbia-

Norway p<0.001). As for the influence of reimbursement of medications available for ADHD treatment in children and adolescents, respondents from Serbia had in average decreasing score of -0.11 (SD 0.96), while Norwegian and Icelandic respondents had in average increasing scores of 1.00 (SD 0.67) and 0.33 (SD 1.04) respectively. Differences were statistically significant (H(2)=16.05 p<0.001, Serbia-Norway p<0.001).

Considering the influence of variety of medications available for ADHD treatment in adults, respondents from Serbia had in average decreasing score of -0.83 (SD 0.92), while Norwegian and Icelandic respondents had in average increasing scores of 0.29 (SD 1.09) and 0.33 (SD 0.91) respectively (Figure 16). Differences are statistically significant (H(2)=15.67 p<0.001, Serbia-Norway p=0.001, Serbia-Iceland p=0.003).

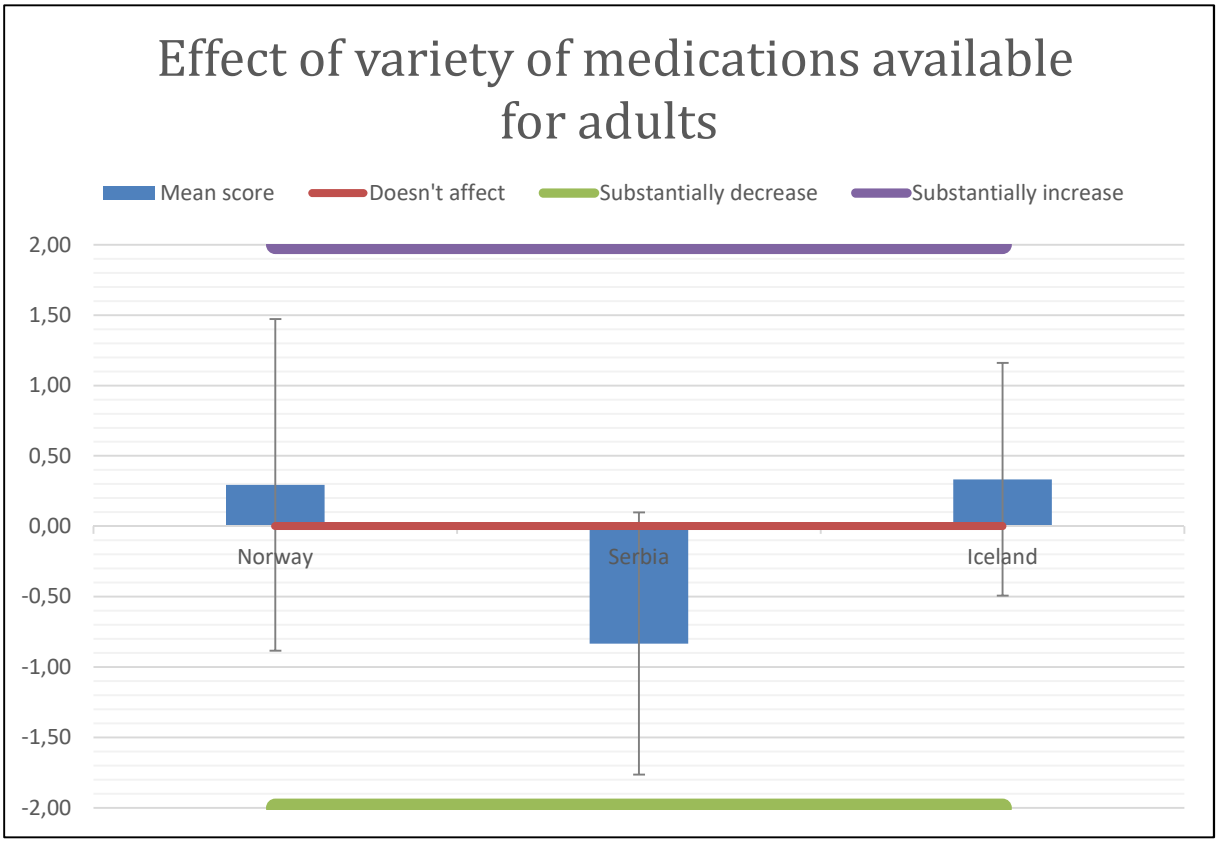

Figure 16. Influence of variety of medications available for adults on the number of patients treated, according to respondents. Data used to create this figure is available in Appendix 14.

As for the influence of reimbursement of medications available for ADHD treatment in adults, respondents from Serbia had in average decreasing scores of -0.65 (SD 0.93), while respondents from Norway and Iceland had in average increasing scores of 0.35 (SD 1.18) and 0.73 (SD 0.83) respectively (Figure 17). Differences are statistically significant ($H(2)=15.40$ $p<0.001$, Serbia-Norway $p<0.005$, Serbia-Iceland $p<0.001$).

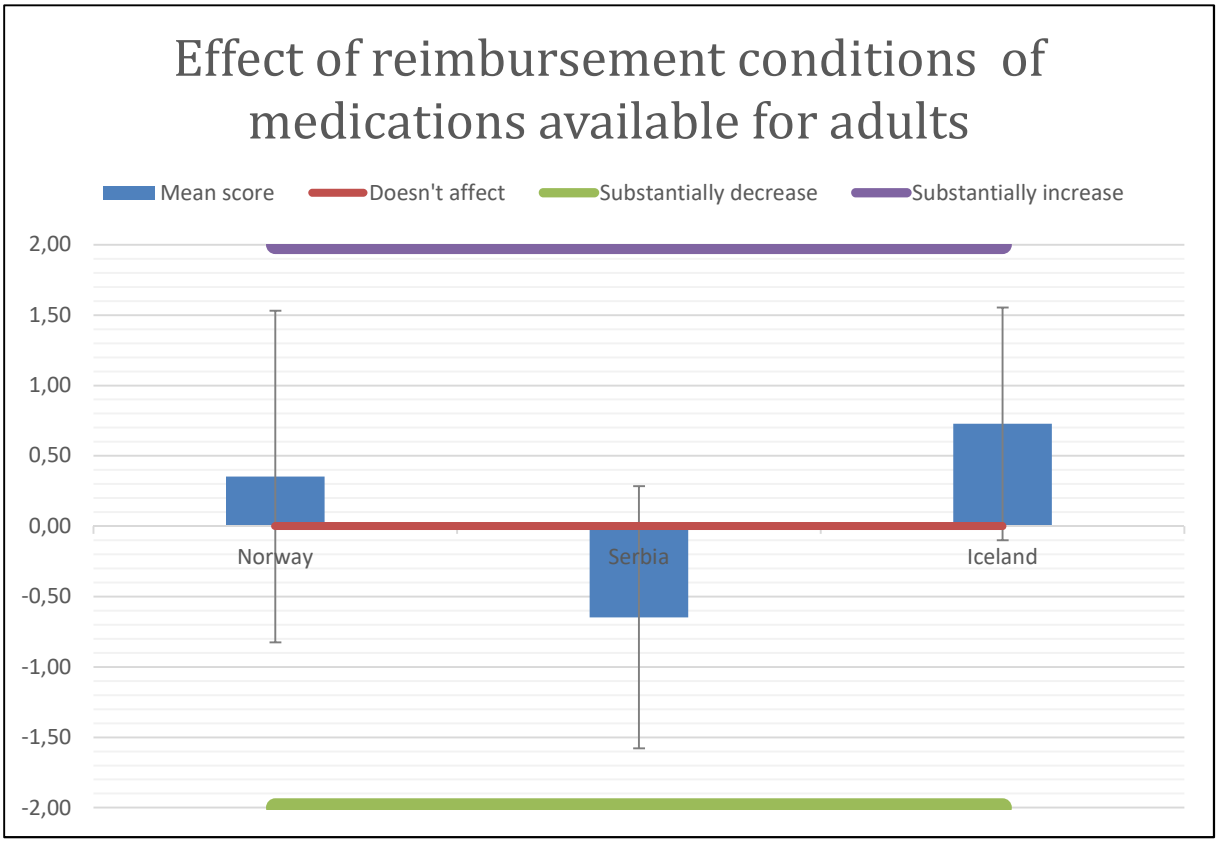

Figure 17. Influence of reimbursement conditions of medications available for adults on the number of patients treated, according to respondents. Data used to create this figure is available in Appendix 14.

3.5 Attitudes and awareness

The psychiatry stigma was present in medium or high levels according to 88.2% of Serbian respondents, followed by 44.4% of Norwegian and 44.8% of Icelandic respondents (Figure 18). The differences between groups were statistically significant (H (2) = 13.44 p= 0.001; Serbia-Norway p=0.002, Serbia-Iceland p=0.006).

