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# **Overdiagnosis of ADHD and the role of emotion dysregulation in adulthood ADHD**

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# **Überdiagnose von ADHS und die Rolle der Emotionsdysregulation bei ADHS im Erwachsenenalter**

**Dissertation**

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# 1 Summary and abstract

## 1.1 English Abstract

Attention Deficit Hyperactivity Disorder (ADHD) is characterized by the core symptoms of inattention, impulsivity, and hyperactivity. It is one of the most frequently diagnosed disorders of childhood and adolescence, with a pooled worldwide prevalence rate of ~5 %. There are recent findings from different cultural contexts demonstrating a rise in the rate of ADHD diagnoses accompanied by increasing psychostimulant prescription rates (e.g., Dunlop & Newman, 2016; Connor, 2011; Safer, 2000) that lead to justifiable concerns about ADHD overdiagnosis. In this relation, age and gender biases are shown to cause false positive and false negative diagnosis and as an explanation for such phenomena these biases are shown to be significantly associated with subjective heuristics of diagnosticians (Mertens, Cwik, Margraf and Schneider, 2017). The age bias issue is focused on the occurrence of an ADHD overdiagnosis in which children born close to kindergarten or school cut-off dates, and who are therefore up to a year younger than their classmates, are significantly more likely to be diagnosed with ADHD. The gender bias issue concerns the occurrence of an ADHD overdiagnosis in which distinguished gender related manifestations of ADHD result in more false positive diagnosis to the disadvantage of boys. Such findings suggest that to defend the validity and reliability of diagnoses and treatment of ADHD, it is necessary to work through the debate of overdiagnosis of ADHD in terms of associated socio-economic and individual implications.

In the **first study** of this dissertation, in addition to summarizing the literature on the debate of ADHD overdiagnosis, a discussion on conducting comparative and systematical assessments as tools of working through the factors involved in overdiagnosing ADHD is presented. In this relation, in a seminal study by Bruchmüller, Margraf and Schneider (2012) in a population of licensed German psychotherapists and psychiatrists the application of diagnostic criteria and the specific role of patient gender in therapists' diagnostic decision making was systemically investigated. The first study is a replication of the study of by Bruchmüller, Margraf and Schneider (2012) in a different cultural context, in this case Iran, as ADHS might be perceived differently there. We assessed both gender bias and the impact of potential overdiagnosis on treatment recommendations. Results of this study demonstrated that ADHD overdiagnosis occurred in both girls and boys, although overdiagnosis was 2.45 more likely in boys than in girls. With respect to the psychiatrist's gender, no difference between males or females was detected, as both overdiagnosed ADHD in boys. Furthermore, ADHD overdiagnosis had a direct impact on medication prescription.

Parallel to investigating the issue of ADHD overdiagnosis another aim of this dissertation was to investigate the role of emotion dysregulation (ED) (subsuming symptoms like low frustration tolerance, irritability, ease of negative emotional experience, and emotional lability) in ADHD. In this

relation and as discussed by the **second study** of this dissertation, emotional symptoms are increasingly considered to be a core feature of ADHD. Among those studies and reviews reporting on ED in ADHD, there are at present one meta-analysis by Graziano & Garcia (2016), focusing on features of ED in children with ADHD. Distinguishing the dimensions of ED in children with ADHD, they demonstrated that such patients are more likely to experience intense emotions. The goal of the second study was to quantify the evidence of emotional dysregulation and its respective facets in individuals with adult ADHD compared to healthy controls using meta-analysis. In this relation, two electronic databases (PubMed, PsycINFO) were reviewed to identify studies. After scanning the studies based on the inclusion and exclusion criteria, a total of 13 studies (N = 2535) were included to assess (1) the standardized mean difference in emotion dysregulation (ED) as a general factor and its specific facets (i.e., emotional lability, negative emotional responses, and emotion recognition) between adults with ADHD and healthy controls; and (2) the association between ADHD symptom severity and ED. Findings of this study showed that compared to healthy controls, adults with ADHD revealed significantly higher levels of general ED (Hedges'  $g = 1.17$ ,  $p < 0.001$ ; Hedges'  $g$  is the adjusted effect size). With regard to intermediate dimensions of ED, emotional lability exhibited the strongest weighted effect (Hedges'  $g = 1.20$ , CI [0.57, 1.83],  $p < 0.001$ ). Furthermore, symptom severity and general ED correlated significantly ( $r = 0.54$ ,  $p < 0.001$ ). Regarding intermediate dimensions of ED, negative emotional responses correlated closely with ADHD symptom severity ( $r = 0.63$ ,  $p < 0.001$ ) and emotional lability ( $r = 0.52$ ,  $p < 0.001$ ).

Moreover, dealing with the meta-analysis conducted in the second study and thus encountering the field of meta-analysis tools, provided the context of an interest worked through by the **third study**. Systematic reviews in general and meta-analysis specifically are broadly applied methods for synthesizing currently available studies in order to reach a better understanding of related problems in a certain field. For conducting such analyses, there are currently four rather popular online services, namely MAVIS, MetaInsight, M-A and Health Decision Strategies Meta-Analysis Calculators that can be used as complementary tools along with statistical software products in order to facilitate the main process of effect size calculations. As the first goal of this study, a comparative description of the pros and cons of these web-apps is summarized. In addition and as the second objective of this study, the development of Meta-Mar is introduced. Meta-Mar is a free online and user-friendly meta-analysis service able to calculate effect sizes based on standardized mean differences as well as correlation coefficients and risk ratios, weighted effects for both fixed and random effect models, and presents the heterogeneity of the analysis as well as forest and funnel plots. Moreover, regarding the bias of the meta-analysis, reports of Fail-Safe N are part of the presented results. Furthermore, a meta-regression tool is available to include moderator variables as predictors of effect size. A subgroup analysis tool is also developed to categorize effect sizes and identify the between group variance.

All in all, findings of this dissertation confirmed the occurrence of ADHD overdiagnosis in cultural context of Iran and patient gender's significant role and also suggest that diagnosticians should strictly adhere to diagnostic criteria to minimize diagnostic error. Moreover, findings support ED symptoms as a core feature of ADHD's psychopathology and with respect to dimensions of ED, emotional lability, and negative emotional responses play a more definitive role in the psychopathology of adults with ADHD.

**Keywords**

ADHD overdiagnosis, adulthood ADHD, emotion dysregulation, meta-analysis, Meta-Mar

## **Zusammenfassung**

Die Aufmerksamkeitsdefizit-Hyperaktivitätsstörung (ADHS) ist durch die Kernsymptome Unaufmerksamkeit, Impulsivität und Hyperaktivität gekennzeichnet charakterisiert. Es ist eine der an den häufigsten diagnostizierten Erkrankungen im Kindes- und Jugendalter mit einer gepoolten weltweiten Prävalenzrate von ~ 5%. Es gibt neuere Erkenntnisse aus verschiedenen kulturellen Kontexten, die einen Anstieg der ADHS-Diagnoserate bei gleichzeitig steigenden Verschreibungsraten für Psychostimulanzien belegen (z. B. Dunlop & Newman, 2016; Connor, 2011; Safer, 2000), die zu berechtigten Bedenken hinsichtlich einer ADHS-Überdiagnose führen. In dieser Beziehung wird gezeigt, dass Alters- und Geschlechtsverzerrungen eine falsch positive und falsch negative Diagnose verursachen, und als Erklärung für solche Phänomene wird gezeigt, dass diese Verzerrungen signifikant mit subjektiven Heuristiken von Diagnostikern assoziiert sind (Mertens, Cwik, Margraf und Schneider, 2017). Das Problem der Altersverzerrung konzentriert sich auf das Auftreten einer ADHS-Überdiagnose, bei den Kindern, die kurz vor dem Stichtag des Kindergartens oder der Schule geboren wurden und daher bis zu einem Jahr jünger als ihre Klassenkameraden sind, signifikant häufiger mit ADHS diagnostiziert werden. Das Problem der geschlechtsspezifischen Verzerrung betrifft das Auftreten einer ADHS-Überdiagnose, bei den unterschiedlichen geschlechtsspezifischen Manifestationen von ADHS zu einer falscheren Diagnose zum Nachteil von Jungen führen. Solche Ergebnisse legen nahe, dass zur Verteidigung der Gültigkeit und Zuverlässigkeit von Diagnosen und Behandlungen von ADHS die Debatte über eine Überdiagnose von ADHS im Hinblick auf die damit verbundenen sozioökonomischen und individuellen Auswirkungen durchgearbeitet werden muss.

In der ersten Studie dieser Dissertation wird neben der Zusammenfassung der Literatur zur Debatte über die Überdiagnose von ADHS eine Diskussion über die Durchführung vergleichender und systematischer Bewertungen als Instrumente zur Bearbeitung der Faktoren bei der Überdiagnose von ADHS vorgestellt. In diesem Zusammenhang wurde in einer wegweisenden Studie von Bruchmüller, Margraf und Schneider (2012) in einer Population zugelassener deutscher Psychotherapeuten und Psychiater die Anwendung diagnostischer Kriterien und die spezifische Rolle des Patientengeschlechts bei der diagnostischen Entscheidungsfindung von Therapeuten systematisch untersucht. Die erste Studie ist eine Replikation der Studie von Bruchmüller, Margraf und Schneider (2012) in einem anderen kulturellen Kontext, in diesem Fall dem Iran, da ADHS dort möglicherweise anders wahrgenommen wird. Wir haben sowohl die geschlechtsspezifische Verzerrung als auch die Auswirkungen einer möglichen Überdiagnose auf die Behandlungsempfehlungen bewertet. Die Ergebnisse dieser Studie zeigten, dass eine ADHS-Überdiagnose sowohl bei Mädchen als auch bei Jungen auftrat, obwohl eine Überdiagnose bei Jungen mit 2,45 wahrscheinlicher war als bei Mädchen. In Bezug auf das Geschlecht des Psychiaters wurde kein Unterschied zwischen Männern und Frauen festgestellt, da beide bei Jungen ADHS überdiagnostizierten. Darüber hinaus hatte die Überdiagnose von ADHS einen direkten Einfluss auf die Verschreibung von Medikamenten.

Parallel zur Untersuchung des Problems der ADHS-Überdiagnose bestand ein weiteres Ziel dieser Dissertation darin, die Rolle der Emotionsdysregulation (ED) (subsumierende Symptome wie geringe Frustrationstoleranz, Reizbarkeit, leichte negative emotionale Erfahrung und emotionale Labilität) bei ADHS zu untersuchen. In dieser Beziehung und wie in der zweiten Studie dieser Dissertation diskutiert, werden emotionale Symptome zunehmend als Kernmerkmal von ADHS angesehen. Unter diesen Studien und Übersichten, die über ED bei ADHS berichten, gibt es derzeit eine Metaanalyse von Graziano & Garcia (2016), die sich auf die Merkmale von ED bei Kindern mit ADHS konzentriert. Sie unterschieden die Dimensionen der ED bei Kindern mit ADHS und zeigten, dass solche Patienten mit größerer Wahrscheinlichkeit intensive Emotionen erfahren. Das Ziel der zweiten Studie war es, die Hinweise auf emotionale Dysregulation und ihre jeweiligen Facetten bei Personen mit ADHS bei Erwachsenen im Vergleich zu gesunden Kontrollen mithilfe von Metaanalysen zu quantifizieren. In diesem Zusammenhang wurden zwei elektronische Datenbanken (PubMed, PsycINFO) überprüft, um Studien zu identifizieren. Nach dem Scannen der Studien anhand der Einschluss- und Ausschlusskriterien wurden insgesamt 13 Studien (N = 2535) eingeschlossen, um (1) den standardisierten mittleren Unterschied in der Emotionsdysregulation (ED) als allgemeinen Faktor und seine spezifischen Facetten (dh) zu bewerten. emotionale Labilität, negative emotionale Reaktionen und Emotionserkennung) zwischen Erwachsenen mit ADHS und gesunden Kontrollpersonen; und (2) die Assoziation zwischen der Schwere der ADHS-Symptome und der ED. Die Ergebnisse dieser Studie zeigten, dass Erwachsene mit ADHS im Vergleich zu gesunden Kontrollen signifikant höhere allgemeine ED-Werte aufwiesen (Hedges'  $g = 1,17$ ,  $p < 0,001$ ; Hedges'  $g$  ist die angepasste Effektgröße). In Bezug auf die mittleren Dimensionen der ED zeigte die emotionale Labilität den stärksten gewichteten Effekt (Hedges'  $g = 1,20$ , CI [0,57, 1,83],  $p < 0,001$ ). Darüber hinaus korrelierten der Schweregrad der Symptome und die allgemeine ED signifikant ( $r = 0,54$ ,  $p < 0,001$ ). In Bezug auf die mittleren Dimensionen der ED korrelierten negative emotionale Reaktionen eng mit der Schwere der ADHS-Symptome ( $r = 0,63$ ,  $p < 0,001$ ) und der emotionalen Labilität ( $r = 0,52$ ,  $p < 0,001$ ).

Darüber hinaus bildete die Auseinandersetzung mit der in der zweiten Studie durchgeführten Metaanalyse und damit die Begegnung mit dem Gebiet der Metaanalysewerkzeuge den Kontext eines Interesses, das in der dritten Studie bearbeitet wurde. Systematische Übersichten im Allgemeinen und Metaanalysen im Besonderen sind breit angewandte Methoden zur Synthese derzeit verfügbarer Studien, um ein besseres Verständnis der damit verbundenen Probleme in einem bestimmten Bereich zu erreichen. Für die Durchführung solcher Analysen stehen derzeit vier recht beliebte Onlinedienste zur Verfügung: MAVIS-, MetaInsight-, MA- und Gesundheitsentscheidungsstrategien. Metaanalyse-Rechner, die zusammen mit statistischen Softwareprodukten als ergänzende Tools verwendet werden können, um den Hauptprozess der Effektgröße zu vereinfachen Berechnungen. Als erstes Ziel dieser Studie wird eine vergleichende Beschreibung der Vor- und Nachteile dieser Web-Apps zusammengefasst. Zusätzlich und als zweites Ziel dieser Studie wird die Entwicklung von Meta-Mar vorgestellt. Meta-Mar ist ein kostenloser Online- und benutzerfreundlicher Metaanalysedienst, der

Effektgrößen basierend auf standardisierten mittleren Differenzen sowie Korrelationskoeffizienten und Risikoverhältnissen, gewichteten Effekten für Modelle mit festen und zufälligen Effekten berechnen kann und die Heterogenität des Modells darstellt Analyse sowie Wald- und Trichtergrundstücke. In Bezug auf die Verzerrung der Metaanalyse sind Berichte über Fail-Safe N Teil der vorgestellten Ergebnisse. Darüber hinaus steht ein Meta-Regressions-Tool zur Verfügung, mit dem Moderatorvariablen als Prädiktoren für die Effektgröße aufgenommen werden können. Ein Untergruppenanalysetool wurde ebenfalls entwickelt, um Effektgrößen zu kategorisieren und die Varianz zwischen Gruppen zu identifizieren.

Insgesamt bestätigten die Ergebnisse dieser Dissertation das Auftreten einer ADHS-Überdiagnose im kulturellen Kontext des Iran und die wichtige Rolle des Patientengeschlechts und legen nahe, dass Diagnostiker die diagnostischen Kriterien strikt einhalten sollten, um diagnostische Fehler zu minimieren. Darüber hinaus unterstützen die Ergebnisse die ED-Symptome als Kernmerkmal der ADHS-Psychopathologie. In Bezug auf die Dimensionen der ED spielen emotionale Labilität und negative emotionale Reaktionen eine eindeutigere Rolle in der Psychopathologie von Erwachsenen mit ADHS.

### **Schlagwörter**

ADHS-Überdiagnose, ADHS im Erwachsenenalter, Emotionsdysregulation, Metaanalyse, Meta-Mar

## **2 Introduction**

This dissertation focuses on two main areas, namely overdiagnosis of ADHD and the associative role of emotion dysregulation (ED) in adulthood ADHD. In this relation, after a brief introduction of the prevalence and core features of the disorder, the issue of ADHD overdiagnosis is worked through. In addition, the role of gender in ADHD overdiagnosis is discussed. Furthermore, main implications of the seminal study of Bruchmüller, Margraf and Schneider (2012) and the study of Achenbach et al. (2008) for study 1 are presented, as these studies provided the backgrounds for the systematic investigation of ADHD overdiagnosis in Iran. Then and with respect to the second focus of the dissertation, the role of ED as a substantial feature of ADHD is introduced. In addition, along with summarizing the conceptual models of ED, implications of a systematic review by Shaw, Stringaris, Nigg, & Leibenluft (2014) and a meta-analysis by Graziano & Garcia (2016) as backgrounds of the meta-analysis conducted in study 2 are presented. Finally, regarding study 3 a comparative description of four popular online meta-analysis web-applications are summarized, and accompanied by an introduction to Meta-Mar, an alternative online meta-analysis service.