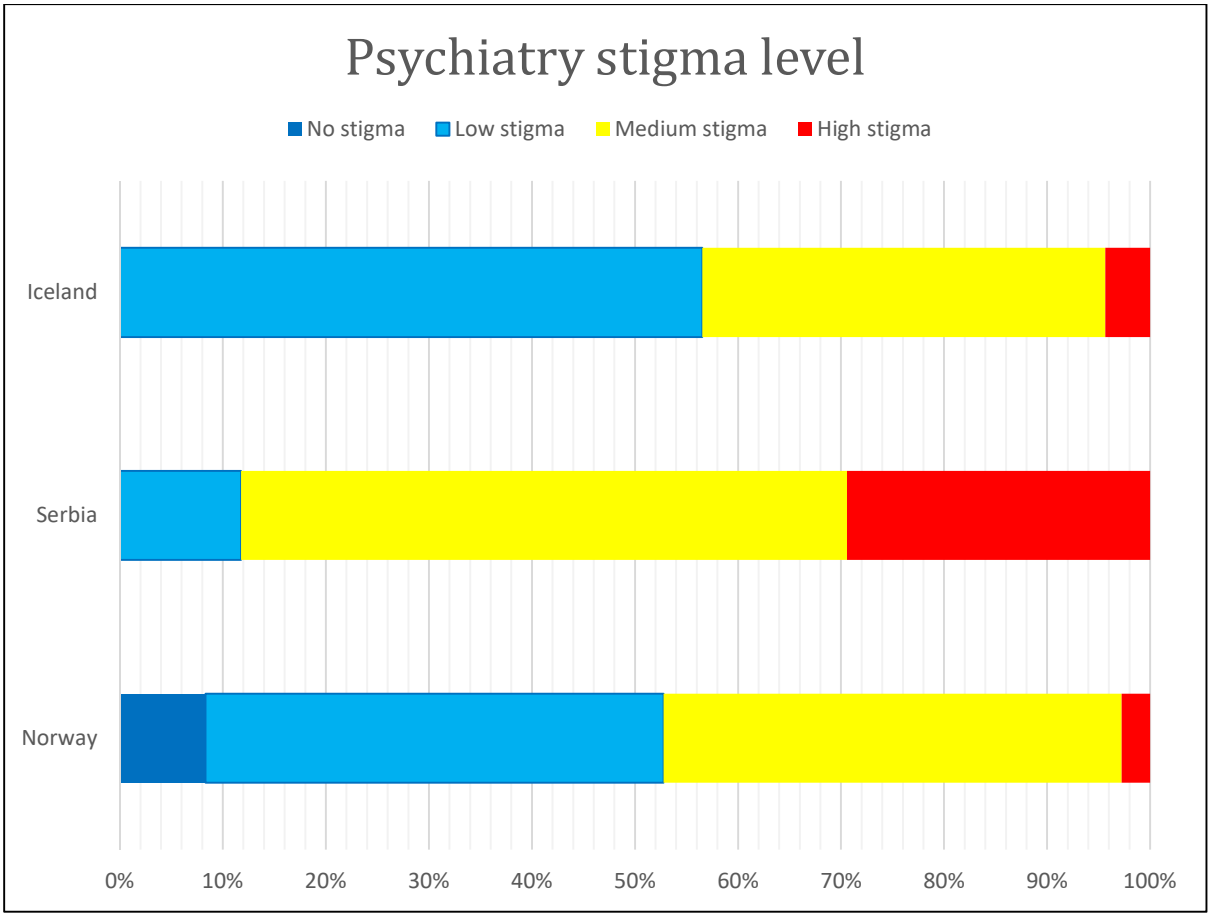

Figure 18. Psychiatry stigma level in general population, according to respondents. Data used to create this figure is available in Appendix 15.

Fifty-eight percent of Serbian respondents reported that general population perceive ADHD as a psycho-social/situational condition or phase in child development rather than mental and/or behavioural illness, while just 19.4% of Norwegian and 22.7% of Icelandic respondents reported the same. The differences between groups were statistically significant (H(2)=10.97 p=0.004; Serbia-Norway p=0.005, Serbia-Iceland p=0.02).

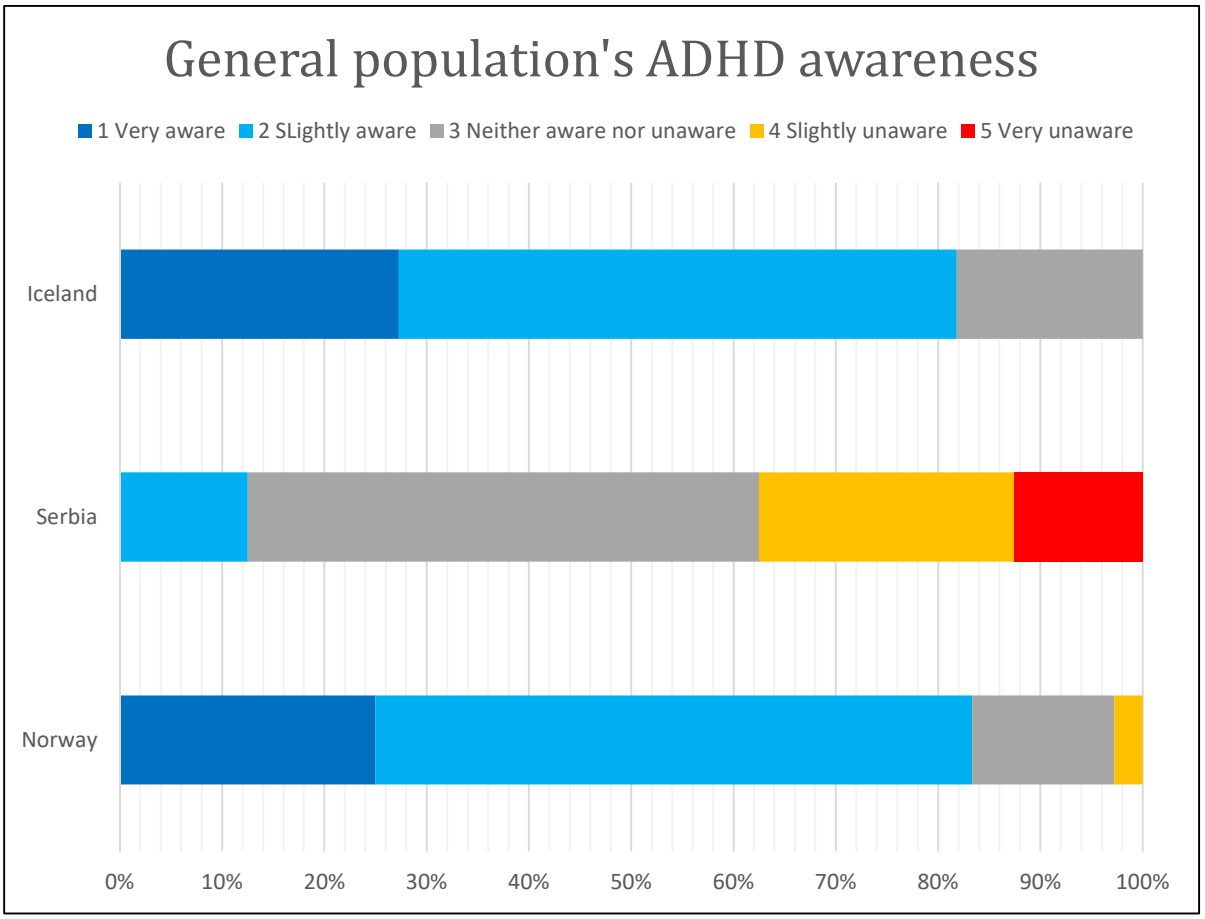

Figure 19. Awareness of general population about ADHD, according to respondents. Data used to create this figure is available in Appendix 16.

The general population's awareness of ADHD was rated by 81.8% of Icelandic, 83.3% of Norwegian and 12.5% of respondents from Serbia as either very or slightly aware of ADHD (Figure 19). The differences between groups were statistically significant ($H(2)=26.3$ $p<0.001$; Serbia-Norway $p<0.001$, Serbia-Iceland $p<0.001$). The teachers' awareness for ADHD were rated by 83.3% of respondents from Norway, 75% of respondents from Iceland and 52.9% of respondents from Serbia either to be slightly or very aware of ADHD. The differences between groups were statistically significant ($H(2)=10.22$ $p=0.006$; Serbia-Norway $p=0.004$).

ADHD awareness of other healthcare professionals (non-prescribing MDs and nurses) was rated to be 36.4% of Icelandic, 38.9% of Norwegian and 0% of Serbian respondents, as very aware. However, it was rated as slightly aware by 50% of Icelandic, 41.7% of Norwegian and 52.9% of Serbian respondents (Figure 20). The differences between groups were statistically significant (H(2)=12.49 p=0.002; Serbia-Norway p=0.003, Serbia-Iceland p=0.008).

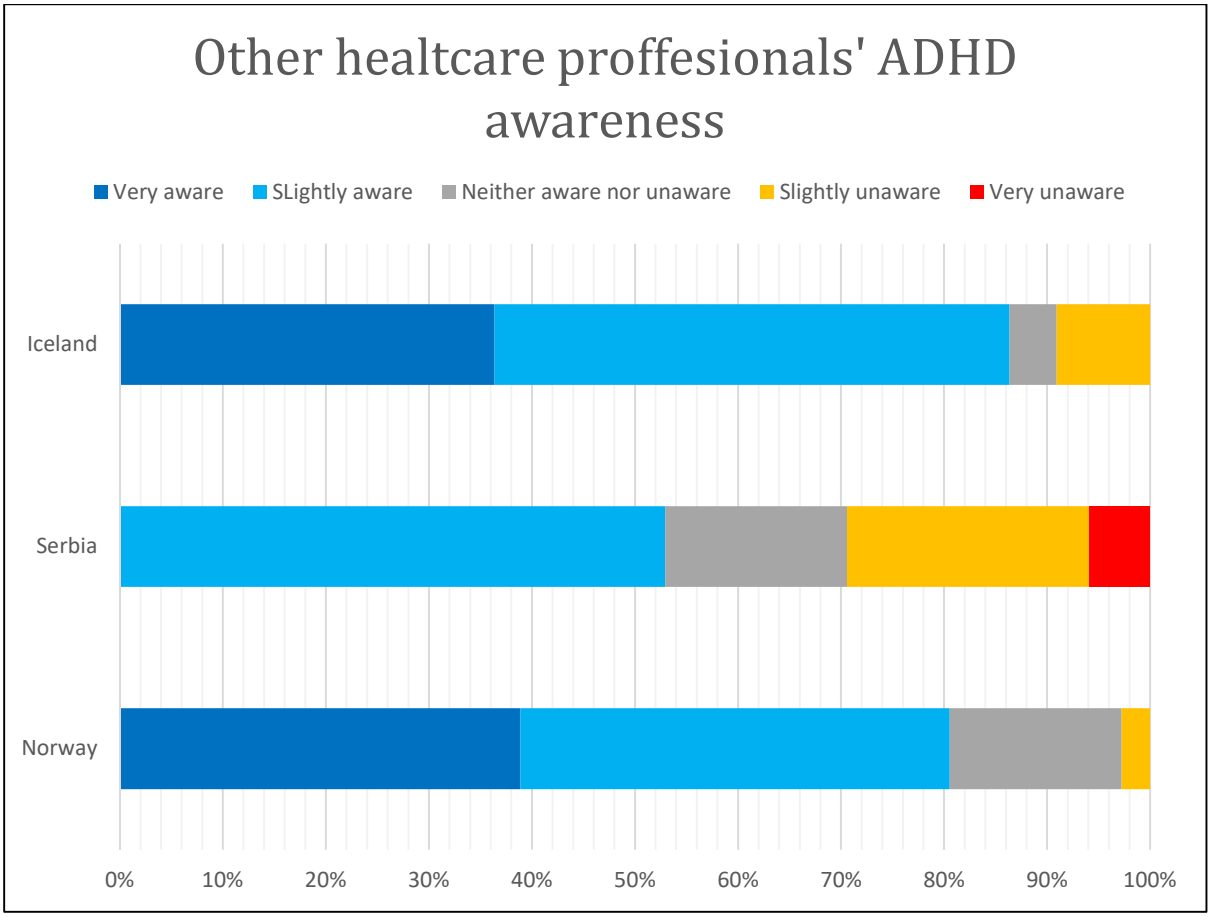

Figure 20. Awareness of other non-prescribing healthcare professionals about ADHD, according to respondents. Data used to create this figure is available in Appendix 17.

ADHD was perceived as a mental and/or behavioural illness by other healthcare professionals (non-prescribing MDs and nurses) according to 88.9% of Norwegian, 85.7% of Icelandic and 35.3% of Serbian respondents. The rest of respondents have reported either psycho/social/situational condition or phase in child development (Figure 21). The differences between groups were statistically significant ($H(2)=17.97$ $p<0.001$; Serbia-Norway $p<0.001$, Serbia-Iceland $p=0.003$).

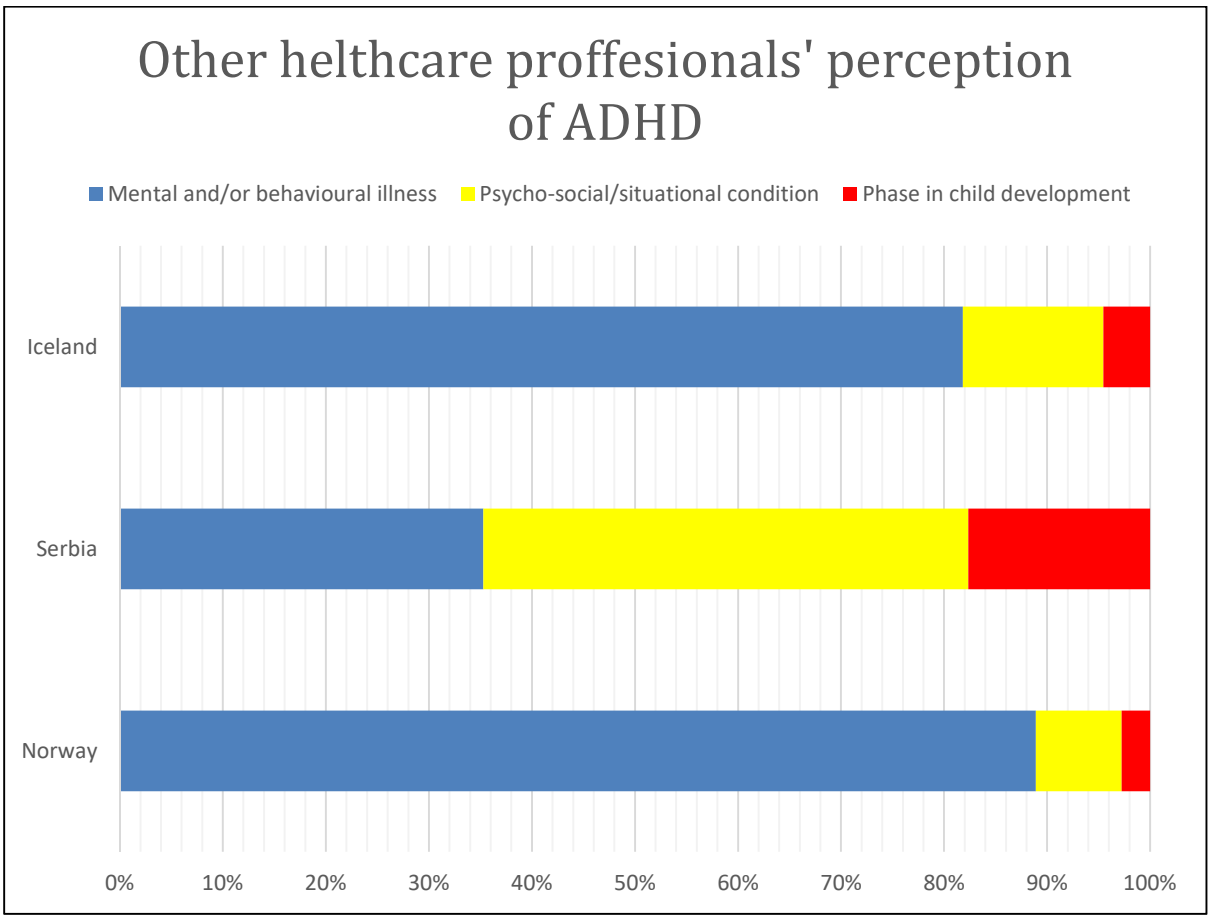

Figure 21. Perception of ADHD of other non-prescribing healthcare professionals, according to respondent. Data used to create this figure is available in Appendix 18.

The readiness/diligence of other health care professionals (non-prescribing MDs and nurses) to refer patients to right institutions, was scored by 50% of Norwegian, 18.2% of Icelandic and 0% of Serbian respondents as very diligent. While 36.1% of Norwegian, 54.5% of Icelandic and 64.7% of Serbian respondents rated their colleagues as slightly diligent (Figure 22). Differences were statistically significant (H (2)= 14.56 p=0.001; Serbia-Norway p=0.001).

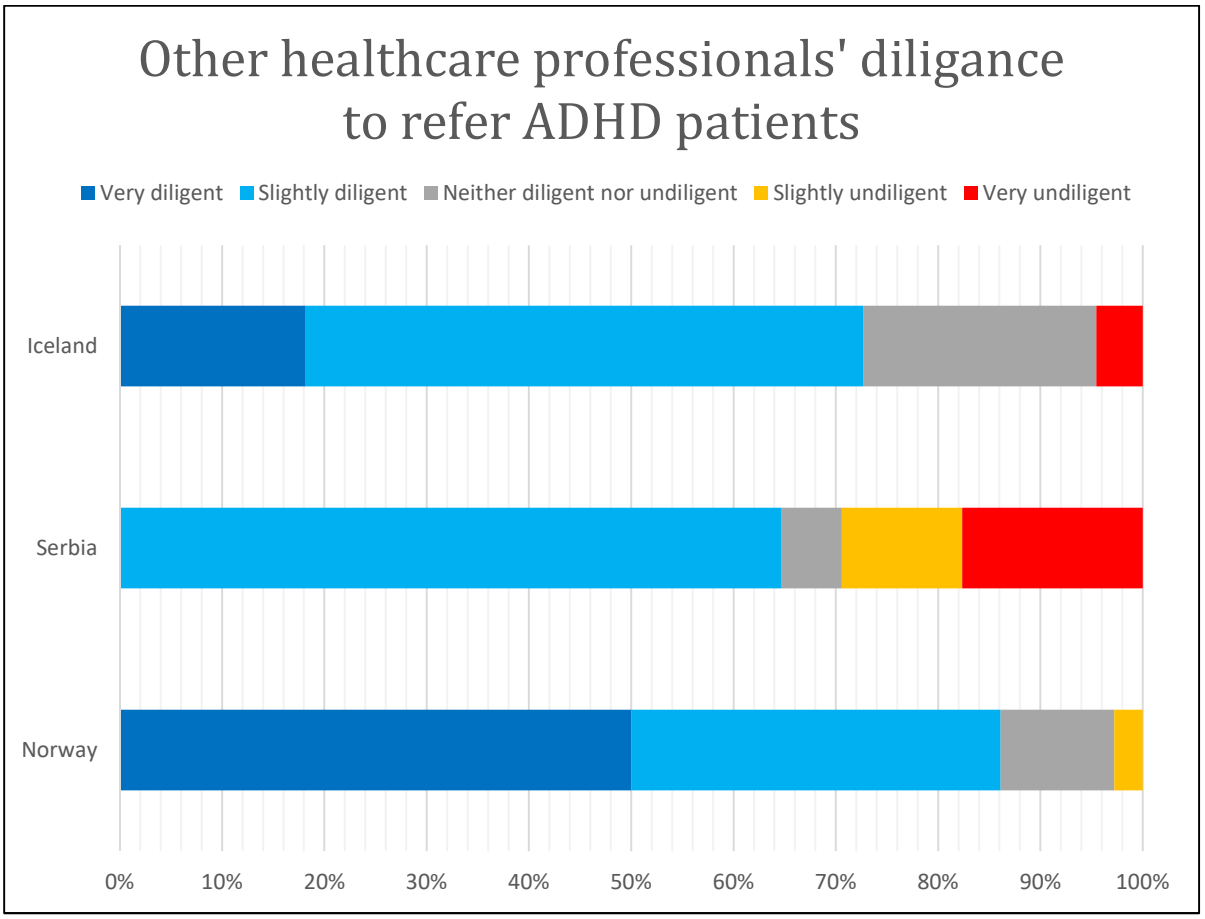

Figure 22. Diligence of other non-prescribing healthcare professionals to refer suspected ADHD patient to right institution, according to respondents. Data used to create this figure is available in Appendix 19.