### **2.1 ADHD, diagnostic core features and prevalence**

ADHD is characterized by the three core symptoms of inattention, impulsivity, and hyperactivity. The DSM-5 combines those for three presentations of the disorder based on the presence of the main symptoms: the predominantly inattentive (ADHD-PI), the predominantly hyperactive/impulsive (ADHD-PHI), and the combined presentation (ADHD-C) (American Psychiatric Association, 2013). For diagnosis, a symptom onset prior to the age of twelve years, and inappropriate functioning with respect to the developmental level are required (Kessler et al., 2006; American Psychiatric Association, 2013; Thomas et al. 2015; Fayyad et al., 2017). Moreover, ADHD is one of the most frequently diagnosed disorders of childhood and adolescence, with a pooled worldwide prevalence rate of ~5 % (Polanczyk et al. 2014; American Psychiatric Association 2013; Polanczyk et al., 2007). A meta-regression analysis of 102 studies by Polanczyk et al. (2007) demonstrated that variation in methodological diagnostic procedures is considered the main source of variability in prevalence estimates. The three parameters diagnostic criteria, information source (parent ratings vs. teacher ratings vs. clinical interviews), and functional impairment reveal a significant association with the variability of estimates in this context (Polanczyk et al., 2014). There are recent studies demonstrating a rise in the rate of ADHD diagnoses. For instance, Xu et al. (2018) analyzed data collected by the National Health Interview Survey during the past 20 years and reported an overall ADHD prevalence rate of 10.2 % among US children and adolescents aged 4 to 17 years (6.3 % in boys and 6.1 % in girls) for the years 2015 to 2016. Compared to a rate of 6.1 % in the years 1997 to 1998, that is a significant increase for all subgroups (Polanczyk et al., 2007; 2014).

## **2.2 ADHD and the debate of overdiagnosis**

With respect to such high rates of ADHD diagnosis, there are justifiable concerns about ADHD overdiagnosis that can be categorized into the two main topics of age gender bias, that both show to cause false positive and false negative diagnosis. The age bias issue focuses on the occurrence of an ADHD overdiagnosis in which children born close to kindergarten or school cut-off dates, and who are therefore up to a year younger than their classmates, are significantly more likely to be diagnosed with ADHD. The gender bias issue concerns the occurrence of an ADHD overdiagnosis in which distinguished gender related stereotypes of ADHD result in more false positive diagnosis to the disadvantage of boys. Regarding these two biases, findings of the literature are summarized below.

### **2.2.1 The issue of age bias**

A large body of ADHD research shows that children born close to kindergarten or school cut-off dates, and who are therefore up to a year younger than their classmates, are 30 to 60% more likely to be diagnosed with ADHD (Merten et al., 2017). In this regard, there is evidence that a child's birthdate considerably influences the subjective evaluations of teachers in identifying whether that child is exhibiting ADHD symptoms. For example, Elder (2010) showed that according to school entry dates, the youngest children in a class are 1.6 more likely to receive an ADHD diagnosis than the oldest children in the same class, implying a significant age bias that is confounded with development. This finding was replicated by Morrow et al. (2012) in children in British Columbia. In addition to this overdiagnosis of ADHD in younger children, Evans, Allen, Moore & Strauss (2004) showed in a similar study that there is little agreement between teachers' assessments of ADHD symptoms and observational data at the beginning of middle school, though this rate improves during the late fall. Wuppermann, Schwandt, Hering, Schul and Bätzing-Feigenbaum (2015) also made such observations in their study in Germany, concluding that there is a robust association between ADHD diagnosis, psychostimulant treatment and relative age position in the class due to month of birth and school entry dates.

Furthermore, this concept of ADHD overdiagnosis is promulgated by the media as a diagnosis *du jour* (Ray & Hinnant, 2009) accompanied by increasing diagnoses and psychostimulant prescription rates (Dunlop & Newman, 2016; Connor, 2011; Safer, 2000). For instance, Hollingworth et al. (2011) reported that the prescription of methylphenidate rose by 300 % between 2002 and 2009 in Australia, with boys receiving stimulant medication four times more likely than girls. A longitudinal study by McCarthy et al. (2012) investigated pharmacological treatment trends for ADHD in the UK. Their study findings imply an increasing rate of medication prescription from 2003 to 2008: they noted an increase in children from 4.8 (95% CI: 4.5–5.1) to 9.2 (95% CI: 8.8–9.6); in adolescents from 3.6 (95% CI: 3.3–3.9) to 7.4 (95% CI: 7.0–7.8); in youth from 0.3 (95% CI: 0.2–0.3) to 1.1 (95% CI: 1.0–1.3); and in adults from 0.02 (95% CI: 0.01–0.03) to 0.08 (95% CI: 0.06–0.10). Another finding of this study was

that this increase is significantly higher for male than female children, though in adolescence and adulthood this was not the case as the rate was significantly higher for female patients. Bachmann et al. (2017) compared the prevalence of ADHD medication use in five countries and reported an increase from 1.8% to 3.9% in the Netherlands (relative increase: +111.9%), from 3.3% to 3.7% in the US (rel. increase +10.7%), from 1.3% to 2.2% in Germany (rel. increase +62.4%), from 0.4% to 1.5% in Denmark (rel. increase +302.7%), and from 0.3% to 0.5% in the UK (rel. increase +56.6%).

On the other hand, and in order to defend the validity and reliability of diagnoses and treatment by the professional, it is necessary to work through this debate of overdiagnosis of ADHD in terms of associated socio-economic and individual implications (Barkley et al., 2002). After all, if our field provides interventions, we should also be able to defend our diagnoses. However, without conducting comparative studies that systematically assess the factors involved in overdiagnosing ADHD, potential indicators such as the variation in prevalence or increasing rates of stimulants prescriptions should not be interpreted as indicative of overdiagnosis (Mertens, Cwik, Margraf and Schneider, 2017). In this regard, Sciutto & Eisenberg (2007) suggest investigating the occurrence of overdiagnosis by reexamining referred patients and by conducting comprehensive, multimethodical evaluations to be compared with the actual diagnoses. Such arguments address type I or false-positive diagnostic errors. Sciutto and Eisenberg (2007) criticize such focusing on false-positive and the disregard of false-negative errors (type II), however. Instead, they suggest examining the presence of potential overdiagnosis via a ratio of these two errors. Accordingly, ADHD overdiagnosis should be based on the odds ratio of type I to type II error while also considering the significance of this ratio. In this regard, comorbidity, diagnostic inaccuracy and changes in diagnostic criteria are sources of false-positive or type I errors, while gender, cultural norms and barriers to diagnostic assessment and treatment are false-negative or type II errors (Sciutto and Eisenberg, 2007).

## **2.2.2 The issue of gender bias**

Overall, the majority of studies report an ADHD gender bias that puts boys at a disadvantage. The rate of boys to girls diagnosed with ADHD is reported to be 3 to 1 in representative population-based studies (Xu et al., 2018), and 5 to 1 or 9 to 1 in clinically-based studies (Young, Moss, Sedgwick & Fridman, 2015), and such gender differences may play a significant role in the case of ADHD overdiagnosis (Bruchmüller, Margraf and Schneider, 2012). In addition to and regarding the pharmacological treatments of ADHD, there are studies demonstrating that boys are given significantly more medication than girls i.e. 3 to 1 in the US (Rowland et al., 2002), 7 to 1 in the UK (McCarty et al., 2012) and 5 to 1 in western European countries (Knopf et al., 2012). As reviews suggest, an explanation for such differences between boys and girls in ADHD diagnosis and medication prescription is that symptom manifestation in boys and girls differs in such a way that girls display more inattentive symptoms that are not found to be as disruptive at school or home (Arnett et al., 2014; Biederman et al., 2006), while

boys exhibit more hyperactive, impulsive and aggressive behaviors that parents and teachers find to be more burdensome and thus result in higher referral rates (Bruchmüller, Margraf & Schneider, 2011; Tung et al., 2016).

Regardless of the diverse manifestations of ADHD symptoms in boys and girls, another explanation for the different ratios in boys and girls is clinicians' subjectivity. Bonati and Reale (2015) state that although ADHD practice guidelines highlight the assessment of symptom severity based on developmental, medical and psychosocial parameters, the degree of impairment is still determined subjectively by the clinician. Mertens, Cwik, Margraf and Schneider (2017) suggest that diagnosticians may not be adhering strictly enough to diagnostic criteria and that instead, their clinical judgment is being affected by heuristics and biases. They demonstrate that diagnosticians are prone to making mistakes in the decision-making process. Adopting a heuristic approach, clinicians tend to base their diagnostic decision primarily on their subjective perception of the patient. As patient gender moderates symptom manifestations, boys are more likely to receive an ADHD diagnosis even when not all the criteria have been met (false-positive diagnostic error), while girls are less likely to receive a diagnosis of ADHD even when they fulfill the criteria (false-negative diagnostic error). Therefore, considering the heuristics effect in the diagnostic process is another possible explanation for the differences we observe between clinical and epidemiological data in ADHD. In support of this are results from a meta-analysis that estimated the agreement between diagnoses made from clinical evaluations and standardized diagnostic interviews. Overall, such agreement was low to moderate and depended on the disorder, with ADHD resulting in moderate agreement ( $\kappa = 0.49$ ,  $CI = [0.46, 0.52]$ ) (Rettew et al. 2009). However, the studies included in the meta-analysis reported kappas varying from 0.12 to 0.92, indicating that the accordance between ADHD diagnoses derived from clinical evaluation and standardized diagnostic interviews requires further systematic examination.

### **2.3 Systematic investigation of ADHD overdiagnosis**

The application of diagnostic criteria and the specific role of patient gender in therapists' diagnostic decision making was systemically investigated in a seminal study by Bruchmüller, Margraf and Schneider (2012) in a population of licensed German psychotherapists and psychiatrists ( $N = 473$ ). The participants rated eight different case vignettes that differed with respect to the number of symptoms (in vignette 1, all ADHD symptoms were fulfilled; in vignette 2 two criteria and in vignette 3 three criteria were missing, while vignette 4 described a different disorder – generalized anxiety disorder of childhood/adolescence) and child gender (all vignettes described either a boy named Leon or a girl, named Lea). Overall, 80 % of the girls and 77 % of the boys were correctly diagnosed with ADHD; for vignette 2, 11 % of the girls and 30 % of the boys received an ADHD diagnosis; in vignette 3 9 % of the girls and 20 % of the boys, and in vignette 4 that described a totally different disorder, still 13 % of the girls and 18 % of the boys received a diagnosis of ADHD (see Fig. 1).

#### ADHD DIAGNOSES AND DIAGNOSTIC CRITERIA

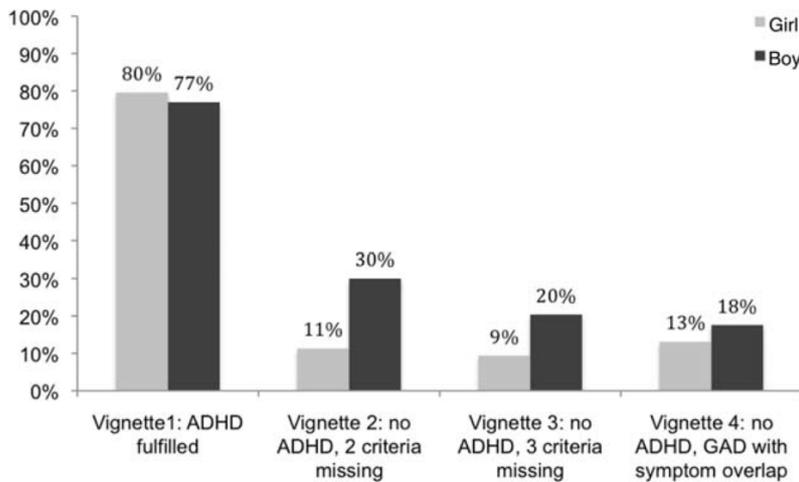


Fig. 1 Percentage of ADHD diagnosis for the eight different case vignettes (Bruchmüller, Margraf and Schneider, 2012).

GAD = Generalized Anxiety Disorder

Overall, there were significantly more false-positive than false-negative diagnoses confirming the assumption of overdiagnosis, and boys were given significantly more false-positive diagnoses, thus indicating a gender bias to their disadvantage. This gender bias was boosted by the fact that male psychotherapists and psychiatrists were more likely to falsely rate boys positively than their female counterparts. In addition, Bruchmüller, Margraf and Schneider (2012) reported that in vignettes 2-4, those therapists who had made an ADHD diagnosis recommended medication and psychotherapeutic treatments significantly more often than other therapists who had not diagnosed ADHD. They thus provided evidence that ADHD overdiagnosis has a direct impact on treatment recommendation. Aim of study 1 of this dissertation was to replicate this study, but based on an Iranian population of psychiatrists.

Iran is especially interesting for such a study, as a large survey in 2008 on the multicultural assessment of child and adolescent psychopathology via the Achenbach System of Empirically Based Assessment (ASEBA) and the Strength and Difficulties Questionnaire (SDQ) indicated that mean ASEBA and SDQ scores are nearly identical for both genders in large, representative samples speaking 76 languages, except Iran (Achenbach et al. 2008). In this regard, both parents and teachers in nearly all the countries studied other than Iran rated boys higher than girls on DSM-oriented ADHD scales, and such gender differences on Attention Problems, Rule-Breaking Behavior, and Aggressive Behavior Syndromes were larger in teachers' ratings than in parents' ratings. However, Youth Self Report on ADHD scales revealed no significant gender difference in these societies. Regarding the Iranian sample of this study, girls and boys in Iran attend single-gender schools, and girls in this study were given higher ADHD scores than girls in most other populations, while Iranian boys scored at about the middle

of the overall population. Achenbach et al. (2008) hypothesize that “the absence of boys in the Iranian girls’ classrooms lowered teachers’ thresholds for endorsing ADHD items in girls, thereby producing higher scale scores than those found in populations whose boys and girls attend class in the same classroom. Unfortunately for this hypothesis, Iranian parents also rated girls as high as boys on statistically-derived and DSM-oriented scales of ADHD problems, unlike parents in the other populations. The similar findings for Iranian parent and teacher ratings indicate cross-informant and cross-situational consistency in Iranian adults’ tendency to rate Iranian girls as high as boys on ADHD problems” (Achenbach et al., 2008, p. 268).

Furthermore, a recent meta-analysis of 27 studies (N = 15124) for the years of 2001 to 2016 reported a prevalence rate of ADHD of 12 % (CI 95%: 9.0 - 15) for children aged six to 14 years in Iran (Yadegari et al. 2018). Compared to the aforementioned international rates (Polanczyk et al. 2007 & 2014; Xu et al. 2018), that rate is significantly higher. Taken together, these studies’ results make Iran a particularly interesting country in which to investigate the potential overdiagnosis and gender effects of ADHD.

## **2.4 Emotion dysregulation**

There is no consensus on defining and distinguishing emotion and emotion regulation by applying an ontological approach. Instead, theories of emotion and emotion regulation present conceptual models based on phenomenological approaches that depict emotional processes in a descriptive manner (Cole et al., 2004; Izard, 2009). One of the prominent models of emotional generation is the modal model of emotion (Gross & Thompson, 2007) in which the core features of emotion are sequentially conceptualized: a psychologically relevant situation attracts attention and the individual evaluates what the situation means in light of relevant goals. Those appraisals generate a multifaceted response (experiential, behavioral, and physiological/neurobiological) and those responses might change the situation it originally started from. Emotion regulation now can roll in at each step of emotion generation in order to influence which emotions we have, when we have them, and how we experience and express them (Gross, 1998). In detail, it proposes five types of emotion regulation strategies (Werner & Gross, 2009): (1) taking steps to influence which situation one will be exposed to (situation selection), (b) changing relevant aspects of the situation (situation modification), (c) influencing which portions of the situation are perceived and attended to (attentional deployment), (d) altering the way of thinking about it (reappraisal), and (e) directly modifying emotion-related actions (response modulation) (see Fig. 2).

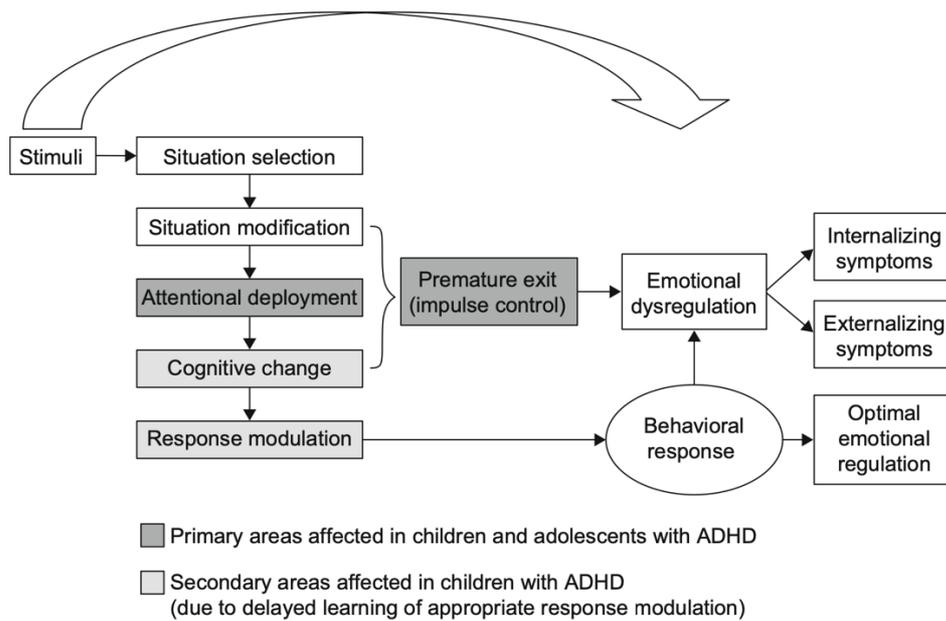


Fig. 2 Conceptual model of ED in childhood ADHD (van Stralen, 2016; Gross, 1998).