ADHD medications were perceived as effective by parents according to 76.5% of Icelandic, 48.3% of Norwegian and 18.8% of Serbian respondents, while the rest of respondents rated the perceived effectiveness of ADHD medications as slightly effective. The differences were statistically significant (H(2)=11.15 p=0.004 ; Serbia-Iceland p=0.003). Parents regarded ADHD medications as safe or slightly safe according to 73.5% of Norwegian, 25% of Serbian and 21.2% of Icelandic respondents. Parents regarded ADHD medications as slightly unsafe according to 11.8% of Norwegian, 31.6% of Icelandic and 25% of Serbian respondents.

Difference between groups were statistically significant (H(2)=14.01 p=0.001 Serbia-Norway p=0.003, Serbia-Iceland p=0.002).

The highest score for misuse and diversion potential of ADHD medications was on Iceland, followed by Norway and the lowest is in Serbia. On scale from one to ten, where one is the lowest and ten is the highest potential for misuse and diversion, Icelandic respondents have rated with average of 6.24 (SD 2.57), Norwegian with 5.06 (SD 2.10) and Serbian respondents with 3.29 (SD 1.77) (Figure 23). The differences between groups were statistically significant (H(2)=13.25 p= 0.001; Serbia-Norway p=0.043, Serbia-Iceland p=0.001).

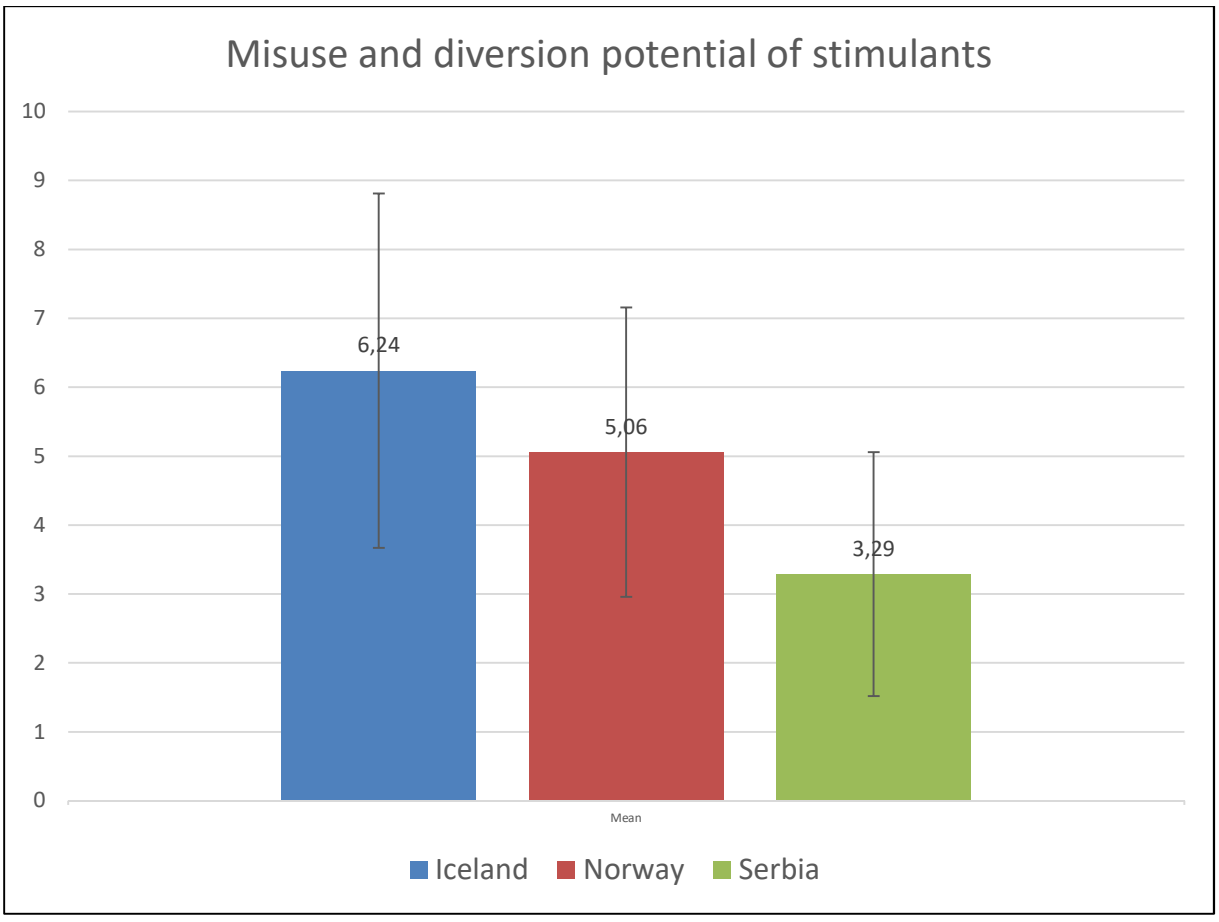

Figure 23. Misuse and diversion potential of stimulants, according to respondents. Data used to create this figure is available in Appendix 21.

4 Discussion

4.1 Study population

Norwegian group was the largest in terms of number of respondents, almost twice as large as Serbian and Icelandic. The total sample had similar number of female and male respondents, while groups had some differences. Icelandic group had the least percentages of females, while the Serbian had the least male respondents. The average age was almost the same in Norwegian and Serbian groups, unlike Icelandic group that had significantly higher age average. However, the experience of respondents in the treatment of ADHD was evenly distributed between groups, with over 50% of those with more than 10 years of experience in ADHD treatment. The most pronounced difference between groups was in terms of adult/children prescribers' ratio. Both Norwegian and Serbian group had a majority of children and adolescents prescribers, while Icelandic group consisted of a majority of adult prescribers. Due to the different sizes of groups, we chose to present results of this study in percentages, even though the number of respondents is limited.

4.2 Main findings

Significant differences in terms of treatment approaches, attitudes and awareness and variety and reimbursement, but also some unexpected similarities in terms of diagnosing and referring process were observed between Serbian group compared to Icelandic and Norwegian groups. On the other hand, Norwegian and Icelandic group were much more similar, leaving mostly subtle differences, which is in accordance with similar structures of healthcare around ADHD, availability/reimbursement of medications and similar cultural backgrounds.

4.2.1 Differences

Diagnosing

A majority of Norwegian and Icelandic respondents receive patients after referral made from general practitioners from public healthcare services. This finding is in accordance with the system structure where general practitioners are primary level for both children and adults in these countries. However, in Serbia paediatricians from public healthcare services represent primary level for children and major referring entity, since very high share of ADHD patients in Serbia are children and adolescents. Almost one-half of respondents from Norway and Iceland have reported social services and psychologist as often source of referring of suspected ADHD. It can indicate active involvement of other non-medical organisation in ADHD surveillance, which is in accordance with results of large Norwegian study, where school services and social services were the second and third most frequent referral sources to child and adolescent psychiatry, behind somatic healthcare institutions [124].

Respondents from Norway were the most satisfied with both referring process and transition to adult services, while respondents from Iceland were those who were the least satisfied. Since Serbia has neither approved indication nor registered medications for treatment of adult ADHD, it was expected that they were not satisfied with transition to adult services. However, the ADHD was perceived as "child" illness not so long ago, thus transition to adult services can be still challenging for both patients and physicians in many European countries [125]. However, the dissatisfaction of Icelandic respondents could be related to the fact that majority of Icelandic respondents treat adult population, while the abuse of ADHD medications in Iceland is common. Additionally, Icelandic respondents rated highest stimulants' misuse potential which could indicate dissatisfaction of prescribers with the system around ADHD that does not provide tools to distinguish between patients and drug dealers/misusers.

Treatment

There were substantial differences in using non-medical treatments such as behavioural therapy, family interventions, school interventions and neurofeedback. The share of those who are prescribing behavioural therapy as a standalone treatment is highest in Serbia. More than half of respondents have stated using behavioural therapy as a standalone treatment that is in accordance with previous research conducted in Serbia [111]. On the other hand, in Norway and Iceland, prescribing behavioural therapy as a standalone treatment was marginal, that is in

accordance with guidelines, where non-pharmacological treatment as a standalone is recommended for preschool children only [88]. Both Icelandic and Norwegian guidelines recommend use of non-pharmacological treatment options in addition to medications for both children and adults [39, 104]. We can assume that a restrictive government policy towards prescription rate and unavailability of other ADHD medications in Serbia affects treatment choices to great extent. However, we cannot exclude the possibility that prescribers' attitudes and practices are simply different, which affect the prescription rates also. Although, the highest share of satisfied respondents with behavioural therapy as a standalone was from Serbia, followed by Norway and least satisfied were from Iceland, overall differences were not statistically significant. As an example from the Western Europe is Italy, where the prescription rates of ADHD medications are as low as in Serbia, while the utilization of behavioural therapy is also high [114].