It is assumed that flexible, context-dependent modification of emotions is essential for mental health and that health-impairing deficits could occur at different stages. Individuals can experience problems (1) with identifying situations when to regulate emotions, or (2) with selecting an appropriate strategy to regulate emotions, or with (3) implementing a particular tactic suited to the present situation and monitoring regulation processes and success (Gross & Thompson, 2007). With regard to psychopathology, some emotion regulation strategies and specific difficulties at the stages of the regulation process such as overuse of a strategy or absence of the skill for proper use of the regulatory strategy are assumed to be risk factors for psychopathology (Gross & Jazaieri, 2014). Recent studies in the field of emotion have shown that 40 % to 70 % of psychological/psychiatric disorders are characterized by emotion dysregulation – with ADHD being one of them (Cole et al., 1994; Thayer & Lane, 2000; Berenbaum et al., 2003; Kring, 2008; Kring, 2010).

## 2.5 ADHD and Emotion dysregulation

Apart from the core symptoms of ADHD, i.e., inattention, impulsivity, and hyperactivity, emotion regulation contributes independently to functional impairments in patients with ADHD (Hirsch, Chavanon, Christiansen, (2019), Barkley et al., 2008; Bunford et al., 2018; Corbisiero et al., 2013). In this regard, several studies reported that emotion dysregulation (ED) (subsuming symptoms like low frustration tolerance, irritability, ease of negative emotional experience, and emotional lability) is highly frequent in children, adolescents, and adults with ADHD (Skirrow & Asherson, 2013; meta-analysis by

Graziano & Garcia, 2016 and qualitative reviews by Ramsay & Rostain, 2008 and Martel, 2009). About 70% of adult patients with ADHD report ED or emotional lability (Skirrow & Asherson, 2013; Barkley & Fischer, 2008; Skirrow et al, 2014). Furthermore, ED also exists in patients with ADHD not suffering from any other comorbid mental disorder (Hirsch, Chavanon, Christiansen, (2019); Skirrow & Asherson, 2013). Those findings reveal ED as a core component of the disorder or at least as a substantial feature in a subgroup of patients with ADHD (e.g., Retz et al., 2012; Hirsch et al., 2018). Two decades after Wender (1995) recognized features of ED as part of the clinical presentation of adult ADHD, DSM-5 refrains from including such symptoms as indicative of the disorder. Instead, the DSM-5 recommends considering ED as an associated feature of ADHD supporting its diagnosis (Diagnostic and statistical manual of mental disorders, 2013).

According to Kring and Sloan (2009), such a limitation occurred due to the fact that ED is still a transdiagnostic concept and can be applied to psychopathological aspects of various disorders not limited to ADHD. Although focusing on emotion regulation and dysregulation might provide a) new insights into the underlying pathophysiological mechanisms (e.g., Shushakova, Ohrmann & Pedersen, 2017), b) a more accurate differentiation of symptoms and disorders (e.g., ODD/CD vs. ADHS), and c) novel treatment approaches (Faraone et al., 2018; Hoxhaj et al., 2018; Shaw et al., 2014), research on ED still lacks a consensual and refined definition and depiction of ED and related constructs in general (e.g., Cole et al., 2004; Izard, 2009), and theoretical frameworks and conceptual models of ED in ADHD in particular. Terms like ED, emotional lability, emotional instability (i.e., irregular shifting between emotional states) and emotional impulsivity (i.e., overshooting emotional responses) are often applied interchangeably or rather idiosyncratically (for a review see Faraone et al., 2018). This lack of consensus and clarity regarding the construct of emotion regulation and ED makes summarizing and integrating empirical findings in ADHD complicated (Ryckaert, Kuntsi & Asherson, 2018). To avoid working in “conceptual and definitional chaos” (Buck, 1990, p. 330), we briefly define emotion regulation, ED, and facets of ED that contribute to functional and psychosocial impairments in patients with ADHD as emotion recognition, emotional lability and negative emotional responses. Emotion recognition refers to the perception and awareness of the self and other’s verbal and nonverbal emotions; emotional lability points to an unstable shifting between states of emotions; negative emotional responses refer to irritability and impulsivity of the emotional reactions (Shaw, Stringaris, Nigg, & Leibenluft, 2014).

Among those studies and reviews reporting on ED in ADHD, there are at present one systematic review (Shaw, Stringaris, Nigg, & Leibenluft, 2014) and one meta-analysis (Graziano & Garcia, 2016), both focusing on ED in childhood ADHD. The overview by Shaw, Stringaris, Nigg, & Leibenluft (2014) summarizes the debate of conceptualizing ED with respect to ADHD by considering ED as a core yet distinct feature that correlates with ADHD. The meta-analysis by Graziano and Garcia (2016) analyzed features of ED in children with ADHD. Distinguishing the dimensions of ED in children with

ADHD, they demonstrated that such patients are more likely to experience intense emotions. The authors reported that this association between emotional reactivity and the ADHD symptom burden becomes stronger with age, a finding consistent with published reports acknowledging that ED's impairment persists over the life-span (Helfer et al., 2019; Shaw, Stringaris, Nigg, & Leibenluft, 2014; Schweren et al., 2019).

## **2.6 Online meta-analysis services**

Since there was no previous review on ADHD and ED in adulthood, conducting a meta-analysis on this subject was the objective fulfilled through the second study. This aim came up with the question of meta-analysis tools. In this regard, this chapter identifies comparative features of online meta-analysis services after a brief introduction of the importance of the investigation in the area of online meta-analysis services.

To gain a broader understanding of results, meta-analysis emerged as a coherent, persuasive and cross-disciplinary statistical framework for synthesizing results across numerous studies (Borenstein et al., 2009; Dixon-Woods et al., 2005; Hanji, 2017; Higgins & Green, 2011; Wallace et al., 2009). Meta-analysis became an influential and yet essential method over the past decades, especially within the fields of psychology, psychotherapy, medicine and public health (Egger, Smith and Altman, 2008; Jackson and Waters, 2005; Petticrew and Roberts, 2008). For instance, Bax et al. (2009) have demonstrated that with regard to meta-analysis, 12.000 studies have been included in such analyses on various medical topics through PubMed search between 1990 and 2005. In addition, based on our own PubMed analysis, we estimate that this amount has increased to approximately 108.000 studies between 2005 and 2018, including nearly 80.000 studies in clinical fields. Meta-analysis can - without any doubt - be acknowledged as one of the key methods of evidence-based practice and health care policy. Research across the fields of clinical psychology, medicine and public health rely on meta-analysis as it informs health professionals and scholars about which treatment works or works better for a specific medical or mental condition. Acknowledging the importance of meta-analysis as a key method for life sciences, it is of major interest for researchers, students and educators to have access to freely available meta-analysis tools that are instantly ready to use and easy to handle. As laid out by Owen and colleagues (2019), complicated software and heavily code-based tools are still major barriers to a greater adoption and proficiency of new methods in general and meta-analysis in particular. After inspecting established meta-analysis software and recent software reviews (Wallace et al., 2017, Bax et al., 2009; Sterne, Egger & Sutton, 2008; Sutton et al., 2005), two main aspects that discourage meta-analysis novices can be identified: 1) accessibility of tools, and 2) their functionality.

## 2.6.1 Accessibility

With regard to accessibility, freely available web-based meta-analysis tools can be distinguished from offline software solutions. Online tools can directly be accessed via standard internet browsers without any further installation as requirement. However, offline software needs to be installed on an operating system. Thus, online software is much more accessible and ready to use than its offline alternative. Currently there are powerful open-access meta-analysis tools as well as open source libraries available such as RevMan<sup>1</sup>, and the MetaFor R-package that need installation or users need to be skilled in using R. On the other hand, with respect to online meta-analysis services there are four rather popular online web-apps, namely MAVIS<sup>2</sup>, MetaInsight<sup>3</sup>, M-A Calculator<sup>4</sup> and Health Decision Strategies Meta-Analysis Calculator (HDS)<sup>5</sup>, that offer meta-analysis procedures without confronting users to be skilled in R. All of those applications are freely available and require no specialist software, beyond a modern web browser for the user to install, but leverage established analysis routines. The focus of the third study was to investigate the comparative features of such online applications which lead to an introduction of the available online meta-analysis services.

## 2.6.2 Application development and functionality

Each of the four web-apps of MAVIS, MetaInsight, M-A and HDS Calculator is developed based on the different methods programming and meta-analysis organization. Regarding the methods of programming two levels of backend and frontend development can be distinguished. At the backend level, R and Python packages such as, metaphor and Scikit, respectively, are two main programming languages having the advantage of entailing meta-analysis specific libraries. At the frontend level that targets the graphical user interface (GUI) there is a broad range of web development languages such as but not limited to HTML & CSS, JavaScript and Shiny.

Regarding meta-analysis organization, we identified four aspects of conducting a meta-analysis by online services as a) types of analysis, b) models of analysis, c) outcomes of analysis, and d) data entry. After framing the raw data of the meta-analysis by user, such data can be entered manually and in hands of predefined sections in each web-app, or be uploaded as an Excel/svc file. Furthermore, each meta-analysis web-app, is developed for conducting at least one type of meta-analysis such as standard mean difference (smd), correlation and binary data. In addition, each type of analysis deals with distinct models of calculation. In this relation, possibility of calculations for fixed and random effect models, bias of analysis (heterogeneity, Fail-N safe), meta-regression and subgroup analysis are distinguished

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<sup>1</sup> <https://community.cochrane.org/help/tools-and-software/revman-5>

<sup>2</sup> <http://kylehamilton.net/shiny/MAVIS/>

<sup>3</sup> <https://crsu.shinyapps.io/metainsightc/>

<sup>4</sup> <http://www.lyonsmorris.com/mal/index.cfm>

<sup>5</sup> <http://www.healthstrategy.com/meta/metainput.htm>

models that a meta-analysis web-app might provide. Moreover, desired outcomes of a meta-analysis expected to be fulfilled by an online application can be differentiated by the way each app represents the results of analysis in forms of data frames, forest and funnel plots, network plots, etc.

All in all, based on the identified aspects of online meta-analysis, services are summarized in Fig. 3. Each of the four web-apps of MAVIS, MetaInsight, M-A and HDS Calculator has its pros and cons. In addition to these services, a free online meta-analysis application, namely Meta-Mar, was developed in the third study. Full introduction to functionality of Meta-Mar accompanied with a comparative review of online meta-analysis tools is presented in the result section of the third study.

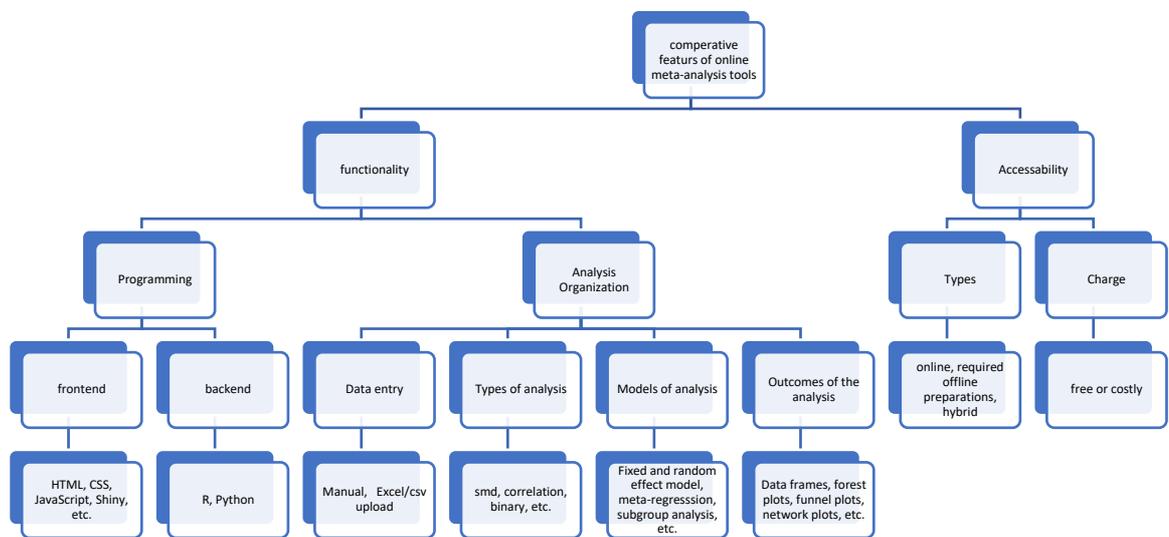


Fig. 3 Comparative features of online meta-analysis services

### **3 Objectives of the dissertation**

#### **3.1.1 Objectives of the first study**

As previously introduced, the seminal study by Bruchmüller, Margraf and Schneider (2012) through a systematical assessment confirmed the assumption of overdiagnosis of ADHD. In this relation, there were significantly more false-positive than false-negative diagnoses, and boys were given significantly more false-positive diagnoses, thus indicating a gender bias to their disadvantage. In addition, the large survey of Achenbach et al. (2008) revealed that Iranian parents and teachers, contrary to nearly all other countries, rated boys and girls similarly on DSM-oriented ADHD scales. Relying on such backgrounds, the first study aimed to investigate the occurrence of ADHD overdiagnosis and its facets in Iran.

##### **Summary of the questions of the first study**

- Is ADHD overdiagnosed in Iran?
- Is the gender bias to boys' disadvantage confirmed in Iran?
- Do Iranian psychiatrists reveal a gender bias when diagnosing boys and girls with ADHD?
- Does ADHD overdiagnosis have an impact on treatment recommendations?

#### **3.1.2 Objectives of the second study**

Relying on the ED facets derived by Graziano and Garcia (2016) for children and adolescents, the goal of the second study was to conduct a meta-analysis for adult patients with ADHD and ED, as this has not been done so far. As previous empirical work on ADHD symptoms suggests there are differences in symptoms and their trajectories from childhood to adulthood (Thomas et al. 2015; Asherson, 2016; Fayyad et al., 2017), this might apply to ED and ED facets in conjunction with ADHD as well.

##### **Summary of the questions of the second study**

- What is the magnitude of the associations between ADHD status (patient with ADHD vs. healthy control), ED and its facets?
- What is the magnitude of the associations between ADHD symptom scores, ED and its facets?

### 3.1.3 Objectives of the third study

After identifying the characteristics of the online meta-analysis apps with respect to their accessibility and functionality, the third study aimed to review four web-apps of MAVIS, MetaInsight, M-A and HDS Calculator, and summarize the pros and cons each app. In addition, this study aimed to introduce Meta-Mar as an alternative online meta-analysis service and to discuss how Meta-Mar discriminates from the above mentioned web-apps.

#### Summary of the objectives of the third study

- Identifying comparative features of online meta-analysis services and in this regard summarizing a review of four web-apps of MAVIS, MetaInsight, M-A and HDS Calculator.
- Introducing Meta-Mar, a free online meta-analysis web-app, with respect to its programming development, methods of data entry and models of analysis.
- Comparing features of Meta-Mar to those of other alternative tools and arguing how Meta-Mar improve the possibility of running an online meta-analysis as well as gathering the features that are considered to be advantages of other available web-apps?

## 3.2 Methods

In study 1, a total of 344 licensed Iranian psychiatrists (mean age = 45.17, SD = 9.50) participated, among them 165 individuals from Isfahan and 179 individuals from Tehran. In contrast to Germany, where licensed psychotherapists and psychiatrists are legitimized to diagnose children with ADHD, Iran only allows psychiatrists to make a diagnosis following the Islamic Republic of Iran's Medical Council law. Each therapist received a cover letter as a brief introduction of this study, attached by a case vignette and a questionnaire. According to the study of Bruchmüller, Margraf and Schneider (2012), the same four case vignettes were used for this study. Based on the ICD-10 and DSM-IV criteria, Vignette 1 satisfies an ADHD diagnosis while no diagnosis of ADHD can be applied to Vignette 2 & 3. Finally, Vignette 4 fulfills the criteria of making a diagnosis of GAD. The four vignettes were duplicated for boys and girls as in the original study to arrive at 4 vignettes for girls and 4 vignettes for boys. The original vignettes were translated to Farsi and reviewed by four Iranian clinicians to ensure their validity for use in the Iranian psychiatrist community. Furthermore, attached to the case vignette, all clinicians received a questionnaire that asked for diagnosis, treatment recommendation and their sociodemographic information. With respect to the first aim of this study, to determine whether ADHD is overdiagnosed in Iran, we applied the chi-square test to compare the proportion of ADHD diagnosis in non-ADHD cases (false positive) to the proportion of non-ADHD diagnosis in the ADHD cases (false negative). Moreover, with respect to our second study aim, we applied multiple logistic regression

analysis to evaluate the role of gender in the therapist's diagnostic decision. Furthermore, to investigate the effect of the psychiatrist's gender, age, therapeutic approach and years of job experience, we included those factors in the analysis. Finally, we repeated calculations regarding the overdiagnosis separately for male and female therapists. Moreover, by running chi square tests, we compared the treatment recommendations by those therapists who made an ADHD diagnosis in vignettes 2-4 with treatment recommendations by those therapists who did not diagnose ADHD.