The highest number of respondents who stated prescribing medications as a standalone treatment were in Icelandic, followed by Serbian and least in Norwegian group. This is one of just few differences observed in this study between Icelandic and Norwegian groups. Respondents from Icelandic group stated four times more frequent use of medications as a stand-alone treatment than Norwegian respondents did. Additionally, no one from Icelandic group does exclude the use of medications in ADHD, unlike Serbian and Norwegian groups, where there were two respondents in each group. It could indicate that Icelandic prescribers are more prone to prescribe medications, rather than any other treatment option. However, the non-pharmacological therapies are not reimbursed for adults in Iceland, which might additionally move prescribers from these treatment options.

The majority of respondents have stated that they consider using medications in ADHD treatment, which is expected considering the level of recommendation for treating the condition with medications [88]. Although there are differences between groups regarding first line treatment, methylphenidate was used by a majority of physicians in all three countries. Such a finding is in accordance with some guidelines, but also with the consumption of ADHD medications in these countries [109, 111]. Icelandic respondents have also reported use of atomoxetine as the first line. Such a finding may be the consequence of high percentage of adult-prescribing respondents in Iceland, while atomoxetine can be prescribed as the first line treatment under a suspicion of substance abuse [39]. One part of Serbian respondents has also reported use of dexamphetamine and antipsychotics as the first line treatment. Since

dexamphetamine are unregistered in Serbia, we can just assume that medications were being brought from one of surrounding countries, emphasizing the need for other medications to be registered in Serbia.

More than one-half of Norwegian respondents reported use of lisdexamphetamine as the second line, while other part is using atomoxetine. In Iceland, preferred second line treatment according almost one-half respondents is atomoxetine. Use of both atomoxetine and lisdexamphetamine are in accordance with the medical treatment guidelines [55]. Serbian respondents have reported use of antipsychotics as the second line. Although, antipsychotics are not recommended in a treatment of ADHD as a second line, it can be seen as justified in the absence of other treatment options. Use of all other medications in ADHD treatment is "off-label" in Serbia. As for the third line, more than one-half of Norwegian respondents reported use of atomoxetine, while one third of Icelandic respondents reported the use of bupropion.

There were just respondents from Serbia who reported use of antipsychotics in the treatment of ADHD, mainly risperidone and aripiprazole. Although, atypical antipsychotics are not regarded as a standard ADHD treatment, the prescription rates of these medications are substantial [56]. Other medications reported in this study were modafinil, antidepressants, anxiolytics and mood stabilizers, that are being used "off label" in ADHD. Modafinil is medication approved for narcolepsy, while being under testing for ADHD [126].

A level of confidence in identifying the side effects of stimulants was significantly higher among physician from Norway and Iceland than among those from Serbia. Although methylphenidate is the first choice medication in Serbia for children and adolescents, the use of methylphenidate is less frequent than in Norway or Iceland [109, 111]. It can lead to assumption that Serbian prescribers do not have the same level of experience in prescribing methylphenidate. Furthermore, adult prescribers in Serbia have very limited experience with methylphenidate, due to the policy makers' unrecognition of adult ADHD treatment with methylphenidate. However, the results for managing side effects of stimulants were similar across the three countries.

Availability/reimbursement of medications

The main findings were that Serbian respondents think that both the variety and reimbursement of medications available had a negative impact on the number of patients treated, unlike Norwegian and Icelandic respondents who reported the opposite. Both, the reimbursement and variety of medications were rated significantly lower from Serbian perspective in contrast to Icelandic/Norwegian. The fact that Serbian respondents think that variety of medication and reimbursement conditions had a negative impact on the number of patients treated can be seen in a light that there is only one medication registered; sustained release methylphenidate formulation, Concerta®. It is the only medication available in Serbia with paediatric ADHD indication, with the prescriptions only from specialists from government appointed institutions [107].

Since adult ADHD patients do not have any registered medication at all, adult-prescribers have no other option than to use Concerta® "off label" with the full payment by the patient or to use some other "off label" treatment options such as bupropion, clonidine or antipsychotics. It can lead much often to therapy failure and discontinuation of therapy, while the cost of unreimbursed medications could be unbearable from the patients' perspectives, and consequently leaving a number of patients without treatment.

On the other hand, both Icelandic and Norwegian respondents reported that availability of medications and reimbursement conditions were increasing the number of patients treated. It can be put in context that conditions and variety of medications did not limit the number of patients treated. Hence, the variety of medications available was allowing prescribers to try out different medications in case of partial response or non-response, while reimbursement conditions endorsed it. As a result, it possibly increases a number of patients treated [127].

Attitudes and awareness

The results are showing significantly higher stigma levels reported by physicians in Serbia, where a majority of Serbian respondents has stated medium or high levels of stigma, compared with around one-half of Norwegian and Icelandic respondents. It indicates higher level of stigma that can be aggravating for patients and resulting in lower rates of self-referring and seeking help, even when the consequences of not seeking help might be severe [128].

According to the results of this research there is substantially lower public awareness, as well lower awareness of teachers and non-prescribing healthcare professionals in Serbia compared to Norway and Iceland. Previous researches done in Serbia, have also come to a

similar conclusion regarding ADHD awareness [111, 129]. Public awareness is important facilitating factor that have large impact on diagnosing rates of ADHD [119]. Furthermore, the results indicate that ADHD is predominantly perceived as non-mental illness in Serbia by the general population and other healthcare professionals such as non-prescribing physicians or nurses, who seems additionally to be the least diligent/ready to refer patients to right institution. However, these findings are projection of respondents believes, therefore, measuring these values in direct way would be necessary to draw more valid conclusions. Health behaviours are under strong influence of individual's beliefs about the illness. In case of paediatric ADHD, parental health beliefs and beliefs about origins of the behaviuor affect referral rates and their children's medical care in general [130].

4.2.2 Similarities

Diagnosing

Waiting-time for receiving ADHD diagnose and specific treatment was without a statistical significance. This finding is unexpected regarding the fact that Serbia has only 25 specialist entitled to prescribe ADHD medications by the National Health Insurance Fund, and at the same time Serbia is the most populous country with more than 7 million inhabitants, which leave us with one ADHD specialist per around 280 000 inhabitants [131]. On the other hand Norway has more than 2 800 specialist entitled to diagnose and treat ADHD per 5.2 million inhabitants, meaning one ADHD specialist per around 2000 inhabitants [132, 133]. Considering the result, we can hypothesize that the referral rates in Serbia are more than 100 times less frequent compared to Norway [108], which is in accordance with low awareness, and higher stigma levels reported in this study as well. This finding can be interesting for further research in the field of ADHD in Serbia. We did not have opportunity to ask those who refer patients about their estimations and opinions about referring process and waiting-times. They could provide significant information, since they are on the other side of the referring process.

Majority of respondents from all countries have answered that they are using the ICD–10 classification system. In both Norway and Iceland, physicians can follow both the ICD and DSM classification according to their guidelines [39, 104]. Considering the high consumption of ADHD medications in Norway and especially Iceland, this finding was unexpected, since the DSM criteria has lower threshold for diagnosing ADHD [41]. Hence, the ICD-10 criteria is restrictive and focused on the severe form of combined subtype ADHD in children, thus leading

to unrecognition and underdiagnosing of ADHD in adults [134]. This finding is not in accordance with diagnostic trends and oncoming the ICD-11 classification that defines ADHD in the same way as the DSM-5 [6].

Treatment

Satisfaction levels with pharmacological treatment options were different but statistically insignificant between countries. The overall satisfaction with effectiveness of medications was highest with sustained release methylphenidate in all three countries. It is in accordance with superior effect size of stimulants over other medications used in ADHD [135]. However, immediate release methylphenidate formulations were rated in average lower than sustained release. Although pharmacokinetic of methylphenidate limits the use of immediate release formulations as the first choice, it allows combining with sustained release formulations in order to achieve better symptoms control throughout the day [136].

Although amphetamines have the same level of recommendations as methylphenidate, they are not used so often in Europe as in the USA [137]. However, both Norwegian and Icelandic reimbursement systems imply the use of methylphenidate as the first line. All types of amphetamines are seldom used as the first line treatment according to respondents. Satisfaction with effectiveness of amphetamines is highest in Norway, where lisdexamphetamine are preferred form of amphetamine. However, that is not surprising when considering the benefits of lisdexamphetamine in comparison to other forms of amphetamines, in terms of kinetic and misuse/diversion potential [138].

4.3 Strengths

The strength of this research lies in the fact that this is maybe the first study of its kind in this regions, that is mapping and comparing diagnosing/prescribing practices, believes and attitudes of prescribing physicians. Furthermore, the response rate of Serbian paediatric prescribers was more than satisfactory; we managed to reach about one-half of them. This is the first research that enrolled Serbian adult psychiatrists regarding ADHD.

By using an online survey method, we managed to reach a significant number of specialists diagnosing and treating ADHD in a short time. In order to capture as broader information as possible, we have added a portion of open-ended questions that provided information we could not predict in designing the questionnaire. The questionnaire is developed under the supervision of expert in the field of child psychiatry and undergone pilot-testing and content validity testing. The number of answers from the same IP address was limited to one, to protect us from multiple attempts of answering a survey.

4.4 Limitations

One of the main limitations for this study was the absence of qualitative research on the topic, which could lead us in specific areas of concern. The qualitative approach, focused group interview, was considered, but could not materialise due to many factors. The unavailability of respondents, physicians specialised in child and adolescent psychiatry, psychiatrist and neurologists involved in the treatment of ADHD, and different geographical locations, were some of the main reasons to abandon the focus group interview approach. Additionally, the fact that study involves Norwegian, Serbian and Icelandic physicians involved in treatment of ADHD, have led to a language barrier in materialising the interviews.

A questionnaire as a method is also limiting, because of all the questions are pre-prepared. Therefore, deep understanding of the subject was hard to get. Hence, direct contact with respondents was not an option, thus further explanations and clarification of questions and answers were out of the reach. The questionnaire was developed for this study, so validity and reliability can be questioned, since it was never used in research purposes before. As we were not able to get mailing lists, we had to use intermediaries and indirectly distribute questionnaire to targeted specialists. Therefore, we were unable to track response rates in Norway and Iceland, which can be seen as a limitation because of possible risk of low response rates in these two

countries. The sample size from Norway is limited, considering the number of potential respondents, while uneven distribution of child and adult prescribers could also affect the results of this study. Despite the fact that physicians are expected to understand English language, we cannot exclude the possibility that some of the participants were not so competent in understanding English language.

Finally, the parents of children treated for ADHD, non-prescribing paediatricians and lay people were not included to study the awareness and stigma of the disorder.

4.5 Further research

Future studies need to focus of identifying risk and protective factors for the current attitudes, practices and believes of those who treat ADHD in all three countries.

It could be of particular interest to conduct research with non-prescribing paediatricians in Serbia, who are numerous, but unable to independently diagnose and treat the condition. Their views regarding referral, waiting time as well awareness could be different from those observed in prescribers.

Of particular importance would be to study epidemiological and prescribing patterns in adults ADHD in Serbia.

Further research about threshold for utilization of medications, as well as misuse/diversion of stimulants is necessary in order to address the higher consumption rates of stimulants in Iceland.

5 Conclusion

Considering referring and diagnostics, this study has shown that source of ADHD referral are paediatricians in Serbia, while in Norway and Iceland it is general practitioners. The waiting time for diagnostics and specific ADHD treatment are not significantly different in these three countries, in average 3 to 6 months for diagnostics and 1 to 6 months for specific treatment. However, the satisfaction with referring process seems to be the highest in Norway. The preferred classification system used in diagnosing ADHD in all three countries is ICD-10.

We came to the conclusion that the treatment approaches to ADHD are different between these three countries. The dominant pharmacological treatment approach to ADHD is observed in Iceland, while high non-pharmacological treatment utilization as stand-alone is present in Serbia. This study showed that the choice of medications is different in these three countries. However, sustained release methylphenidate is regarded as a the most effective and dominant in the fist line treatment. Hence, it seems that methylphenidate is the only medication that is being used in Norway as the first line treatment, unlike Serbia and Iceland, where atypical antipsychotics and atomoxetine are also a part of the first line. At the same time, the confidence level in identifying adverse effects of stimulants is lower in Serbia, compared to Norway and Iceland.

This study concludes that the healthcare system around ADHD in terms of variety and reimbursement of available specific ADHD medications has negative impact on the number of patients treated in Serbia, unlike Norway and Iceland.

Results of this study indicate lower ADHD awareness and dominant non-mental illness characterization of ADHD in Serbia, unlike Iceland and Norway where ADHD is considered as a disorder. These findings might indicate much lower referral rates of ADHD patients, and consequently under-diagnosing of the disorder in Serbia.

However, further research is needed to capture effect sizes of our findings in order to draw valid conclusions.

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Appendix

Appendix 1

The table shows number of male and female respondents in this survey.

	Norway	Serbia	Iceland
Number of female respondents	22	13	9
Number of male respondents	15	6	14
Total	37	19	23

Appendix 2

This table presents number of respondents with predefined experience level in treatment of ADHD

Respondents experience with ADHD treatment	Norway	Serbia	Iceland
Under 1 year	2	1	0
1-3 years	1	1	0
3-5 years	5	3	1
5-10 years	7	3	7
more than 10 years	22	11	15

Appendix 3

This table presents number of respondents according population they are treating.

	Norway	Serbia	Iceland
Child and adolescent psychiatry	24	11	3
Adult psychiatry	10	6	19
Both	3	2	1

Appendix 4

This table presents number of respondents who gave a specific answer about adequacy of referring process for ADHD patients

	Norway	Serbia	Iceland
Very adequate	11	0	7
Slightly adequate	16	8	3
Neither adequate nor inadequate	6	6	5
Slightly inadequate	3	2	3
Very inadequate	1	3	5

Appendix 5

This table presents number of respondents with specific answer about waiting time from suspicion on ADHD to diagnose

	Norway	Serbia	Iceland
Less than a month	2	1	6
1-2 months	8	4	2
3-4 months	11	2	4
5-6 months	13	1	2
more than 9 months	3	11	9
Total	37	19	23

Appendix 6

This table presents number of respondents distributed by classification criteria used in diagnosing of ADHD

	Norway	Serbia	Iceland
DSM - 5	4	3	6
ICD - 10	32	16	16
Both	1	0	1

Appendix 7

This table presents number of respondents distributed by treatment options they are prescribing to ADHD patients

	Norway	Serbia	Iceland
Medications	35	17	23
Behavioural therapy	25	9	7
Cognitive-Behavioural therapy	15	8	12
Family inteventions	31	14	4
School interventions	26	10	3
Neurofeedback	5	4	1

Appendix 8

This table presents number of respondents distributed by usage of behavioural therapy as a stand-alone treatment and usage of medications as a stand-alone treatment in ADHD

	Behavioural therapy as a stand-alone treatment		Medications as a stand-alone treatment	
	Yes	No	Yes	No
Norway	5	32	59	86
Serbia	10	9	8	7
Iceland	3	19	35	51

Appendix 9

This table presents the number of respondents distributed by first line treatment.

	Norway	Serbia	Iceland
Methylphenidate	35	10	16
Amphetamine	1	0	0
Dexamphetamine		3	0
Lisdexamphetamine		0	1
Atomoxetine		0	6
Bupropione		1	0
Antipsichotics		2	0
Total	36	16	23

Appendix 10

This table presents number of respondents distributed by satisfaction level with sustained release methylphenidate formulations.

	Effectiveness of sustained release methylphenidate formulations		
	Norway	Serbia	Iceland
Very satisfied	12	6	11
Slightly satisfied	20	6	9
Neither satisfied nor unsatisfied	4	4	0
Slightly unsatisfied	0	0	0
Very unsatisfied	0	0	1

Appendix 11

This table presents mean scores of satisfaction with effectiveness of different types of medications and standard deviations, on the five grade Likert like scale from one to five, where one represents Very unsatisfied and five represents Very satisfied.

	Mean score	SD
Sustained release methylphenidate	4,16	0,85
Prefered amphetamine	3,71	0,99
Immediate release methylphenidate	3,38	0,96
Atomoxetine	3,11	1,07

Appendix 12

This table presents number of respondents distributed by confidence level in identifying adverse effects in stimulants

	Norway	Serbia	Iceland
Very confident	22	5	13
Slightly confident	11	6	9
Neither confident nor unconfident	3	4	1
Slightly unconfident	1	2	0
Very unconfident	0	2	0

Appendix 13

This table presents mean and standard deviation values for rating scores of variety and reimbursement of available ADHD medications, according to respondents.

		Variety of ADHD medications available for children and adolescents	Variety of ADHD medications available for adults	Reimbursement of ADHD medications for children and adolescents	Reimbursement of ADHD medications for adults
Norway	Mean	7,29	6,06	8,39	6,10
	Std. Deviation	1,811	2,394	1,308	2,343
Serbia	Mean	4,06	3,18	5,19	3,25
	Std. Deviation	2,407	2,430	2,455	2,145
Iceland	Mean	6,83	6,40	6,64	6,95
	Std. Deviation	1,642	1,569	1,748	1,596

Appendix 14

This table presents mean and relative scores given for influence of variety and reimbursement of medications available for adults. Mean scores are gathered from Likert like scale, and coded where one represents substantial decreasing effect, two represents slightly decreasing effect, three represents no effect (neither decrease or increase), four represents slightly increasing effect and five represents substantially increasing effect. Relative scores are obtained by subtraction of 3 from mean score, in order to get more representable comparison, where positive values implies increasing effect, while negative values decreasing effect.