In study 2, first in order to run a systematic literature search, the electronic databases PubMed and PsychINFO were searched. Our search in PubMed yielded 1316 and PsychINFO 714 abstracts. We also checked the reference lists of included studies for other studies eligible for inclusion. After removing duplicates, abstracts of all articles were screened based on pre-defined inclusion criteria independently by the first author. Inclusion criteria were: (i) report of any self- or third-party measure of emotion, affect, or mood (dys)regulation or emotional lability, (ii) inclusion of clinical samples of adults (>18 years of age) with ADHD characterized by clinical criteria (e.g., DSM, ICD) and diagnostic procedures, (iii) inclusion of non-ADHD healthy controls. Exclusion criteria were: case reports, conference abstracts, reviews, duplicates and non-English studies. After scanning a total number of 2030 studies, ultimately 13 studies remained for data extraction. In order to code these studies, three main dimensions of ED were identified based on the narrative synthesis of the literature: Emotion recognition, emotional lability and negative emotional responses. Finally, we differentiated the included studies in two parts: the first concerned studies that examined ED between groups with and without ADHD (related to the study's question of magnitude of the associations between ADHD status, ED and its facets), and the second concerned studies that investigated ED within the groups with ADHD (related to the study's question of magnitude of the associations between ADHD symptom scores, ED and its facets). To conduct the meta-analyses and demonstrate results via forest and funnel plots, initial calculations were carried out by Cochrane RevMan 5 and then repeated by Meta-Mar.

In study 3, first we identified comparative features of online meta-analysis services with respect to their accessibility and functionality. Based on the identified features, four web-apps of MAVIS, MetaInsight, M-A and HDS Calculator were reviewed. In addition, development process and functionality of Meta-Mar was introduced. In this relation, with respect to the literature (Borenstein et al., 2010; Brockwell & Gordon, 2001; Cleophas & Zwinderman, 2012; Ellis, 2010), the mathematical background of conducting a meta-analysis was reviewed for providing the calculation framework of Meta-Mar's development. Then, the development of Meta-Mar was illustrated regarding two steps of programming: Python based backend, which is focused on the calculation process of meta-analysis, and JavaScript based frontend that regards the experience of the user while working with the application. In this relation and via an illustrative example it is shown how Meta-Mar works. In addition, we compared the features of Meta-Mar with those applications we reviewed in the previous step and highlighted how Meta-Mar improves the possibility of running an online meta-analysis as well as gathering the features

that are considered to be advantages of these web-apps. Finally, to validate the function of Meta-Mar, the results of an illustrative meta-analysis were compared with those provided by RevMan 5 and MAVIS.

## 4 Summary of the studies and their results

### 4.1 ADHD overdiagnosis and the role of patient gender among Iranian psychiatrists

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**Theoretical background:** As mentioned previously, ADHD is one of the most frequently diagnosed disorders of childhood and adolescence, with a pooled worldwide prevalence rate of ~5 % (American Psychiatric Association 2013; Polanczyk et al. 2007). In addition, the rate of boys to girls diagnosed with ADHD is reported to be 3 to 1 in representative population-based studies (Xu et al. 2018), and 5 to 1 or 9 to 1 in clinically-based studies (Young, Moss, Sedgwick & Fridman 2015). Recent studies also demonstrate a rise in the rate of ADHD diagnoses and thus an increase in prescribing ADHD medication (Xu et al., 2018; Bachmann et al., 2017). In this respect, there are justifiable concerns about ADHD's overdiagnosis and thus stimulants overprescription as well as occurrence of such overdiagnosis to the boys' disadvantage. As Mertens, Cwik, Margraf and Schneider (2017) suggest, such variation in prevalence or increasing rates of stimulants prescriptions should not be interpreted as indicative of overdiagnosis without conducting comparative studies that systematically assess the factors involved in overdiagnosing ADHD. In this respect, Bruchmüller, Margraf and Schneider (2012) conducted a systematical investigation of clinicians' ADHD diagnosis in a population of licensed German psychotherapists and psychiatrists (N = 473). Their results showed that not only false-positive diagnoses were significantly more frequent than false-negative ones (confirming the assumption of overdiagnosis), but boys were also given significantly more false-positive diagnoses. Furthermore, Achenbach et al. (2008) showed that contrary to the samples included in their study, Iranian parents and teachers rated girls higher than boys on DSM-oriented ADHD scales compared to all other countries. The aim of study 1 was to replicate the study of Bruchmüller, Margraf and Schneider (2012), but based on an Iranian population of psychiatrists to address whether ADHD is overdiagnosed in Iran, and to identify whether the gender of the patients and psychiatrists bias the diagnosis. Finally, another goal of this study was to investigate whether ADHD overdiagnosis leads to medication overprescription.

**Methods:** Replicating the study of Bruchmüller, Margraf and Schneider (2012), there were four case vignettes constructed based on the ICD-10 and DSM-IV criteria applied in this study. Among these vignettes, one case fulfilled the criteria of ADHD diagnosis (Vignette 1), and the three categorized as non-ADHD cases either lacked two or three criteria for making an ADHD diagnosis (Vignette 2 & 3,

respectively), while the fourth vignette targeted a totally different disorder, namely GAD. These four vignettes were duplicated for boys and girls. All vignettes were translated into Farsi and reviewed by four Iranian clinicians to ensure their validity for use in the Iranian psychiatrist community. In addition to the vignettes, a cover letter, as a brief introduction to study 1, accompanied by a questionnaire, to investigate the diagnosis, treatment recommendation and psychiatrists' sociodemographic information, and a consent form were provided. These materials were distributed to Iranian psychiatrists (N = 344 licensed Iranian psychiatrists; mean age = 45.17, SD = 9.50), with n = 165 individuals from Isfahan and n = 179 individuals from Tehran who participated in this study. We compared demographics of these two cities by running t-tests. Regarding the question of ADHD overdiagnosis in Iran, the proportion of ADHD diagnosis in non-ADHD cases (false positive) to the proportion of non-ADHD diagnosis in the ADHD cases (false negative) was compared via a chi-square test. Moreover, with respect to question of gender bias in ADHD diagnosis, multiple logistic regression analysis was applied. Furthermore, to investigate whether psychiatrist's gender, age, therapeutic approach and years of job experience effect the diagnosis, those factors were included in the multiple logistic regression analysis. Then, these calculations were repeated separately for male and female therapists. Moreover, by running chi square tests, we compared the treatment recommendations by those therapists who made an ADHD diagnosis in vignettes 2-4 with treatment recommendations to those therapists who did not diagnose ADHD. All of the above-mentioned analyses were conducted via SPSS (v. 25) and Microsoft Excel (v. 2016).

**Results:** Comparison of the demographics of psychiatrists from Isfahan and Tehran showed no significant difference of the two cities (age:  $t = 1.95$ ; years of job experience:  $t = 1.23$ ). With respect to the first aim of this study, the odds ratio of overdiagnosis amounted to 5.46 and chi square analysis results confirmed a substantial difference between the non-ADHD and ADHD vignettes ( $\chi^2(1, N = 344) = 14.91, p < 0.01$ ). This implies the occurrence of ADHD overdiagnosis among Iranian psychiatrists. By excluding the answers of therapists who stated no clear diagnosis due to a lack of information, or asserted a suspected diagnosis, we conducted the analysis again. In this regard, odds ratio was calculated as 3.45 and the analysis of chi square again showed a significant difference between groups ( $\chi^2(1, N = 277) = 7.16, p < 0.01$ ), and thus also confirming the overdiagnosis of ADHD. In addition, adjustment disorder was the most likely diagnosed disorder with a probability of 0.76 and 0.79 in vignettes 1 and 2, respectively, and GAD with a probability of 0.83 was the most frequent diagnosis in vignette 4. To explore whether a positive gender bias to the disadvantage of boys is present in Iran, a logistic regression analysis was conducted to examine whether the gender in vignettes predicts an ADHD diagnosis. The chi square analysis of the adopted model in the logistic regression was statistically significant ( $\chi^2(9, N = 344) = 105.31, p < 0.01$ ) and this showed that the probability of an ADHD diagnosis is calculated better when the predictors are included in the equation. Results of the logistic regression analysis showed that in comparison to girls, odds of diagnosing ADHD in boys were more than twice (OR = 2.45,  $p < 0.05$ ) as high. Furthermore, as Fig. 4 indicates, this only applied to

vignettes 3 and 4 in which the percentages of receiving an ADHD diagnosis were 30.8 % in boys and 17.5 % in girls for vignette 3, and 15.9 % in boys and 8.1 % in girls for vignette 4.

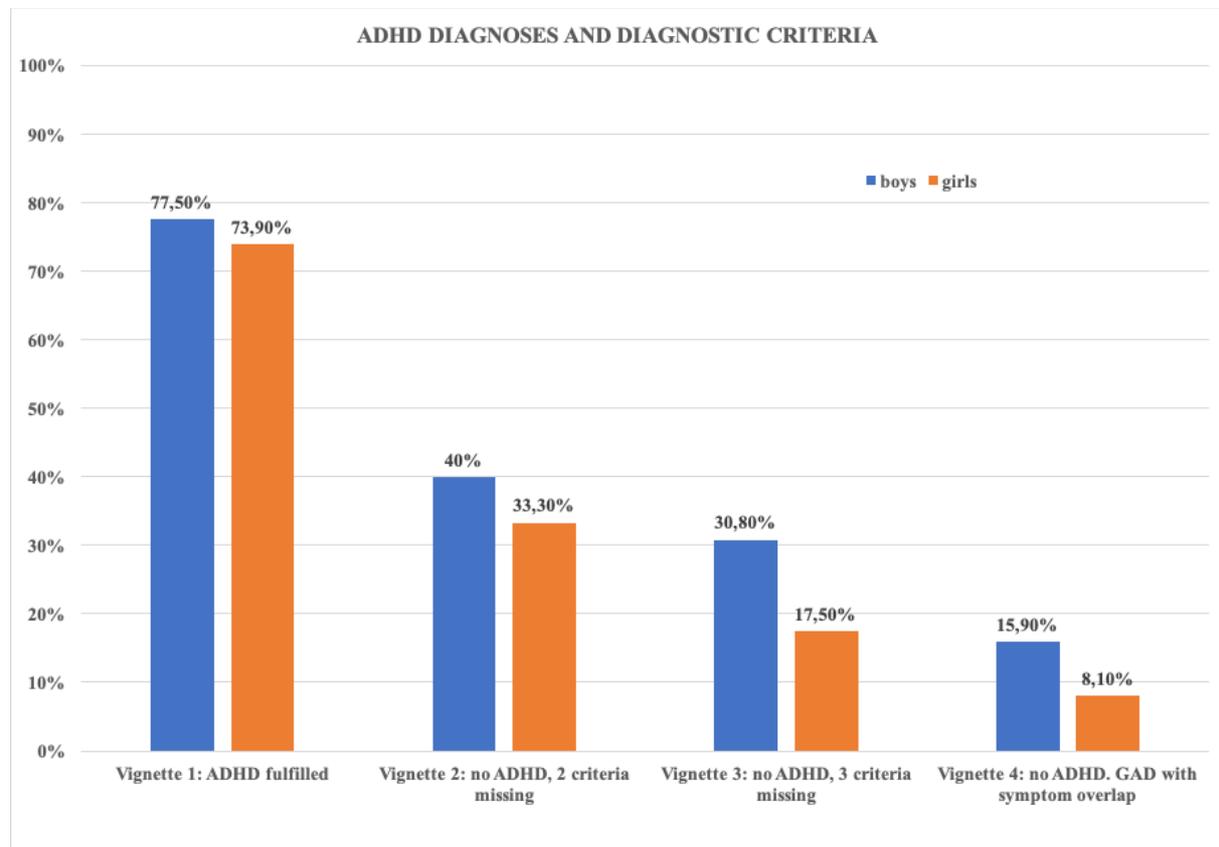


Fig. 4 Percentage of attention-deficit/hyperactivity disorder (ADHD) diagnoses for the eight different case vignettes. GAD = generalized anxiety disorder.

Moreover, the overdiagnosis of ADHD was examined separately for boy and girl vignettes. The girls' analysis resulted in an odds ratio of 3.76 and a significant chi square ( $\chi^2(1, N = 171) = 4.86, p < 0.01$ ). The same analysis for boys was also significant ( $\chi^2(1, N = 173) = 10.1, p < 0.01$ ) with an odds ratio of 7.9. These results imply that ADHD is being overdiagnosed in both boy and girl vignettes. However, by comparing the rates of false-positive diagnosis between boy and girl cases, our results demonstrate that boys are given significantly more false-positive diagnoses of ADHD ( $\chi^2(1, N = 258) = 5.87, p < 0.01$ ). Next, we examined the occurrence of psychiatrists' overdiagnoses based on their gender. In this relation, at the first level calculations were based on the overall case vignettes, i.e., irrelevant of child gender. Results of odds ratio amounted to 7.12 and 4.3 for male and female therapists, respectively and chi square was significant for both groups, implying that overdiagnosis of ADHD is independent of psychiatrist's gender (*female psychiatrist*:  $\chi^2(1, N = 173) = 6.22, p < 0.01$ ; *male psychiatrist*:  $\chi^2(1, N = 171) = 7.12, p < 0.01$ ). On level two, we repeated the analysis once again by separately examining the occurrence of psychiatrists' overdiagnosing ADHD in the boy and girl vignettes. Our results indicate that in female psychiatrists' group chi squares of girl

vignettes were not significant ( $\chi^2(1, N = 85) = 2.2, ns, OR = 3.16$ ), while the same statistic was significant for boy vignettes ( $\chi^2(1, N = 88) = 4.17, p < 0.01, OR = 6.8$ ), showing that ADHD is overdiagnosed by female psychiatrists only in boy vignettes. In the male psychiatrists' group, chi squares of girl vignettes were not significant ( $\chi^2(1, N = 86) = 2.66, ns, OR = 4.9$ ), while the same statistic was significant for boy vignettes ( $\chi^2(1, N = 85) = 5.89, p < 0.01, OR = 9.0$ ). These results indicate that similar to female psychiatrists, ADHD is overdiagnosed by male psychiatrists only in boy vignettes. With respect to the third aim of this study, we examined the impact of overdiagnosis on treatment recommendation. Findings showed that making an ADHD diagnosis significantly increases treatment recommendations entailing medication ( $\chi^2(1, N = 84) = 4.39, p < 0.01$ ), whereas recommendations for psychotherapy were not significant ( $\chi^2(1, N = 79) = 4.27, p = 0.052$ ).

**Discussion:** Results of study 1 indicate that ADHD overdiagnosis is present in Iran and to boys' disadvantage. It is also significantly associated with treatment recommendations entailing medication. As an explanation, supported by Mertens, Cwik, Margraf and Schneider (2017), ADHD is overdiagnosed where therapists instead of adhering to the diagnostic guidelines rely on general heuristics. Our findings are generally in line with those of Bruchmüller, Margraf & Schneider (2012), as they also reported the occurrence of ADHD overdiagnoses among German therapists. However, contrary to their findings that ADHD overdiagnosis occurred only by male therapists, our results imply that this is the case by both male and female psychiatrists in Iran. In addition, based on our findings boys were more than twice as likely to receive a false-positive diagnosis of ADHD in comparison to girls, contradicting the conclusion by Achenbach et al. (2008) who established that Iranian parents and teachers revealed no such gender differences on ADHD symptom measures. It seems to be either that ADHD is perceived differently by health professionals in Iran, in this case by psychiatrists compared to teachers and parents or that we are witnessing a change in ADHD symptom perceptions since 2008. Overall, our results imply that clinicians should strictly adhere to the criteria offered by ICD or DSM guidelines. In addition, to avoid the overdiagnosis of ADHD, we need to develop strategies to help overcome heuristic biases and reduce diagnostic error.

## **4.2 Emotion dysregulation in adults with attention deficit hyperactivity disorder: A meta-analysis**

Beheshti, A., Chavanon, M. L., & Christiansen, H. (2020). Emotion dysregulation in adults with attention deficit hyperactivity disorder: a meta-analysis. *BMC psychiatry*, 20(1), 1-11.

**Theoretical background:** ADHD, characterized by its core symptoms inattention, impulsivity, and hyperactivity, is shown to persist into adulthood (Barkley, 2010; Kessler et al., 2006; Retz, Stieglitz, Corbisiero, Retz-Junginger, & Rösler, 2012). Apart from the core symptoms, emotion regulation

contributes independently to functional impairments in children, adolescents, and adults with ADHD (Skirrow & Asherson, 2013; meta-analysis by Graziano & Garcia, 2016 and qualitative reviews by Ramsay & Rostain, 2008). Furthermore, ED also exists in patients with ADHD not suffering from any other comorbid mental disorder (Skirrow & Asherson, 2013). Among those studies and reviews reporting on ED in ADHD, there are at present one systematic review (Shaw, Stringaris, Nigg, & Leibenluft, 2014) and one meta-analysis (Graziano & Garcia, 2016), both focusing on ED in childhood ADHD. The overview by Shaw, Stringaris, Nigg, & Leibenluft (2014) summarizes the debate of conceptualizing ED with respect to ADHD by considering ED as a core yet distinct feature that correlates with ADHD. The meta-analysis by Graziano and Garcia (2016) analyzed features of ED in children with ADHD. Distinguishing the dimensions of ED in children with ADHD, they demonstrated that such patients are more likely to experience intense emotions. The authors reported that this association between emotional reactivity and the ADHD symptom burden becomes stronger with age, a finding consistent with published reports acknowledging that ED's impairment persists over the life-span (Helfer et al., 2019; Shaw, Stringaris, Nigg, & Leibenluft, 2014; Schweren et al., 2019). Relying on the ED facets derived by Graziano and Garcia (2016) for children and adolescents, the goal of the present study was to conduct a meta-analysis continuing their work for adult patients with ADHD, as this has not been done so far, in order to identify features of ED in adult ADHD with a literature review and to examine a) the magnitude of the associations between ADHD status ED and its facets, and b) the magnitude of the associations between ADHD symptom scores, ED and its facets.