	Variety of medications for adults			Reimbursement of medications for adults		
	Mean score	SD	Relative score (Mean score - 3)	Mean score	SD	Relative score (Mean score - 3)
Norway	3,29	1,088	0,29	3,35	1,178	0,35
Serbia	2,17	0,924	-0,83	2,35	0,931	-0,65
Iceland	3,33	0,913	0,33	3,73	0,827	0,73

Appendix 15

This table presents number of respondents distributed by stated stigma level

	Norway	Serbia	Iceland
No stigma	3	0	0
Low stigma	16	2	13
Medium stigma	16	10	9
High stigma	1	5	1

Appendix 16

This table presents the number of respondents distributed by awareness level stated for general population

	Norway	Serbia	Iceland
Very aware	9	0	6
SLightly aware	21	2	12
Neither aware nor unaware	5	8	4
Slightly unaware	1	4	0
Very unaware	0	2	0

Appendix 17

This table presents number of respondents distributed by stated awareness level of other non-prescribing healthcare professionals

	Norway	Serbia	Iceland
Very aware	14	0	8
SLightly aware	15	9	11
Neither aware nor unaware	6	3	1
Slightly	1	4	2
Very unaware	0	1	0

Appendix 18

This table presents number of respondents distributed by stated perception of ADHD by other non-prescribing healthcare professionals

	Norway	Serbia	Iceland
Mental and/or behavioural illness	32	6	18
Psycho-social/situational condition	3	8	3
Phase in child development	1	3	1

Appendix 19

This table presents number of respondents distributed by referring diligence level stated for other non-prescribing healthcare professionals

	Norway	Serbia	Iceland
Very diligent	18	0	4
Slightly diligent	13	11	12
Neither diligent nor undiligent	4	1	5
Slightly undiligent	1	2	
Very undiligent	0	3	1

Appendix 20

This table present number of different specialist entitled to prescribe ADHD medications independently. Adapted from Norwegian Medical Association [133]

Associations of specialist	The number of members with approved specialisation
Norwegian child and adolescent psychiatric association	324
Norwegian psychiatric association	1485
Norwegian neurological association	401
Norwegian paediatric association	620
Total	**2830**

Appendix 21

This table presents means and standard deviation values for rating scores for misuse and diversion potential of stimulants on the scale from 1 to 10, where 1 represents the lowest, while 10 the highest potential for misuse and diversion.

	Mean	SD
Serbia	3,29	1,77
Norway	5,06	2,1
Iceland	6,24	2,57

Appendix 22

The questionnaire used in research

1. How old are you?

2. What is your gender?

◯ Female

◯ Male

3. What country and city do you work in?

◯ Norway

◯ Serbia

◯ Iceland

City (optional) :

4. How would you describe the municipality where you reside?

◯ Urban ◯ Rural

5. If possible choose how many people live in municipality where you reside:

◯ Less than 10 000

◯ Between 10 000 and 50 000

◯ Between 50 001 and 150 000

◯ Between 150 001 and 500 000

◯ Between 500 001 and 1000 000

◯ More than 1000 000

◯ Can't tell

6. You are directly involved or have been involved in diagnosing ADHD in:

- [ ] children and adolescents up to age of 18 years
- [ ] adult population
- [ ] Other (please specify)

7. How many years in total have you been working in jobs that brought you into contact with ADHD patients?

- ○ Under 1 year
- ○ 1-3 years
- ○ 3-5 years
- ○ 5-10 years
- ○ More than 10 years

8. Who refers patients for ADHD assessment to you?

- [ ] Paediatricians or nurses from public health services
- [ ] Paediatricians or nurses from private health services
- [ ] General practitioners
- [ ] Teachers and/or school staff
- [ ] Other (please specify)

9. How much time passes on average once a person is ADHD suspected until he/she receives the diagnosis?

- ○ Less than a month
- ○ 1-2 months
- ○ 3-4 months
- ○ 5-6 months
- ○ 7-8 months
- ○ More than 9 months

10. How much time passes on average once a person is diagnosed with ADHD until he/she receives specific treatment?

- ○ Less than a month
- ○ 1-2 months
- ○ 3-4 months
- ○ 5-6 months
- ○ 7-8 months
- ○ More than 9 months

11. How would you describe referring process for ADHD diagnosis/treatment?

- ○ Very adequate
- ○ Slightly adequate
- ○ Slightly inadequate
- ○ Very inadequate

◯ Neither adequate nor inadequate

12. Which classification system do you rather follow for ADHD diagnosis?

◯ DSM-5

◯ ICD-10

◯ Other (please specify)

13. Which therapy options do you consider for ADHD treatment?

☐ Medications

☐ Behavioural therapies

☐ Cognitive-behaviour therapy

☐ Other (please specify)

☐ Family interventions

☐ School interventions

☐ Neurofeedback

14. Do you prescribe behavioural therapy as a standalone treatment?

◯ Yes

◯ No

15. Do you prescribe ADHD medications as a standalone treatment?

◯ Yes ◯ No

16. How satisfied or dissatisfied are you with effectiveness of behavioural therapy only?

◯ Very satisfied

◯ Slightly satisfied

◯ Neither satisfied nor dissatisfied

◯ Other (please specify)

◯ Slightly dissatisfied

◯ Very dissatisfied

17. What is your preferred medical treatment for ADHD?

	Amphetamine	Dexamphetamine	Lisdexamphetamine	Methylphenidate	Atomoxetine	Guanfacine	Clonidine	Imipramine	Bupropion	Antipsychotics
First line	○	○	○	○	○	○	○	○	○	○
Second line	○	○	○	○	○	○	○	○	○	☐
Third line	○	○	○	○	○	○	○	○	○	○

If you are using antipsychotics in treatment of ADHD please specify which?

18. Are there some other medications that you are using in treatment of ADHD?

○ Yes

○ No

If yes, please specify which

19. How satisfied or dissatisfied are you with effectiveness of sustained release methylphenidate formulations?

○ Very satisfied
○ Slightly satisfied
○ Neither satisfied nor dissatisfied
○ Slightly dissatisfied
○ Very dissatisfied
○ Not applicable

20. How satisfied or dissatisfied are you with the effectiveness of immediate release methylphenidate formulations?

○ Very satisfied
○ Slightly satisfied
○ Neither satisfied nor dissatisfied
☐ Slightly dissatisfied
☐ Very dissatisfied
☐ Not applicable

21. How satisfied or dissatisfied are you with the effectiveness of amphetamine which you prefer to prescribe?

○ Very satisfied
○ Slightly satisfied
○ Neither satisfied nor dissatisfied
○ Slightly dissatisfied
○ Very dissatisfied
○ Not applicable

Please specify which

22. How satisfied or dissatisfied are you with the effectiveness of atomoxetine?

- ◯ Very satisfied
- ◯ Slightly satisfied
- ◯ Neither satisfied nor dissatisfied
- ◯ Slightly dissatisfied
- ◯ Very dissatisfied
- ◯ Not applicable

23. How satisfied or dissatisfied are you with the effectiveness of other medications in treatment of ADHD?

- ◯ Very satisfied
- ◯ Slightly satisfied
- ◯ Neither satisfied nor dissatisfied
- ◯ Slightly dissatisfied
- ◯ Very dissatisfied
- ◯ Not applicable

please specify which

24. Do you combine two or more medications for ADHD treatment?

- ◯ Yes
- ◯ No

If yes, please specify:

25. What is your level of confidence in identifying adverse effects of stimulants?

- ◯ Very confident
- ◯ Slightly confident
- ◯ Neither confident nor unconfident
- ◯ Slightly unconfident
- ◯ Very unconfident

26. What is your level of confidence in the management of stimulants' adverse effects?

- ◯ Very confident
- ◯ Slightly confident
- ◯ Neither confident nor unconfident
- ◯ Slightly unconfident
- ◯ Very unconfident

27. How would you describe adherence to ADHD treatment with stimulants?

◯ Low ◯ Medium ◯ High

28. What are the reasons for discontinuing a stimulant medication?

☐ Ineffectiveness

☐ Side effects

☐ Other (please specify)

29. What is your level of confidence in identifying adverse effects of other ADHD medications (e.g. atomoxetine, clonidine, antipsychotics)?

◯ Very confident

◯ Slightly confident

◯ Neither confident nor unconfident

◯ Other (please specify)

◯ Slightly unconfident

◯ Very unconfident

30. Which of the following treatment options is/are in any way reimbursed for ADHD treatment for children and adolescents in your country:

☐ Amphetamine

☐ Dexamphetamine

☐ Lisdexamfetamine

☐ Methylphenidate

☐ Atomoxetine

☐ Clonidine

☐ Other (please specify)

☐ Guanfacine

☐ Imipramine

☐ Bupropione

☐ Behavioural treatment

☐ Cognitive behavioural treatment

☐ None

31. How would you describe the influence of variety of medications available in your country on the number of paediatric patients treated?

◯ It substantially decreases the number of patients treated

◯ It slightly decreases the number of patients treated

◯ It doesn't affect the number of patients treated

◯ It slightly increases the number of patients treated

◯ It substantially increases the number of patients treated

32. How would you rate variety of ADHD medications available for children and adolescents in your country on the scale from 1 to 10, where 1 is the lowest and 10 is the highest?

1	2	3	4	5	6	7	8	9	10	Not applicable
○	○	○	○	○	○	○	○	○	○	○

33. How would you rate reimbursement of ADHD medications for children and adolescents available in your country on the scale from 1 to 10, where 1 is the lowest and 10 is the highest?

1	2	3	4	5	6	7	8	9	10	Not applicable
○	○	○	○	○	○	○	○	○	○	○

34. How would you describe the influence of reimbursement of ADHD medications on the number of paediatric patients treated in your country?

- ○ It substantially decreases the number of patients treated
- ○ It slightly decreases the number of patients treated
- ○ It doesn't affect the number of patients treated
- ○ It slightly increases the number of patients treated
- ○ It substantially increases the number of patients treated

35. How would you describe the transition of ADHD patients to adult services?

- ○ Very adequate
- ○ Slightly adequate
- ○ Neither adequate nor inadequate
- ○ Slightly inadequate
- ○ Very inadequate

36. How important is to continue with ADHD treatment in adulthood?

- ○ Very important
- ○ Slightly important
- ○ Neither important nor unimportant
- ○ Slightly unimportant
- ○ Very unimportant

37. Which of the following treatment options is/are in any way reimbursed for adult ADHD treatment in your country?

- [ ] Methylphenidate
- [ ] Atomoxetine
- [ ] Dexamphetamine
- [ ] Lisdexamfetamine
- [ ] Amphetamine
- [ ] Imipramine
- [ ] Other (please specify)
- [ ] Bupropion
- [ ] Clonidine
- [ ] Guanfacine
- [ ] Behavioural treatment
- [ ] Cognitive behavioural treatment
- [ ] None

38. How would you describe the influence of variety of medications available in your country on the number of adult patients treated?