**Methods:** A systematic literature search was undertaken using the electronic databases PubMed and PsychINFO. The literature search was consistent with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) statement (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2009). We defined the inclusion criteria of the meta-analysis as follows: (i) report of any self- or third-party measure of emotion, affect, or mood (dys)regulation or emotional lability, (ii) inclusion of clinical samples of adults diagnosed with ADHD, (iii) inclusion of non-ADHD healthy controls. Exclusion criteria were case reports, conference abstracts, reviews, duplicates and non-English studies. The primary search in PubMed yielded 1316 and in PsycINFO 714 abstracts. Based on inclusion and exclusion criteria abstracts of all articles were screened. In this relation, 858 studies failed to be included after removing duplicates and then 1109 studies were excluded as the theme of ADHD in adulthood and measurements of ED were absent. Finally, excluding studies in languages other than English as well as reviews, 63 studies remained to be scanned in full-text of which 13 studies were selected for data extraction. These studies were then coded based on the identified dimensions of ED, adopted from final scanning step, as emotion recognition, emotional lability and negative emotional responses. Ultimately, studies categorized into two parts: the first part included studies that examined ED between groups with and without ADHD (related to the first aim of the study). In this regard, meta-analysis was carried out using random-effects models and average effect sizes were estimated; Hedges' *g* criteria

were adopted as small = 0.2, medium = 0.5 and large  $\geq 0.8$  (Turner & Bernard, 2006). The second part included studies that investigated ED within the groups with ADHD (related to the second aim of the study). In this relation, effect sizes were originally reported based on correlations. Each correlation factor ( $r$ ) was converted to Fischer's  $z$ . Finally, to report all of a study's effect sizes in a corresponding unit, Fischer's  $z$  was converted to Hedges'  $g$ . To run all the above-mentioned analyses and demonstrate results, Cochrane RevMan 5 and Meta-Mar were used.

**Results:** With respect to the first aim of the current study, which was to identify features of ED in adult ADHD with a literature review, facets of ED were determined as emotion recognition, emotional lability and negative emotional responses. In addition, of 13 studies selected for the meta-analysis, ten (Bisch et al., 2016, Bodalski, Knouse & Kovalev, 2018; Cavelti et al., 2018; Corbisiero et al., 2107; Irastorza & Bellon, 2016; Miller et al., 2011; Mitchell et al., 2012; Rapport et al., 2012; Richard-Lepouriel et al., 2015; Rüfenacht et al., 2019; Skirrow & Asherson, 2013; Surman et al., 2015) were used to run between-group analysis, as they reported data for both groups with ADHD and healthy controls. Each of these studies reported that either general ED or specified facets of ED are significantly different between the control and ADHD groups. Furthermore, four studies (Corbisiero et al., 2107; Mitchell et al., 2012; Reimherr et al., 2005; Richard-Lepouriel et al., 2015) were included to run our within-group analysis, as they only reported data on clinical groups. Each of these studies also reported that either general ED or specified facets of ED are significantly associated with severity of ADHD symptoms. Moreover, Conners' Adult ADHD Rating Scale, Emotion Regulation Skills Questionnaire, Deficient Emotional Self-Regulation, Current Behavior Scale, Wender-Reimherr Adult Attention Deficit Disorder Rating Scale, Diagnostic Assessment of Nonverbal Accuracy, The Affect Intensity Measure, Affective Lability Scale, Deficient Emotional Self-Regulation Scale and Emotion Reactivity Scale were the measures adopted by the included studies to determine the status of ED and its dimensions. Furthermore, after conducting the meta-analysis to examine whether groups with and without ADHD differ in emotion regulation, results showed a large average effect size of  $g = 1.17$  (95% CI [0.70, 1.64],  $p < 0.001$ ) for general emotion dysregulation according to the random effects model. In addition, emotional lability was revealed to have a medium to large effect size ( $g = 1.20$  (95% CI [0.57, 1.83],  $p < 0.001$ ). The effect size for negative emotional responses and emotion recognition was calculated as  $g = 1.12$  (95% CI [0.57, 1.68],  $p < 0.001$ ) and  $g = 0.63$  (95% CI [0.40, 0.85],  $p < 0.001$ ), respectively (see table 1). However, results of an analysis of the variance (ANOVA) showed that the difference between those specific dimensions was not significant ( $F = 1.33$ , ns).

Table 1. Average effect Sizes for differences in ED dimensions between adults with and without ADHD

	<b>ED</b>	<b>ER</b>	<b>EL</b>	<b>NE</b>
<b>Hedges'g</b>	1.17	0.63	1.20	1.12
<b>95% CI</b>	[0.70,1.64]	[0.40, 0.85]	[0.57, 1.83]	[0.57, 1.68]
<b>Hedges'g Criteria</b>	Large	Moderate	Large	Large
<b>I<sup>2</sup></b>	94%	40%	90%	91%
<b>Criteria of I<sup>2</sup></b>	High	Moderate	High	High
<b>Number of studies</b>	12	6	4	6
<b>Number of participants</b>	1926	767	695	933

Notes. ED=Emotion Dysregulation, ER=Emotion Recognition, EL= Emotional Lability, NE=Negative Emotions.  
*I<sup>2</sup>*: Heterogeneity of the study.

Conducting the meta-analysis to investigate the association between ADHD symptoms in adults and emotion dysregulation dimensions, findings showed a strong correlation between the severity of ADHD symptoms and ED in general with an average effect size of  $r = 0.54$  (95% CI [0.48, 0.61],  $p < 0.001$ ). Moreover and regarding the facets of ED, results revealed that negative emotional responses contribute more with a weighted effect of  $r = 0.63$  (95% CI [0.30, 0.99],  $p < 0.001$ ) whereas emotional lability revealed a slightly smaller weighted effect of  $r = 0.52$  (95% CI [0.31, 0.73],  $p < 0.001$ ) (see table 2). However, results of an ANOVA showed that the difference between those specific dimensions was not significant ( $F = 0.27$ , ns). In addition, the total heterogeneity of ED's average effect size in between-group studies was 94 % and for emotion recognition, emotional lability, and negative emotional responses 40 %, 90 % and 91 %, respectively. In the within-group studies, the total heterogeneity of the average effect size was 71 %, and for emotional lability and negative emotional responses 54 % and 68 %, respectively. In addition, Fail-safe N test results showed that 1481 studies need to be added to our analysis to reduce the effect size to statistical non-significance. Similar analysis for within group analysis showed that 732 studies need to be added to our analysis to reduce the effect size to statistical non-significance.

Table 2. Average effect sizes for correlation between ED dimensions and symptoms of adult ADHD

	<b>ED</b>	<b>EL</b>	<b>NE</b>
<b>Correlation Coefficient (r)</b>	0.54	0.52	0.63
<b>95 % CI (random-model)</b>	[0.48, 0.61]	[0.31, 0.73]	[0.30, 0.99]
<b>r criteria</b>	Large	Large	Large
<b>I<sup>2</sup></b>	71 %	54 %	68 %
<b>Criteria of I<sup>2</sup></b>	High	Medium	Medium
<b>Number of studies</b>	4	2	2
<b>Number of samples</b>	1097	168	168

Notes. ED=Emotion Dysregulation, ER=Emotion Recognition, EL= Emotional Lability, NE=Negative Emotions.  
I<sup>2</sup>: Heterogeneity of the study.

**Discussion:** In line with a previous meta-analysis by Graziano & Garcia (2016) and a systematic review by Shaw et al. (2014) which respectively summarizes the debate of conceptualizing ED with respect to ADHD and analyzed features of ED in children with ADHD, we conducted a meta-analysis focusing on the role of ED in adulthood ADHD. Based on the 13 studies included in this meta-analysis, facets of ED were identified as emotion recognition, emotional lability and negative emotional responses. Findings of this study implied that compared to a control group, ED is a distinct feature of adult ADHD. In this relation, results are in line with previous studies that demonstrated the relevance of ED for mental and somatic health in general (e.g., Kring, 2008; Kring, 2010), and for ADHS in particular (e.g., Shaw et al., 2014; Barkley & Fischer, 2012). Furthermore, our findings suggested that the severity of ADHD symptoms significantly correlates with dimensions of ED. These results are also in accordance with the literature (e.g., Evren, Evren, Dalbudak, Topcu, & Kutlu, 2018; Helfer et al., 2019; Shushakova, Ohrmann, & Pedersen; 2018), and compatible to the study by Graziano & Garcia (2016) that reported a stronger correlation between emotional responses and ADHD symptoms in older adolescents. All in all, findings of this study suggest that assessing and targeting emotion regulation in clinical practice might prove to be a valuable strategy for diagnosing and treating adult ADHD.

### 4.3 Meta-Mar: a free online meta-analysis service

Ashkan Beheshti, Mira-Lynn Chavanon, Björn Albrecht and Hanna Christiansen (under review at Journal of Educational and Psychological Measurement)

**Theoretical background:** Acknowledging the importance of meta-analysis as a key method for life sciences, it is of major interest for researchers, students and educators to have access to freely available meta-analysis tools that are instantly ready to use and easy to handle. In this relation, when inspecting established meta-analysis software and recent software reviews (Wallace et al., 2017, Bax et al., 2009; Sterne, Egger & Sutton, 2008; Sutton et al., 2005), we identified two main aspects that discourage meta-analysis novices :1) accessibility of tools, and 2) methods of application development, data entry and calculation. With regard to accessibility and in comparison to offline software solutions, online tools can directly be accessed via standard internet browsers without any further installation as requirement. As the focus of study 3 is to investigate the free online tools available for conducting a meta-analysis, we limited our review to four rather popular online tools, MAVIS<sup>6</sup>, MetaInsight<sup>7</sup>, M-A Calculator<sup>8</sup> and Health Decision Strategies Meta-Analysis Calculator<sup>9</sup>. Each of these web-apps have their own pros and cons. The first aim of study 3 was to review and summarized features of the four above mentioned web apps. The second aim of the study was to introduce Meta-Mar, a free online meta-analysis web-app developed as an alternative tool for running a meta-analysis. The third aim of this study was to compare the features of Meta-Mar with other available web-apps in this field.

**Methods:** Concerning the first aim of the study, we reviewed and compared MAVIS, MetaInsight, M-A Calculator and Health Decision Strategies Meta-Analysis Calculator based on their application development, methods of data entry and models of the analysis. Furthermore, with regard to the second aim of the study, development of Meta-Mar was discussed. In this relation, first mathematical background of meta-analysis process is summarized. We then explained how Meta-Mar was developed during two steps of programming, namely, Python based backend, which is focused on the calculation process of meta-analysis, and JavaScript based frontend that regards the experience of the user while working with the application. Furthermore, the instructions of using Meta-Mar were explained. In this relation, methods of data entry and models of analysis were introduced. Furthermore, we compared the features of the four web-apps reviewed in the first step with those of Meta-Mar. In addition, to show how results of a meta-analysis are presented in Meta-Mar, we used an illustrative example. Finally, to

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<sup>6</sup> <http://kylehamilton.net/shiny/MAVIS/>

<sup>7</sup> <https://crsu.shinyapps.io/metainsightc/>

<sup>8</sup> <http://www.lyonsmorris.com/mal/index.cfm>

<sup>9</sup> <http://www.healthstrategy.com/meta/metainput.htm>

validate Meta-Mar, results of this illustrative meta-analysis were compared to those of MAVIS and RevMan.

**Results:** With respect to first objective of this study, comparative features of online meta-analysis services were identified as accessibility and functionality. In this regard, accessibility referred to availability of the service (online, offline or hybrid) and its costs. On the other hand, functionality targets data entry as well as types (SMD, correlation or binary), models (calculations of fixed and random effect models, bias of analysis, subgroup analysis, etc.), and outcomes (forest and funnel plots, data frames, etc.) of analysis. With respect to such characteristics, four rather popular meta-analysis web-apps of MAVIS, MetaInsight, M-A and HDS Calculator were reviewed and pros and cons of each app were distinguished. Advantages such as variety of analysis calculations, like in MAVIS, or the possibility of converting different types of effect sizes to each other, like in M-A, or the option of cvs file upload and visualization of network plots in MetaInsight were enumerated. Furthermore, limitation of the analysis types and models were considered as disadvantages. For instance, MetaInsight and M-A lack the reports of heterogeneity, analysis bias and funnel plots and meta-analysis can only be conducted for continuous data (mean differences). M-A and Health Decision Strategies Meta-Analysis Calculator also lack the comparison between fixed and random models. Of the described online-tools, only MetaInsight and MAVIS fulfill the inclusion of both fixed and random effect models. Furthermore, analysis based on multiple models other than mean differences (i.e., correlations and ratios) is a lack in all the apps except MAVIS. MAVIS is capable of running a meta-analysis by covering its A to Z aspects including subgroup moderator analysis. However, subgroup analysis is developed to include only categorical variables and the user is not able to add a continuous moderator variable to conduct a regression analysis between such predictor variables and the effect sizes. In addition, with MAVIS the user can set the raw data based on the application instructions in an Excel or cvs file, however instead of uploading such files to the program, she/he has to manually copy and paste the data from the file to the related section in the application. A direct upload option, like in MetaInsight, would make the data entry method of MAVIS even more flexible. With respect to the second objective of this study, we developed Meta-Mar by adopting the mathematical backgrounds introduced in the literature (Borenstein et al., 2010; Brockwell & Gordon, 2001; Cleophas & Zwinderman, 2012; Ellis, 2010) as methods of meta-analysis calculations, Python (v 3.6.3) and Vue.Js (v 2.5.2) as backend and frontend programming languages, respectively. In this relation, Meta-Mar was developed to conduct meta-analysis based on three models of standardized mean difference (SMD), correlation and ratio. In each model and with respect to data entry, the user is able to select between manual data entry or an Excel file upload. As an example, we discussed the results of a meta-analysis calculated for the SMD model by uploading an Excel file. In this relation, Meta-Mar demonstrated the results for the entered data in predefined columns of Study, Group1-sample size, Group1-mean, Group1-sd, Group2-sample size, Group2-mean, Group2-sd, moderator variable and subgroup. Results are illustrated in eight parts, namely, 5 tables and 3

figures. The first table is a summary of studies included, the value of the calculated effect size, standard errors, weights for fixed and random models, and 95 % CI based on Hedges'  $g$ . The second table presents a summary of the average effect size of the analysis with 95 %CI, z-score, p-value and heterogeneity of the analysis ( $I^2$ ,  $\text{Chi}^2$  and  $\text{Tau}^2$ ) for both fixed and random models. The third table is assigned to report the bias of analysis in terms of Fail-Safe-N based on methods of Rosenberg (2005) and Rosenthal (1979). The fourth table shows the meta-regression results. Table 5 demonstrates the results of subgroup analysis for fixed and random effect models. The first figure is assigned to demonstrate the results by drawing two comparable forest plots regarding fixed and random effect models. The second figure visualizes funnel plots of the meta-analysis for fixed and random effect models. Finally, the third figure visualizes the intervals of effect sizes for subgroups of fixed and random effect models. To validate the calculations of Meta-Mar, we compared the results of the illustrative example with those of MAVIS and RevMan. In general, results from Meta-Mar are highly comparable with RevMan5 and MAVIS, though due to the difference in adopting weighting methods, there are some insignificant differences. Furthermore, besides the meta-analysis service we developed an effect size calculator that calculates an effect size for a single study based on SMD, correlation or ratio models. Finally, the comparison of the features of Meta-Mar and other alternative web-apps included in the review section of this study are summarized in table 3.