- ○ It substantially decreases the number of patients treated
- ○ It slightly decreases the number of patients treated
- ○ It doesn't affect the number of patients treated
- ○ It slightly increases the number of patients treated
- ○ It substantially increases the number of patients treated

39. How would you rate variety of ADHD medications available for adults in your country on the scale from 1 to 10, where 1 is the lowest and 10 is the highest?

1	2	3	4	5	6	7	8	9	10	Not applicable
○	○	○	○	○	○	○	○	○	○	○

40. How would you rate reimbursement of ADHD medications for adults available in your country on the scale from 1 to 10, where 1 is the lowest and 10 is the highest?

1	2	3	4	5	6	7	8	9	10	Not applicable
○	○	○	○	○	○	○	○	○	○	○

41. How would you describe the influence of reimbursement of ADHD medications on the number of adult patients treated in your country?

- ○ It substantially decreases the number of patients treated
- ○ It slightly decreases the number of patients treated
- ○ It doesn't affect the number of patients treated
- ○ It slightly increases the number of patients treated
- ○ It substantially increases the number of patients treated

42. Are there any limitations aggravating your everyday practice with diagnosing and treating ADHD?

43. How would you describe attitudes of your community towards psychiatry?

- ◯ Psychiatry is accepted as other branches of medicine, no trace of social stigma at all
- ◯ There is a low level of social stigma, towards psychiatry and psychiatric patients
- ◯ There is medium level of social stigma, towards psychiatry and psychiatric patients
- ◯ There is high level of social stigma, towards psychiatry and psychiatric patients

44. How would you describe attitudes of general population towards ADHD?

- ◯ ADHD is perceived as a mental and/or behavioural illness
- ◯ ADHD is perceived as a psycho-social/situational condition
- ◯ ADHD is not perceived as mental illness rather as a phase in child development

Other (please specify)

45. How would you describe awareness of general population towards ADHD?

- ◯ Very aware
- ◯ Aware
- ◯ Neither aware or unaware
- ◯ Unaware
- ◯ Very unaware

46. How would you describe attitudes of other healthcare professionals (nurses, non-prescribing MDs) towards ADHD?

- ◯ ADHD is perceived as a mental and/or behavioural illness
- ◯ ADHD is perceived as a psycho-social/situational condition
- ◯ ADHD is not perceived as mental illness rather as a phase in child development

Other (please specify)

47. How would you describe awareness of other healthcare professionals (nurses, non-prescribing MDs) towards ADHD?

- ◯ Very aware of ADHD
- ◯ Aware
- ◯ Neither aware or unaware
- ◯ Unaware
- ◯ Very unaware

48. How would you describe readiness/diligence of other healthcare professionals (nurses, non-prescribing MDs) to refer patients with suspicion of ADHD to right institution?

- ◯ Very diligent
- ◯ Slightly diligent
- ◯ Neither diligent nor non-diligent
- ◯ Slightly non-diligent
- ◯ Very non-diligent

49. How would you describe teacher's awareness?

- ◯ Very aware of ADHD
- ◯ Aware of ADHD
- ◯ Neither aware or unaware of ADHD
- ◯ Unaware of ADHD
- ◯ Very unaware

50. What do parents think about the effectiveness of ADHD medications?

- ◯ Effective
- ◯ Slightly effective
- ◯ Ineffective

Other (please specify)

51. What do parents think about the safety of ADHD medications?

- ◯ Very safe
- ◯ Slightly safe
- ◯ Neither safe or unsafe
- ◯ Slightly unsafe
- ◯ Absolutely unsafe

52. On the scale from 1 to 10, where 1 is the lowest and 10 is the highest probability, how would you rate misuse and diversion of stimulant medications used in ADHD treatment in your country?

1	2	3	4	5	6	7	8	9	10	Not applicable
◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

53. Is there anything else that you would like to share about your experience with ADHD treatment?

Appendix 23

Approval from Norwegian centre for research data

Ingunn Björnsdottir
Postboks 1068 Blindern
0316 OSL O

Vår dato: 08.11.2017 Vår ref: 56591 / 3 / OOS Deres dato: Deres ref:

Vurdering fra NSD Personvernombudet for forskning § 31

Personvernombudet for forskning viser til meldeskjema mottatt 13.10.2017 for prosjektet:

56591	Bruk av ADHD-medisin
Behandlingsansvarlig	Universitetet i Oslo, ved institusjonens øverste leder
Daglig ansvarlig	Ingunn Björnsdottir
Student	Dorde Zdravkovic

Vurdering

Etter gjennomgang av opplysningene i meldeskjemaet og øvrig dokumentasjon finner vi at prosjektet er meldepliktig og at personopplysningene som blir samlet inn i dette prosjektet er regulert av personopplysningsloven § 31. På den neste siden er vår vurdering av prosjektopplegget slik det er meldt til oss. Du kan nå gå i gang med å behandle personopplysninger.

Vilkår for vår anbefaling

Vår anbefaling forutsetter at du gjennomfører prosjektet i tråd med:

•opplysningene gitt i meldeskjemaet og øvrig dokumentasjon
•vår prosjektvurdering, se side 2
•eventuell korrespondanse med oss

Vi forutsetter at du ikke innhenter sensitive personopplysninger.

Meld fra hvis du gjør vesentlige endringer i prosjektet

Dersom prosjektet endrer seg, kan det være nødvendig å sende inn endringsmelding. På våre nettsider finner du svar på hvilke endringer du må melde, samt endringsskjema.

Opplysninger om prosjektet blir lagt ut på våre nettsider og i Meldingsarkivet

Vi har lagt ut opplysninger om prosjektet på nettsidene våre. Alle våre institusjoner har også tilgang til egne prosjekter i Meldingsarkivet.

Vi tar kontakt om status for behandling av personopplysninger ved prosjektslutt

Ved prosjektslutt 31.03.2018 vil vi ta kontakt for å avklare status for behandlingen av personopplysninger.

Se våre nettsider eller ta kontakt dersom du har spørsmål. Vi ønsker lykke til med prosjektet!

Marianne H øgetveit Myhren

Øyvind Straume

NSD – Norsk senter for forskningsdata AS Harald Hårfagres gate 29 Tel: +47-55 58 21 17 nsd@nsd.no Org.nr. 985 321 884
NSD – Norwegian Centre for Research Data NO-5007 Bergen, NORWAY Faks: +47-55 58 96 50 www.nsd.no

K ontaktperson: Øyvind Straume tlf: 55 58 21 88 / Oyvind.Straume@nsd.no

Vedlegg: Prosjektvurdering
K opi: Dorde Z dravkovic, djordje.zdravkovic1@gmail.com

Personvernombudet for forskning

Prosjektvurdering - Kommentar

Prosjektnr: 56591

INFORMASJONSKRIV

Personvernombudet viser til informasjonsskriv som ble ettersendt 7.11.2017. Utvalget informeres skriftlig og samtykker til deltakelse. Informasjonsskrivet er godt utformet, og vi har ingen merknader til dette.

DATASIKKERHET

Personvernombudet legger til grunn at forsker etterfølger Universitetet i Oslo sine interne rutiner for datasikkerhet. Dersom personopplysninger skal sendes elektronisk eller lagres på privat pc, bør opplysningene krypteres tilstrekkelig.

PROSJEKTSLUTT

Forventet prosjektslutt er 31.03.2018. Ifølge prosjektmeldingen skal innsamlede opplysninger da anonymiseres. Vi gjør oppmerksom på at anonymisering innebærer å bearbeide datamaterialet slik at ingen enkeltpersoner kan gjenkjennes. Det gjøres ved å slette IP-adresser som blir registrert.

Appendix 24

Informational letter that was used as invitation to the study

Request for participation in the research project

«Use of ADHD medications»

Background and purpose

Purpose with the research is to map and compare the attitudes and practises of those who prescribe ADHD treatment in Serbia, Iceland and Norway. This research is a part of Master thesis in social pharmacy, School of pharmacy, University of Oslo.

Target population

We are trying to reach physicians who treat ADHD patients and proscribe ADHD treatment in Norway, Serbia and Iceland.

What does participation in the study involve?

To take the part in the research means to answer the attached questionnaire. Questionnaire includes questions about ADHD treatment, medications, difficulties and reimbursement in your home country. It contains both multiple choice and open-ended questions.

What happens with your personal information?

All personal information will be treated confidentially. It is only student and supervisors who will have access to the data collected. Intention with the research is not to collect personal data. All personal data we encounter in process will be delete at once.

Participants would not be recognizable in later publications.

Project duration

The project will end in April 2018. Intention with the research is not to collect personal data. All personal data we encounter in process will be delete at once.

Voluntary participation

It is voluntary to participate in research, and you may at any time withdraw your consent without giving any reason.

If you would like to take part, or have any question regarding the research, contact:

1. Djordje Zdravkovic, student, telephone number: +47 47228692,
   E-mail: djordje.zdravkovic1@gmail.com

Or

2. Ingunn Björnsdottir, supervisor, telephone number: +47 22856650
   E-mail: ingunn.bjornsdottir@farmasi.uio.no

The study has been reported to the Personnel Ombudsman for Research, NSD - Norwegian Centre for Research Data AS.