Table 3. Comparison of different meta-analysis online apps

	MAVIS	MetaInsight	M-A Calculator	Health Decision Strategies Meta-Analysis Calculator	Meta-Mar
<b>programming basis</b>	R+Shiny	R+Shiny	HTML+JavaScript	HTML+JavaScript	Python+VueJs
<b>type of analysis</b>	mean differences, correlations, dichotomies	mean differences	mean differences, correlations, p values	mean differences	mean differences, correlations, ratios
<b>data entry</b>	command line/copy-paste form .cvs or Excel	.cvs upload	one by one entered, then gathered in a table	a table with limit number of studies	responsive table/ Excel upload
<b>model of analysis</b>	fixed & random	fixed & random	fixed	fixed	fixed & random
<b>full output (ES<sup>a</sup>, SD<sup>b</sup>, CI<sup>c</sup>, w<sup>d</sup>%, p value, z score, etc.)</b>	✓	-	-	-	✓
<b>plots</b>	forest plots funnel plots	forest plots funnel plots network plots	-	forest plots	forest plots funnel plots
<b>heterogeneity</b>	✓	-	-	-	✓
<b>Fail-N safe</b>	✓	-	-	-	✓
<b>Separate effect size calculator</b>	✓	-	-	-	✓
<b>Continuous moderator variable</b>	-	-	-	-	✓
<b>Subgroup analysis</b>	✓	✓	-	-	✓

a: effect size, b: Standard Deviation, c: Confidence interval, d: weight

**Discussion:** After identifying distinguished characteristics of online meta-analysis services and reviewing the four popular web-apps available for running a meta-analysis, we discussed their pros and cons. Next we introduced Meta-Mar as an alternative solution. Development and function of Meta-Mar were also articulated and compared to those of the four available. In this relation, the Meta-Mar user is able to run a meta-analysis based on mean differences, correlations or ratios and reach the results of fixed and random model analysis attached with forest and funnel plots as well as heterogeneity, bias of

the analysis (Fail-N safe), subgroup analysis. In addition to those facilities developed by the four web-apps, Meta-Mar can upload excel file data besides manual data entry. Moderator analysis, prediction of effect size based on a continuous moderator variable, is another advantage of Meta-Mar. Moreover, regardless of the section of meta-analysis in the app, an adjunctive effect size calculator is also available in order to represent the calculated effect sizes of a single study.

## **5 Final discussion**

### **5.1 Theoretical and practical implications of the studies**

The results of this dissertation provide evidence that ADHD is overdiagnosed to boy's disadvantage. In addition and following the previous studies that specified ED as a core feature of ADHD in children and adolescents, findings of this dissertation demonstrated that ED is also core a characteristic of adult ADHD. These findings imply that on the one hand ADHD should be diagnosed strictly based on the criteria of guidelines instead of including subjective heuristics, and on the other hand considering ED as a main feature of psychopathology of ADHD to not only improve the diagnostic procedure but to also reinforce the treatment of the disorder. In **study 1**, by replicating the German study of Bruchmüller, Margraf & Schneider (2012) in an Iranian cultural context the occurrence of ADHD overdiagnosis was examined. Concerning our first aim, our findings show that similar to the German study ADHD is overdiagnosed in Iran. Such results, however, contradict the findings of the study of Achenbach et al. (2008) that established Iranian parents and teachers to rate boys and girls with respect to ASEBA and SDQ ratings more similar than parents and teacher of all other countries included. Accordingly, we had expected Iranian psychiatrists to rate girls and boys equally. However, as we detected the same false-positive bias to the disadvantage of boys as Bruchmüller, Margraf and Schneider (2012), it seems to be either that ADHD is perceived differently by health professionals in Iran, in this case by psychiatrists compared to teachers and parents or that we are witnessing a change in ADHD symptom perceptions since 2008 when the study by Achenbach et al. was published. As the meta-analysis by Yadegari et. al (2018) reveals a very high prevalence rate of ADHD of 12 % (CI 95%: 9.0 - 15) in children aged 6 to 14 years in Iran, the latter could be the case. Furthermore and concerning the third aim of the study 1, findings demonstrated that both male and female therapists overdiagnosed ADHD only in boys, a finding that does not concur with the results of Bruchmüller, Margraf & Schneider (2011), as they reported ADHD overdiagnosis only by male therapists in boys and as an "unexpected finding with no obvious explanation." Our study results are thus more in line with the assumption that both male and female psychiatrists do not always adhere to ADHD's diagnostic criteria and instead most likely rely on subjective heuristics. In this relation, similarities between the actual patient and an imaginary stereotypical ADHD patient, and prioritizing the diagnostic criteria differently are considered to be the two main sources of the misdiagnosis. In addition, as such a misdiagnosis bias to the disadvantage of

boys might imply that a male patient exhibits significantly more similarities to a stereotypical ADHD patient than does a female patient. Finally and with respect to the fourth objective of study 1, findings showed that psychiatrists who made an ADHD diagnosis in non-ADHD children prescribed medication more frequently than psychiatrists who did not. However, a similar psychotherapeutic-recommendation comparison was not significant. These findings are not fully in line with the study by Bruchmüller, Margraf & Schneider (2012), as their results show that both psychostimulant and psychotherapeutic treatment recommendations were higher in the group of therapists that falsely declared an ADHD diagnosis. Explaining our findings, since all the participants in the present study were psychiatrists and psychologists were not included because they are not allowed to make a diagnosis due to the law of the Medical Council of the Islamic Republic of Iran, this factor might be a reason behind higher medication prescriptions and the lack of psychotherapy recommendations in this study.

**Study 2** is a meta-analysis that established aspects of ED in adulthood ADHD. In this relation, based on the adopted conceptual models of ED (i.e., emotion regulation model by Gross (2009), and regarding features of ED in adulthood ADHD focused by studies included in the meta-analysis) the three dimensions of 1) emotion recognition (ER), 2) emotional lability (EL), and 3) negative emotional responses (NE) were distinguished. A total of 13 studies was selected (N = 2535) and labeled as between-group studies (10), in which data was reported on both groups with ADHD and healthy controls, and within-group studies (4), in which only data on patients with ADHD was available. At the between-group analysis level, results showed that compared to a control group, emotion dysregulation is significantly more pronounced in adults with ADHD with a large effect size (Hedges'  $g = 1.17$ ). Furthermore, regarding ED's intermediate dimensions, emotional lability revealed the largest effect size (Hedges'  $g = 1.20$ ). Previous studies demonstrated the relevance of ED for mental and somatic health in general (e.g., Kring, 2008; Kring, 2010) and for ADHS in particular (Shaw et al., 2014). Barkley & Fischer (2012) demonstrated that adult patients with persisting ADHD reported worse ED than healthy control participants. In addition, at the within-group analysis level a strong correlation between the severity of ADHD symptoms and ED ( $r = 0.54$ ) was observed. In terms of ED dimensions, negative emotional responses exhibited the strongest correlation with the core ADHD symptoms ( $r = 0.63$ ) - findings that concur with the literature (Evren, Evren, Dalbudak, Topcu, & Kutlu, 2018; Helfer et al., 2019; Shushakova, Ohrmann, & Pedersen; 2018), and that are also compatible with the study by Graziano & Garcia (2016) that reported a stronger correlation between emotional responses and ADHD symptoms in older adolescents. Findings of this study demonstrate that emotional lability plays both a significant role in differentiating clinical groups with ADHD from healthy controls and a strong correlation between negative emotional responses and ADHD symptom severity. Articulating explanations for findings of study 2, literature suggests that concerning ADHD's epidemiology in adults, the evidence that hyperactive-impulsive symptoms seem to remit in older age groups may be attributable to adaptive strategies patients develop over the life-span, while inattention symptoms seem

to persist (Barkley, 2014; Polanczyk et al., 2014; Simon et al., 2009). In this respect, these symptoms might be correlated with lack of strategies for monitoring emotion regulation processes and impaired situation identification. As articulated by Posner & Hulvershorn (2014) in their dyscontrol and affectivity hypotheses the severity of ADHD symptoms in adults correlates significantly with negative externalizing behaviors such as aggression and irritation. Based on these hypotheses, negative-emotionally-responsive behavior occurred whether by impairments in the capacity of inhibiting the emotional responses due to anomalies within frontolimbic circuits (dyscontrol hypothesis), or by dysfunctional emotional processing associated with the amygdala and medial prefrontal cortex (affectivity hypothesis).

Furthermore, conducting the meta-analysis on the role of ED in adulthood ADHD requires a closer look at the currently available online meta-analysis services. In this relation, regarding the cons and pros of each of these web applications was the focus of **study 3**, and the subsequent development of a free online application service, namely Meta-Mar, a complementary tool for conducting a meta-analysis. Among online web-apps, MAVIS, MetaInsight, M-A and Health decision Strategies Calculator are four rather popular meta-analysis services. Regarding the disadvantages of these services, such as lack of calculations for random models, meta-regression and subgroup analysis, heterogeneity, Fail-Safe-N and funnel plots, we developed Meta-Mar in order to conduct the meta-analysis process based on the standard mean difference model, correlation model and risk ratio model. Furthermore, Meta-Mar demonstrates results of the analysis in eight parts including the summary of studies, summary of average effect size, forest and funnel plots, meta regression and subgroup analysis, and reports of Fail-Safe-N. Each part can also be downloaded and saved by the user. In addition, as a distinguished feature of Meta-Mar, the user is not only able to enter the data manually but can also upload an Excel file. Comparative consideration of the results between Meta-Mar and RevMan demonstrates high validity of the application. Furthermore, Meta-Mar is also appropriate for users who like to introduce meta-analysis in seminars, lectures, exercises, etc.

## **5.2 Limitations of the studies**

Regarding study 1, as the vignettes in this study were adopted from the study by Bruchmüller, Margraf and Schneider (2012) and were not fully compatible with Iranian culture, the issue of case validity can be raised. In this regard, the lack of the psychiatrist's responsibility in decision-making based on the written vignettes is one source of such a limitation. In addition, compared to written descriptions of patients, psychiatrists in real situations can gather more information about a patient in real-life settings that might facilitate the decision making process. However, as the vignettes are based strictly on the DSM-IV criteria and ICD-10 and as we would expect psychiatrists to strictly adhere to those criteria during the diagnostic procedure, decision-making should be even easier in such a situation than in real life settings (Bruchmüller, Margraf & Schneider, 2012). Another limitation of this study concerns the

problem of generalizing results. As our study investigated the issue of overdiagnosis in a sample of Iranian psychiatrists from Tehran and Isfahan, our results might not transfer well to other cities in the country or to other countries in general. However, as our overall study, results, i.e. the occurrence of overdiagnosing ADHD and the significant role of patient gender in the psychiatrist's diagnosis concur with the study of Bruchmüller, Margraf & Schneider (2012) in their German sample and with regard to highlighting the presence of overdiagnosis in previous studies, we conclude that ADHD overdiagnosis is an issue in Iran and most other countries.

Furthermore and concerning study 2, we assumed that different measures of ED are contingent, though that might not always be the case. As the adopted conceptual models of ED converged in the studies included in our meta-analysis, we did not analyze them accordingly. Moreover, reviews have shown that moderators such as gender and cognitive functions (Bridgett & Walker, 2006; Boonstra, Oosterlaan, Sergeant, & Buitelaar, 2005; Gershon & Gershon, 2002) as well as the presence of comorbidity (Kessler et al., 2006) or medication (Shushakova, Ohrmann & Pedersen, 2017) play a significant role in ADHD. Therefore, if emotion dysregulation is assumed to be a main feature of ADHD in adults, controlling for such moderators should be part of a meta-analysis. However, as the studies included contained a paucity of such statistical data, we could not perform meta-regressions that might have shed light on such moderators. Finally, our funnel plots and Fail-safe N test results imply that (probably) missing studies and thus omitted from our meta-analysis contributed to asymmetrically distributed effect sizes. In between-group analysis, missing studies would strengthen, and in within-group analysis weaken effects. In addition, the lesser degree of heterogeneity (71%) in our within-group analysis compared to the between-group analysis might be a sample-size problem.

Finally and with respect to the third study, network analysis, network plots and fill-and-trim analysis of funnel plot is still not included in the service.

### **5.3 Prospect**

If we want systematic measurements and assessments to prevail in our field and be able to validate interventions critically, we must rely on ADHD's diagnostic guidelines and base diagnostic decisions on them (Safer, 2015; Hollingworth et al., 2011). In this relation, further studies should investigate the dimensions of ADHD overdiagnosis in more details. For instance, to examine whether such overdiagnosis has a specific association with ADHD subtypes can be considered as an aim of such studies. Based on the literature, boys with ADHD are reported to be diagnosed with the hyperactive and impulsive subtype more often than girls. In addition, our findings imply that in comparison to girls boys received a diagnosis of ADHD more than twice as often. With respect to these findings, a future study should replicate study 1 and redesign the case vignettes of this study by articulating two overall types of vignettes: vignettes that fulfil or do not fulfill the criteria of the inattentive presentation (regarding

A.1 DSM-5 ADHD criteria), and vignettes that fulfil or does not fulfil the criteria of the hyperactive and impulsive presentation (regarding A.2 DSM-5 ADHD criteria). On the other hand, in line with findings of the second study that leads us to conclude that ED is not only a core feature of ADHD in children and adolescents but also a significant characteristic of adulthood ADHD, a goal of a further study can be the investigation of the role of the ED in overdiagnosis of ADHD. In this relation, the question that such study has to addresses can be whether including the assessments of ED as an adjunctive tool in ADHD diagnosis affects occurrence of ADHD overdiagnosis. Moreover, further studies should examine the issue of ADHD overdiagnosis in other cultural contexts to provide distinguished and comparative understanding of this issue in such contexts.

In addition and regarding the third study of this dissertation, development of Meta-Mar can be progressed by addressing the following goals: adding the capability of conducting a meta-meta-analysis (i.e., quantitative umbrella review), improving the user interface experience (frontend programming) and possibility of user registration in the application which would facilitate saving, editing and completing the analysis for the user, making Meta-Mar more convenient.

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## RESEARCH ARTICLE

## Open Access



# Emotion dysregulation in adults with attention deficit hyperactivity disorder: a meta-analysis

Ashkan Beheshti<sup>\*</sup> , Mira-Lynn Chavanon and Hanna Christiansen**Abstract**

**Background:** Emotional symptoms are increasingly considered a core feature of attention deficit/hyperactivity disorder (ADHD). We aimed to quantify the evidence of emotional dysregulation and its respective facets in individuals with adult ADHD compared to healthy controls using meta-analysis.

**Methods:** Two electronic databases (PubMed, PsycINFO) were reviewed to identify studies. Studies were eligible for inclusion that had reports on any measure of emotion (dys) regulation in adults (> 18 years of age) in clinically diagnosed patients with ADHD as well as healthy control participants. We included a total of 13 studies ( $N = 2535$ ) to assess (1) the standardized mean difference in emotion dysregulation (ED) as a general factor and its specific facets (i.e., emotional lability, negative emotional responses, and emotion recognition) between adults with ADHD and healthy controls; and (2) the association between ADHD symptom severity and ED.

**Results:** Compared to healthy controls, adults with ADHD revealed significantly higher levels of general ED (Hedges'  $g = 1.17$ ,  $p < 0.001$ ; Hedges'  $g$  is the adjusted effect size). With regard to intermediate dimensions of ED, emotional lability exhibited the strongest weighted effect (Hedges'  $g = 1.20$ , CI [0.57, 1.83],  $p < 0.001$ ). Furthermore, symptom severity and general ED correlated significantly ( $r = 0.54$ ,  $p < 0.001$ ). Regarding intermediate dimensions of ED, negative emotional responses correlated closely with ADHD symptom severity ( $r = 0.63$ ,  $p < 0.001$ ) and emotional lability ( $r = 0.52$ ,  $p < 0.001$ ).

**Conclusions:** Our findings support ED symptoms as a core feature of ADHD's psychopathology. With respect to dimensions of ED, emotional lability, and negative emotional responses play a more definitive role in the psychopathology of adults with ADHD. Due to insufficient statistical reports in the included studies, we could not perform meta-regressions to control the role of moderator variables.

**Keywords:** ADHD, Emotion dysregulation, adults, Meta-analysis

**Background**

Attention Deficit Hyperactivity Disorder (ADHD) is characterized by its core symptoms inattention, impulsivity, and hyperactivity [1]. The past decade of research revealed that ADHD persists into adulthood [2–4]. Apart from the core symptoms, emotion regulation contributes independently to functional impairments in patients with ADHD [5–7]. In this regard, several studies reported that emotion dysregulation (ED) (subsuming symptoms like low frustration tolerance, irritability, ease

of negative emotional experience, and emotional lability) is highly frequent in children, adolescents, and adults with ADHD ([8]; meta-analysis by [9] and qualitative reviews by [10, 11]). About 70% of adult patients with ADHD report ED or emotional lability [5, 8, 12]. Furthermore, ED also exists in patients with ADHD not suffering from any other comorbid mental disorder [8]. Those findings reveal ED as a core component of the disorder or at least as a substantial feature in a subgroup of patients with ADHD (e.g., [4, 13]).

Two decades after Wender [14] recognized features of ED as part of the clinical presentation of adult ADHD, DSM-5 refrains from including such symptoms as

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indicative of the disorder. Instead, the DSM-5 recommends considering ED as an associated feature of ADHD supporting its diagnosis [1]. According to Kring and Sloan [15], such a limitation occurred due to the fact that ED is still a transdiagnostic concept and can be applied to psychopathological aspects of various disorders not limited to ADHD. Although focusing on emotion regulation and dysregulation might provide a) new insights into the underlying pathophysiological mechanisms (e.g., Shushakova, Ohrmann & Pedersen, [16], b) a more accurate differentiation of symptoms and disorders (e.g., oppositional defiant disorder or conduct disorder vs. ADHS), and c) novel treatment approaches [17–19], research on ED still lacks a consensual and refined definition and depiction of ED and related constructs in general (e.g., [20, 21]), and theoretical frameworks and conceptual models of ED in ADHD in particular. Terms like ED, emotional lability, emotional instability (i.e., irregular shifting between emotional states) and emotional impulsivity (i.e., overshooting emotional responses) are often applied interchangeably or rather idiosyncratically (for a review see [17]). This lack of consensus and clarity regarding the construct of emotion regulation and ED makes summarizing and integrating empirical findings in ADHD complicated [22]. To avoid working in “conceptual and definitional chaos” ([23], p. 330), we briefly define emotion regulation, ED, and facets of ED that contribute to functional and psychosocial impairments in patients with ADHD.

Emotion regulation includes all processes that unfold over time and are related to the different emotions people have, the intensity of emotions, and how emotions are experienced and expressed [24]. The major function of ER is to shape emotional states to facilitate adaptive, goal-directed behavior in a certain situation. The most prominent model of emotion regulation is the modal model [24] that proposes five types of emotion-regulation strategies [25]: (1) taking steps to influence which situation one will be exposed to (situation selection); (2) changing relevant aspects of the situation (situation modification); (3) influencing which portions of the situation are perceived and attended to (attentional deployment); (4) altering the way of thinking about it (reappraisal); and (5) directly modifying emotion-related actions (response modulation). In order to apply such emotion regulation strategies, emotions need to be recognized (i.e., perception and awareness of the self and other’s verbal and nonverbal emotions) [19]. Furthermore, with respect to dysfunctional ER Ryckaert et al. [22] consider all processes that are impaired or fail to modify emotions.

Among those studies and reviews reporting on ED in ADHD, there are at present one systematic review [19] and one meta-analysis [9], both focusing on ED in

childhood ADHD. The overview by Shaw et al. [19] summarizes the debate of conceptualizing ED with respect to ADHD by considering ED as a core yet distinct feature that correlates with ADHD. The meta-analysis by Graziano and Garcia [9] analyzed features of ED in children with ADHD. Distinguishing the dimensions of ED in children with ADHD, they demonstrated that such patients are more likely to experience intense emotions. The authors reported that this association between emotional reactivity and the ADHD symptom burden becomes stronger with age, a finding consistent with published reports acknowledging that ED’s impairment persists over the life-span [19, 26, 27].

Relying on the ED facets derived by Graziano and Garcia [9] for children and adolescents, the goal of the present study was to conduct a meta-analysis continuing their work for adult patients with ADHD, as this has not been done so far. As previous empirical work on ADHD symptoms suggests there are differences in symptoms and their trajectories from childhood to adulthood [28–30], this might apply to ED and ED facets as well. We therefore first aimed to identify features of ED in adult ADHD with a literature review. Second, a meta-analysis was conducted to examine a) the magnitude of the associations between ADHD status (patient with ADHD vs. healthy control), ED and its facets; b) the magnitude of the associations between ADHD symptom scores, ED and its facets.

## Methods

### Literature search

This study has been recorded in the international prospective register of systematic reviews (Prospero) in April 2017 with the registration number CRD42017059710. A systematic literature search was undertaken using the electronic databases PubMed and PsychINFO. The literature search was consistent with the ‘Preferred Reporting Items for Systematic Reviews and Meta-Analyses’ (PRISMA) statement [31] and was terminated in December 2019. The Boolean expression used for our search is:

[ADHD\* OR “attention deficit hyperactivity disorder” OR ADD\* OR “attention deficit disorder” OR hyperkinetic\*] AND [“emotion dysregulation” OR “emotion regulation” OR “mood regulation” OR “mood dysregulation” OR “affect regulation” OR “affect dysregulation” OR emotion OR labil\*] AND [adult\*].

### Inclusion and exclusion criteria

Our search in PubMed yielded 1316 and in PsycINFO 714 abstracts. We also checked the reference lists of included studies for other studies eligible for inclusion. After removing duplicates, abstracts of all articles were screened based on pre-defined inclusion criteria independently by the first author. Inclusion criteria were: (i)

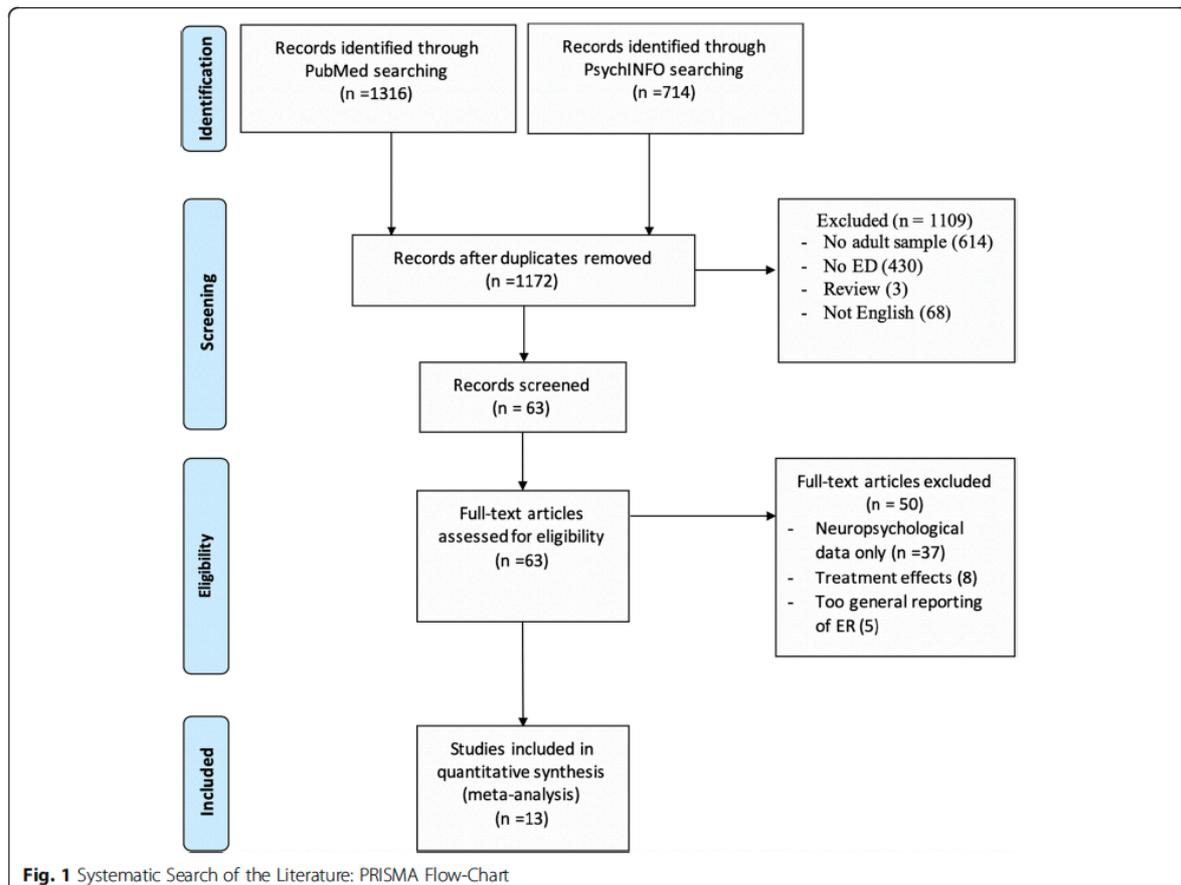
report of any self- or third-party measure of emotion, affect, or mood (dys) regulation or emotional lability, (ii) inclusion of clinical samples of adults (> 18 years of age) with ADHD characterized by clinical criteria (e.g., DSM, ICD) and diagnostic procedures, (iii) inclusion of non-ADHD healthy controls. Exclusion criteria were: case reports, conference abstracts, reviews, duplicates and non-English studies. We included only randomized case-control studies that were published in peer-reviewed journals at any time from the inception of the databases. We limited our search to published studies to ensure a level of methodological adequacy and rigor among included studies and to avoid the inevitable problems with securing access to a full set of unpublished studies and the bias that would introduce [32].

After scanning a total number of 2030 studies in order to remove the duplicates, 858 studies failed to be included. In the next step, the abstracts of the studies were checked to clarify whether the subject matter is proper to our Boolean expressions. In this step, 1109 studies were excluded since the theme of ADHD in adulthood and measurements of ED were absent. In addition,

studies in language other than English as well as reviews were excluded. Next, all titles fulfilling our inclusion criteria (63 studies) were reviewed in full-text. Data were collected and extracted by two independent reviewers that included ADHD status and diagnostic procedures, emotion regulation/dysregulation as defined above, gender composition (male, female), age, comorbidity, and country. When disagreement arose, reviewers consulted with each other until coming to a consensus. Ultimately, 13 studies remained for data extraction (see Fig. 1 for a flow chart of the search).

#### Coding and data extraction

In order to code the studies, after the final scanning, three main dimensions of ED were identified based on the narrative synthesis of the literature: Emotion recognition, emotional lability and negative emotional responses. Emotion recognition refers to the perception and awareness of the self and other's verbal and nonverbal emotions; emotional lability points to an unstable shifting between states of emotions; negative emotional responses refer to irritability and impulsivity of the



emotional reactions [19]. For each study and in addition to information on demographics: our statistical results relied on total ED and its extracted facets (emotion recognition, emotional lability or negative emotional responses). Finally, we differentiated the included studies in two parts: the first concerned studies that examined ED between groups with and without ADHD (related to the study's question of magnitude of the associations between ADHD status, ED and its facets), and the second concerned studies that investigated ED within the groups with ADHD (related to the study's question of magnitude of the associations between ADHD symptom scores, ED and its facets).

Authors who reported ED but who had not provided enough quantitative data (e.g., only a graphic illustration) were contacted in order to request the necessary information to derive effect size estimates and confidence limits on the selected indices. When only the standard error of the mean (SEM) was reported, the standard deviation (SD) was calculated by multiplying the SEM by the square root of the sample size [33]. When descriptive statistics were reported other than the mean, SD or SEM, data were imputed by established procedures where possible [34].

#### Effect estimation and heterogeneity

True effect estimates were computed as adjusted standardized mean differences (Hedges' *g*). Meta-analysis was carried out using random-effects models and the results are reported and graphically displayed, as that better conveys data variability [33]. To estimate the average effect size, Hedges' *g* criteria were adopted: small = 0.2, medium = 0.5 and large  $\geq 0.8$  [35]. Furthermore, as two studies had such small samples ( $n < 20$ ), effect sizes were also calculated with a correction factor converting Cohen's *d* to Hedges' *g*.

Moreover, to calculate the effect sizes based on correlations, each correlation factor (*r*) was converted to Fischer's *z*. Finally, to report all of a study's effect sizes in a corresponding unit, Fischer's *z* was converted to Hedges' *g*.

To examine the consistency of results and estimate to what degree the calculated average effect sizes of a given study are representative, *Q* and  $I^2$  statistics were calculated, in which the adopted interpretation amounts are: zero or small heterogeneity for 0 -40%, medium heterogeneity for 40 -70% and high heterogeneity for 70 -90% [36].

To run all the above-mentioned analyses and demonstrate results via forest plots, we carried out initial calculations using Cochrane RevMan 5 and then repeated the calculations using Meta-Mar (1.1.0), a free online meta-analysis service developed by the first author of this study (Beheshti, in preparation).

## Results

### Summary of systematic review

Our systematic literature search revealed thirteen qualifying studies. We used ten of them ([8, 37–47], to run our between-group analysis, as they reported their data for both groups with ADHD and healthy controls. Furthermore, four studies [38, 41, 45, 48] were included to run our within-group analysis, as they only reported data on clinical groups. Moreover, with respect to the identified dimensions of ED, Bodalski, Knouse & Kovalev [47], Cavelti et al. [46], Corbisiero et al. [38], Irastorza [39], Reimherr et al. [48] and Surman et al. [38] reported overall measures of ED. Cavelti et al. [46] and Irastorza & Bellon [49] additionally provided information on the specific facets of negative emotional responses and emotion recognition. The measures used by Bisch et al. [37], Miller et al. [41] and Rapport et al. [50] match the facet of emotion recognition. Mitchell et al. [41], Richard-Lepouriel et al. [45] and Skirrow & Asherson [8] operationalized ED by using scales that assessed the facets of emotional lability and negative emotional responses. Rufenacht et al., (2019) evaluated all the three dimensions of negative emotional responses, emotion recognition and emotional lability in addition to a total assessment of ED.

Moreover, and with respect to ED measurements, Cavelti et al. [46], Irastorza & Bellon [49] and Mitchell et al. [41] adopted the long version of the Conners' Adult ADHD Rating Scale self-report that contains a subscale on Impulsivity and Emotional Lability, and used the Emotion Regulation Skills Questionnaire to measure emotion regulation skills. Furthermore, Bodalski, Knouse & Kovalev [47] and Irastorza & Bellon [49] employed the Deficient Emotional Self-Regulation (DESR) scale additionally, which is a section of the self-report Current Behavior Scale developed by Barkley [51] for assessing ED. Reimherr et al. [48] and Corbisiero et al. [38] assessed ED via the Affect Lability, Temper and Emotional Overreactivity subscales of the Wender-Reimherr Adult Attention Deficit Disorder Rating Scale. Miller et al. [40] and Rapport et al. [50] administered the Diagnostic Assessment of Nonverbal Accuracy (DANVA [52]); as an assessment to identify facial emotional expression. In addition, Rapport et al. [50] and Richard-Lepouriel et al. [45] administered The Affect Intensity Measure (AIM; [53] to examine experienced aspects of emotion. Richard-Lepouriel et al. [45] and Skirrow & Asherson [8] also employed the Self-rated Affective Lability Scale (ALS [54]) to measure emotional lability and negative emotional responses. Bisch et al. [37] employed the Self-Report Emotional Intelligence Test (SREIT, [55]) to measure the ability to recognize, manage, and engage in one's own and others' emotions. Surman et al. [44] used the Deficient Emotional Self-Regulation scale (DESR [51]); to measure ED (see Table 1 for details).

Rüfenacht et al. [43] administered The Emotion Reactivity Scale (ERS, [56]) which consists of three subscale of emotion sensitivity, intensity and persistence in order to evaluate ED.

Regarding the studies' results, Bodalski, Knouse & Kovalev [47], Cavelti et al. [46], Corbisiero et al. [38], Irastorza [39], Reimherr et al. [48], Rüfenacht et al. [43] and Surman et al. [44] reported a significant difference between ED scores (regardless of its specific dimensions) of the groups with ADHD and healthy controls ( $p < 0.01$ ,  $p < 0.01$ ,  $p < 0.001$ ,  $p < 0.01$ ,  $p < 0.01$ ,  $p < 0.001$  and  $p < 0.01$ , respectively). Cavelti et al. [46], Irastorza & Bellon [49] and Rüfenacht et al., [43] also reported a strong association between negative emotional responses and emotion recognition in their ADHD group ( $p < 0.01$ , for all of them). Moreover, the studies by Bisch et al. [37], Miller et al. [40], Rapport et al. [50] and Rüfenacht et al. [43] demonstrated a distinct difference between groups regarding the facet of emotion recognition ( $p < 0.01$  for all of them). In addition, emotional lability and negative emotional responses were significantly associated in patients with ADHD in investigations by Mitchell et al. [41], Richard-Lepouriel et al. [45], Rüfenacht et al. [43] and Skirrow & Asherson [8] ( $p < 0.01$ , for all of them).

Furthermore, the study by Corbisiero et al. [38] was the only one we included that investigated comorbidity as a moderating variable. In this context, they observed a significant difference between ADHD + ED with comorbidity

and ADHD + ED with no comorbidity ( $p < 0.01$ ). Also, the study by Cavelti et al. [45] was the only one in which ED was not only investigated in differences between patients with ADHD and healthy controls, but also it compared ED in ADHD with ED in another mental disorder: they found that patients with ADHD and borderline personality disorder exhibit significantly higher levels of emotional lability than a healthy group ( $p < 0.001$ ). However, the difference in emotional lability was not significant between patients with ADHD and borderline personality disorders ( $p = 0.81$ ). Table 1 provides an overview of the studies included in this meta-analysis.

### Summary of the meta-analysis

#### ED differences between patients with ADHD and control groups

In answering our study's first question, namely whether groups with and without ADHD differ in emotion regulation, we noted a large average effect size of  $g = 1.17$  (95% CI [0.70, 1.64],  $p < 0.001$ ) for general emotion dysregulation according to the random effects model (for details see Fig. 2 and Table 2). In addition, with respect to specific dimensions, medium to large effect sizes were revealed for emotional lability ( $g = 1.20$  (95% CI [0.57, 1.83],  $p < 0.001$ ), negative emotional responses ( $g = 1.12$  (95% CI [0.57, 1.68],  $p < 0.001$ ), and emotion recognition ( $g = 0.63$  (95% CI [0.40, 0.85],  $p < 0.001$ ). However, results of an analysis of the variance ANOVA showed that

**Table 1** Summary of studies and calculated effect sizes

Study	Age(M ± SD)	sample size	Measurements of ED	ED dimensions	design	Effect size
[37]	28.52 ± 8.53	54	The Self-report of Emotional Intelligence Test	ER	Between	0.70
[47]	30.47 ± 9.20	159	DERS	Total ED	Between	0.92
[46]	33.39 ± 9.4	135	Impulsivity/Emotional Lability scale from the Conners' CAARS	Total ED, ER, NE	Between	1.67
[38]	32.27 ± 10.98	514	Emotional Dysregulation Derived from the Wender-Reimherr Adult Attention Deficit Disorder Rating Scale	Total ED	Between Within	2.04 1.38
[49]	36.29 ± 10.71	105	Impulsivity/Emotional Lability scale from the Conners' CAARS, DERS	Total ED, ER, NE	Between	0.85
[40]	33.82 ± 9.90	51	Diagnostic Analysis of Nonverbal Accuracy	ER	Between	0.30
[41]	23.58 ± 5.31	41	Impulsivity/Emotional Lability scale from the Conners' CAARS	EL, NE	Between Within	0.95 2.10
[50]	34.85 ± 11.20	56	Affect Intensity Measure, Diagnostic Analysis of Nonverbal Accuracy	ER	Between	0.25
[48]	41.20 ± 11.20	536	Emotional Dysregulation Derived from the Wender-Reimherr Adult Attention Deficit Disorder Rating Scale	Total ED	Within	1.09
[45]	38.14 ± 11.43	198	Affective Lability Scale, Affect Intensity Measure	EL, NE	Between Within	0.98 1.31
[43]	35.49 ± 12.86	366	ERS	Total ED, EL, NE, ER	Between	0.59
[8]	28.76 ± 9.98	88	The Affective Lability Scale-Short Form	EL, NE	Between	1.87
[44]	28.42 ± 8.78	232	self-report Current Behavior Scale developed by R. Barkley	Total ED	Between	2.71

ED Emotion Dysregulation, ER Emotion Recognition, EL Emotional Lability, NE Negative Emotions. Between: comparison between ADHD and control group, within: association of ADHD symptoms with emotion dysregulation within the ADHD group

the difference between those specific dimensions was not significant ( $F = 1.33$ , ns).

**Association of ED with severity of ADHD symptoms**

Answering our study’s second question regarding a correlation between ADHD symptoms in adults and emotion dysregulation dimensions, we found a strong correlation between the severity of ADHD symptoms and ED in general with an average effect size of  $r = 0.54$  (95% CI [0.48, 0.61],  $p < 0.001$ ; for details see Fig. 3 and Table 3). However, our data on the correlation between the severity of ADHD symptoms and specific ED dimensions revealed that negative emotional responses contribute more with a weighted effect of  $r = 0.63$  (95% CI [0.30, 0.99],  $p < 0.001$ ) whereas emotional lability revealed a slightly smaller weighted effect of  $r = 0.52$  (95% CI [0.31, 0.73],  $p < 0.001$ ). However, results of an analysis of the variance (ANOVA) showed that the difference between those specific dimensions was not significant ( $F = 0.27$ , ns).

**Heterogeneity of analysis**

$I^2$  values are presented in Tables 2 and 3. The total heterogeneity of ED’s average effect size in between-group studies was 94% and for emotion recognition, emotional lability, and negative emotional responses 40, 90 and 91%, respectively. In the within-group studies, the total heterogeneity of the average effect size was 71%, and for emotional lability and negative emotional responses 54 and 68%, respectively.

To control for any analysis bias, we used funnel plots and Fail-safe N tests. Our between-group analysis results showed that the funnel plot is asymmetric, with the smaller studies tending toward the left of the average effect size. This may indicate that there are studies missing from the right side. Consequently, were there no such probable bias, the average effect size could be larger than the aforementioned amount. In addition, our Fail-safe N test results showed that 1481 studies need to be added

**Table 2** Effect Sizes for differences in ED dimensions between adults with and without ADHD

	ED	ER	EL	NE
Hedges’g	1.17	0.63	1.20	1.12
95% CI	[0.70,1.64]	[0.40, 0.85]	[0.57, 1.83]	[0.57, 1.68]
Hedges’g Criteria	Large	Moderate	Large	Large
$I^2$	94%	40%	90%	91%
Criteria of $I^2$	High	Moderate	High	High
Number of studies	12	6	4	6
Number of participants	1926	767	695	933

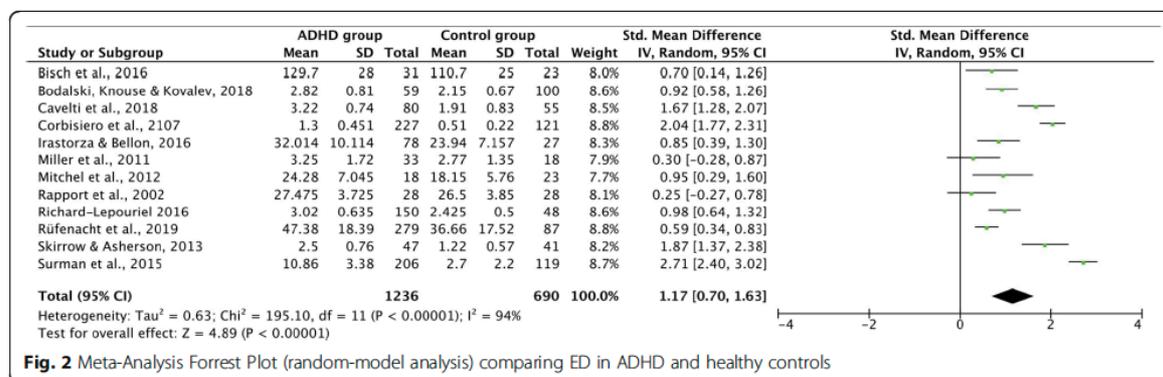
ED Emotion Dysregulation, ER Emotion Recognition, EL Emotional Lability, NE Negative Emotions.  $I^2$ : Heterogeneity of the study

to our analysis to reduce the effect size to statistical non-significance (for details see Fig. 4a).

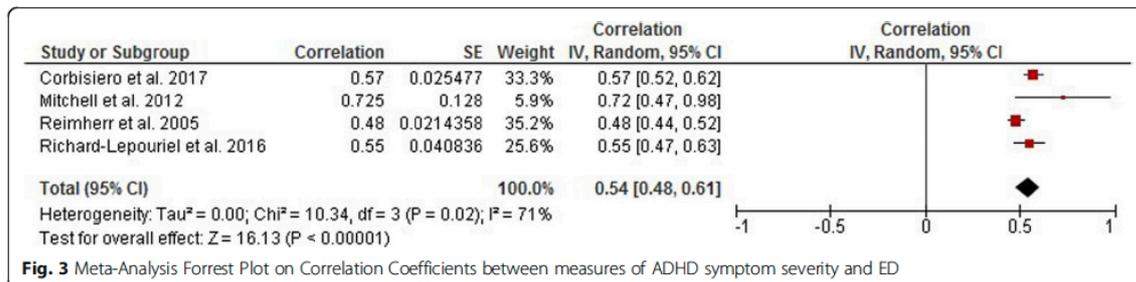
Concerning our within-group analysis, we noted an asymmetric funnel plot with the smaller studies leaning to the right of the average effect size. Four studies were included at this level with sample sizes of 539, 396, 150 and 18 ([38, 41, 45, 48]), respectively. This may indicate studies missing from the left side. Therefore, the average effect size might be smaller than the current estimate. In addition, our Fail-safe N test results showed that 732 studies need to be added to our analysis to reduce the effect size to statistical non-significance (for details see Fig. 4b).

**Discussion**

The present meta-analysis was conducted to establish aspects of ED in adulthood ADHD and to differentiate such aspects between ADHD and healthy control groups. Another goal of our study was to assess any association between ED’s features and ADHD symptoms. In line with these research objectives, we identified dimensions of ED based on our adopted conceptual models of ED (i.e., emotion regulation model by Gross [57], and regarding features of ED in adulthood ADHD that focused on the studies we selected for this study. Three dimensions of



**Fig. 2** Meta-Analysis Forrest Plot (random-model analysis) comparing ED in ADHD and healthy controls



**Fig. 3** Meta-Analysis Forrest Plot on Correlation Coefficients between measures of ADHD symptom severity and ED

emotion recognition (ER), emotional lability (EL), and negative emotional responses (NE) were distinguished.

We then categorized the 13 studies selected ( $N = 2535$ ) by two labels of between-group studies (10), in which data was reported on both groups with ADHD and health controls, and within-group studies (4), in which only data on patients with ADHD was available. At the between-group analysis level, we found that compared to a control group, emotion dysregulation is significantly more pronounced in adults with ADHD with a large effect size (Hedges'  $g = 1.17$ ). Furthermore, regarding ED's intermediate dimensions, emotional lability revealed the largest effect size (Hedges'  $g = 1.20$ ). Previous studies demonstrated the relevance of ED for mental and somatic health in general (e.g., [58, 59]) and for ADHS in particular [19]. Barkley & Fischer [60] demonstrated that adult patients with persisting ADHD reported worse ED than healthy control participants. In another example, Corbisiero et al. [7] differentiated affective lability from reactivity and temper as core features of ED; they reported higher rates of ED in adults with ADHD. Compatible with these findings, our results support the significant difference between the rates of ED in adulthood ADHD and control groups. Skirrow & Asherson [8] also reported that emotional lability contributed independently to impairing the daily life of adults with ADHD.

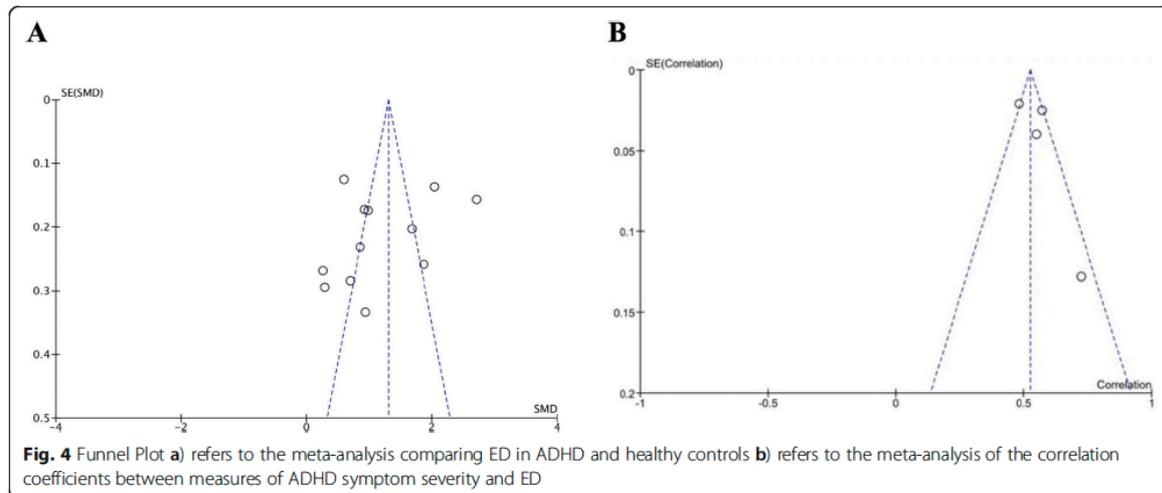
**Table 3** Effect sizes for differences in ED dimensions in adults with ADHD

	ED	EL	NE
Correlation Coefficient ( $r$ )	0.54	0.52	0.63
95% CI (random-model)	[0.48, 0.61]	[0.31, 0.73]	[0.30, 0.99]
$r$ criteria	Large	Large	Large
$I^2$	71%	54%	68%
Criteria of $I^2$	High	Medium	Medium
Number of studies	4	2	2
Number of samples	1097	168	168

ED Emotion Dysregulation, ER Emotion Recognition, EL Emotional Lability, NE Negative Emotions.  $I^2$ : Heterogeneity of the study

Finally, we observed a strong correlation between the severity of ADHD symptoms and ED ( $r = 0.54$ ). In terms of ED, dimensions, negative emotional responses exhibited the strongest correlation with the core ADHD symptoms ( $r = 0.63$ ) - findings that concur with the literature [16, 26, 61], and that are also compatible with the study by Graziano & Garcia [9] that reported a stronger correlation between emotional responses and ADHD symptoms in older adolescents.

Our results demonstrate that emotional lability plays both a significant role in differentiating clinical groups with ADHD from healthy controls and a strong correlation between negative emotional responses and ADHD symptom severity. Referring to adopted conceptual models, these findings might be explained by considering the following: First, the literature suggests that concerning ADHD's epidemiology in adults, the evidence that hyperactive-impulsive symptoms seem to remit in older age groups may be attributable to adaptive strategies patients develop over the life-span, while inattention symptoms seem to persist [62–64];). In this regard, these symptoms might be correlated better with impaired situation identification that requires attention processes, as well as a lack of strategies for monitoring emotion regulation processes – which in turn would trigger higher rates of emotional lability in adults with ADHD. Second, the severity of ADHD symptoms in adults correlated significantly with negative externalizing behaviors such as aggression and irritation, as articulated by Posner et al. [65] in their *dyscontrol hypothesis* and *affectivity hypothesis*. Based on dyscontrol hypothesis, impairments in the capacity of inhibiting the emotional responses occurs significantly more in hyperactive subgroups of ADHD. In this regard, functional neuroimaging shows anomalies within frontolimbic circuits. According to the affectivity hypothesis, negative-emotionally-responsive behavior in ADHD patients emerges through the route of dysfunctional emotional processing associated with the amygdala and medial prefrontal cortex [65]. Emotion recognition seems to be a more serious problem in young people with ADHD. As the Graziano & Garcia [9] analysis implied, emotion



recognition skills are weaker in younger children, and as cognitive abilities develop and adapt, emotion recognition improves. Therefore, although emotion recognition remains a feature of ED in adulthood ADHD, emotional lability and negative emotional responses play a more pronounced role in the ED-associated psychopathology of adults with ADHD.

#### Practical implications of the results

Most likely, ED in adults with ADHD is a problem persisting from childhood that either was addressed with no specific intervention (as juvenile ADHD treatment is predominantly pharmacological [66, 67];), or that was therapy-resistant and continues to be a obvious feature over the course of the disorder [68, 69]. In this regard, our study findings support the consideration of therapeutic approaches entailing ED improvement strategies and reinforcing emotion regulation skills, in addition to standard interventions for the disorder [4, 70]. Furthermore, as our results demonstrate, such therapeutic strategies and interventions would be advisable to focus on a general ED impairment in adults with ADHD while considering emotional lability and negative emotional responses as aspects of ED that need to be targeted in adults with ADHD. Moreover, there is strong evidence of the effectiveness of pharmacological [27, 71, 72]; and psychotherapeutic interventions in alleviating emotion dysregulation and the disorder's core symptoms [4, 6, 11, 73, 74]. In light of the problem of diagnosing ADHD in adulthood and the lack of specific criteria for adults, our meta-analysis findings suggest that adopting an approach that addresses aspects of ED in the diagnosis and

treatment of adults with ADHD would yield a valuable supplementary benefit.

#### Study limitations

We assumed that different measures of ED are contingent, though that might not always be the case. As the adopted conceptual models of ED converged in the studies included in our meta-analysis, we did not analyze them accordingly.

Moreover, reviews have shown that moderators such as gender and cognitive functions ([75–77]; as well as the presence of comorbidity [3] or medication [6] play a significant role in ADHD. Therefore, if emotion dysregulation is assumed to be a main feature of ADHD in adults, controlling for such moderators should be part of a meta-analysis. However, as the studies included contained a paucity of such statistical data, we could not perform meta-regressions that might have shed light on such moderators.

Finally, our funnel plots and Fail-safe N test results imply that (probably) missing studies and thus omitted from our meta-analysis contributed to asymmetrically distributed effect sizes. In between-group analysis, missing studies would strengthen, and in within-group analysis weaken effects. In addition, the lesser degree of heterogeneity (71%) in our within-group analysis compared to the between-group analysis might be a sample-size problem.

#### Conclusions

In conclusion, our results from the present meta-analysis focusing on the role of emotion dysregulation in adulthood ADHD imply that compared to a control group, ED

is a distinct feature of adult ADHD. Furthermore, the severity of ADHD symptoms significantly correlates with dimensions of ED such as emotional lability, emotion recognition, and emotional responses, replicating other studies in the field (e. g., [78]). In addition, classic domains of inattention, hyperactivity, and impulsivity do not sufficiently explain the entire symptom spectrum. In this respect, assessing and targeting emotion regulation in clinical practice might prove to be a valuable strategy for diagnosing and treating adult ADHD. Moreover, future research should clarify how ED interacts with adult ADHD symptoms, comorbid conditions, and other moderators such as demographics.

#### Abbreviations

ADHD: Attention deficit/hyperactivity disorder; AIM: Affect Intensity Measure; ALS: Affective Lability Scale; DANVA: Diagnostic Assessment of Nonverbal Accuracy; DESR: Deficient Emotional Self-Regulation; ED: Emotion dysregulation; EL: Emotional lability; ER: Emotion recognition; ERS: Emotion Reactivity Scale; NE: Negative emotional responses; SD: Standard deviation; SEM: Standard error of the mean; SREIT: Self-Report Emotional Intelligence Test

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Not applicable.

#### Authors' contributions

AB designed the meta-analysis, and conducted the literature search, data coding, and statistical analysis. MLC did the studies' reliability coding. HC provided expert advice throughout these processes. AB wrote the first draft of the manuscript and all authors contributed to and have approved the final manuscript.

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#### Availability of data and materials

The datasets used and analyzed during the present study are available from the corresponding author on reasonable request.

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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## **Statutory declaration**

I hereby declare that I have completed this work independently and without outside help. Text passages that are literally or in essence on publications by other authors are given references as such.

The work has not yet been submitted to any other examination authority and has not yet been published.

25.06.2020, Berlin

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