Ten years (2011-2021) of the Regional ADHD Centre-Based Network Project for the Diagnosis and Treatment of Children and Adolescents with ADHD

Maurizio Bonati[1] Francesca Scarpellini[1] Massimo Cartabia[1] Michele Zanetti[1], and the Lombardy ADHD Group

[1] Laboratory for Mother and Child Health, Department of Public Health, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan, Italy

Abstract

Background: The purpose of this article is to update the diagnostic assessment, therapeutic approach, and 12-18 month follow up of patients added in the Italian Lombardy ADHD Register. **Methods:** Data on patients evaluated by the 18 Regional ADHD Reference Centres in the ten year period from 2011 to April 2021 were analysed. **Results:** 4091 of 5934 added patients received a diagnosis of ADHD. In 20.3% of cases, there was a family history of ADHD. 2879 children (70.4%) had at least one comorbidity disorder, the most common of which was learning disorder (39%). Nearly all (95.9%) received at least one psychological prescription, 17.9% of them almost one pharmacological treatment, and 15.6% a combination of both. Values of ≥ 5 of the Clinical Global Impressions- Severity (CGI-S) are more commonly presented by patients with a pharmacological prescription than with a psychological treatment (p < .0001). A significant improvement was reported in half of the patients followed after 1 year, with Clinical Global Impressions- Improvement (CGI-I ≤ 3). In all, 233 of 4091 are 18 year old patients. **Conclusion:** A ten year systematic monitoring of models of care was a fruitful shared and collaborative initiative in order to promote significant improvement in clinical practice, providing effective and continuous quality of care. The unique experience here reported should spread.

Keywords (3-10)

Attention deficit disorder with hyperactivity, child, adolescent, mental health, chronic disease, register, clinical protocol

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that affects 5.9% - of children and persists into adulthood for two-thirds of them [1,2], with great impairments on academic achievement and work [3]. The core symptoms are inattention, restlessness and impulsivity, which are more frequent in boys than girls (ratio 3:1). In Italy, the prevalence of the disorder ranges from 1.1% to 3.1% of the paediatric population, considering only subjects with diagnosis confirmed by clinical evaluation [4].

The wide variability depends on the different diagnostic procedures adopted to assess children and the criteria used, and the period of time over which it is conducted [5]. The peak age of diagnosis of ADHD is in primary school children aged 5–10 years [6], children born later in the school year are more likely to receive an ADHD diagnosis than their same school-year peers [7]. According to the national and international guidelines [8,9] diagnosis of ADHD is based on a careful and systematic assessment of a lifetime history of symptoms, as childhood onset, and impairment in some contexts (schools, relationships, home) [10]. Information about medical history of psychiatric and neurological problems are also important. Psychiatric comorbidity is thus a clinically important factor that contributes to the persistence of ADHD in adulthood [11] The Oppositional Defiant Disorder (ODD), conduct disorder (CD) and autism spectrum disorder are the most common conditions associated with ADHD [12]. Concerning treatment, the guidelines suggest using a multimodal treatment combining psychosocial interventions with pharmacological therapies. Psychological therapies involve parents and teachers with training and a range of cognitive behavioural approaches to the patient. Medication includes stimulants, in particular methylphenidate, and as a first choice and the most effective therapy. The stimulant medications for ADHD are more effective than non-stimulant medications but, are also more likely to be diverted, misused, and abused [13,14]. Otherwise, non-medication treatments for ADHD are less effective than medication treatments for ADHD symptoms, but are frequently useful to help problems that remain after medication has been optimized [1]. A recent meta-analysis of the literature highlighted the positive effect of psychological interventions on ADHD cognitive symptomatology and supports the inclusion of non-pharmacological interventions in conjunction with the commonly used pharmacological treatments [15]. Despite the existence of clear and specific guidelines, access to services is limited [16,17], the waiting times for diagnosis are too long [18], and the treatment outcomes depend on many factors, such as the presence of comorbidities [19]. In June 2011, an official regional registry was activated in the Lombardy Region. The Regional ADHD Registry was designed as a disease-oriented registry collecting information not only on ADHD patients treated with pharmacological therapy, but also on all patients who access ADHD centres for a diagnosis of

suspected ADHD. The Regional Registry was part of a more general project aimed to ensure appropriate ADHD management for children and adolescents once the disorder is suspected; the data recorded include common diagnostic and therapeutic procedures as well as educational initiatives for healthcare workers of the Lombardy Region health care system [2]. After 10 years of THE project, we aimed to update the diagnostic assessment and therapeutic approaches proposed to youth aged 5 to 17 years old enrolled in any of the 18 ADHD reference centres of the Lombardy Region. In particular, we analysed the clinical characteristics of ADHD patients and the relation with the treatment prescription and the elevation in some scales of the test used for the diagnosis. We explored if there was an improvement on their Clinical Global Impressions – Improvement (CGI-I) scores after 12-18 months of follow up.

Materials and methods

A review of patient medical records was the design of this study. Data were identified from the Regional ADHD Registry. Formal ethical review board approval was not required for the present updating, because previously approved by the Institutional Review Board of the Istituto di Ricerche Farmacologiche Mario Negri IRCCS , Milan, Italy. Written informed consent was obtained for all patients before data collection. We used the methodology previously described and reported data concerning the local health setting [7], the characteristics of the ADHD Registry activated in Lombardy in June 2011 [20,21], the systematic work carried out by the 18 ADHD centres [19], the diagnostic assessment and the treatment conducted by all involved clinicians, according to the national and international guidelines [8,9]. Results on the scales used for the diagnostic evaluation were analysed. In particular, the Conner's Parent Rating Scale (CPRS), rated by the parents, and the Conner's Teacher Rating Scale (CTRS), rated by the teachers, were compared. In the same way rates on the Child Behaviour Checklist rated by the mothers and rated by the fathers were observed. The Clinical Global Impressions-Improvement scores were analysed after 12-18 months of follow up.

Data were extracted from the database and analyses were updated on 1 April 2021, and data referred to patients added between 2011 and 2021 period.

Data Analyses

All data were entered in an SAS/STAT database (SAS Version 9, SAS Institute, Inc., Cary, NC, USA). Descriptive statistics were computed for the entire study population and for subgroups. The student's t test was used to compare continuous variables, whereas chi-square tests were used to

compare categorical variables. A multivariate logistic regression analysis with stepwise selection was also carried out to assess the determinants of disease and treatment. Moreover, interrater agreement (parents VS teachers; mothers VS fathers) on symptom scores for each diagnostic scale was established by Kappa coefficient of agreement (K). The results are presented as the number, frequency (%), and mean or median; p < .05 was considered to be significant.

Results

A total of 7053 children were added to the registry from June 2011 to December 2021, of whom 6188 were children and adolescents accessing the ADHD centres for the first time (range 89-1010 patients per centre, median = 248) for suspected ADHD diagnosis. Most of patients (5934) had completed the diagnostic assessment (Table 1). These patients had a median age of 9 years (range 7-11) at their first visit, most of them were males 4960 (83.6%) and 974 (16.4%) were females. In all 4091 patients met Diagnostic and Statistical Manual of Mental Disorders [22] criteria for ADHD diagnosis; 3484 (85.2%) of whom were males and 607 (14.8%) females. The cumulative incidence of ADHD in the 2011 and 2021 period was estimated to be 0.26% (95% confidence interval [CI] = [0.94-1.24]) of resident population of the same age range, with a peak at 8 years of age (Figure 1).

Figure 1. Age of the sample population
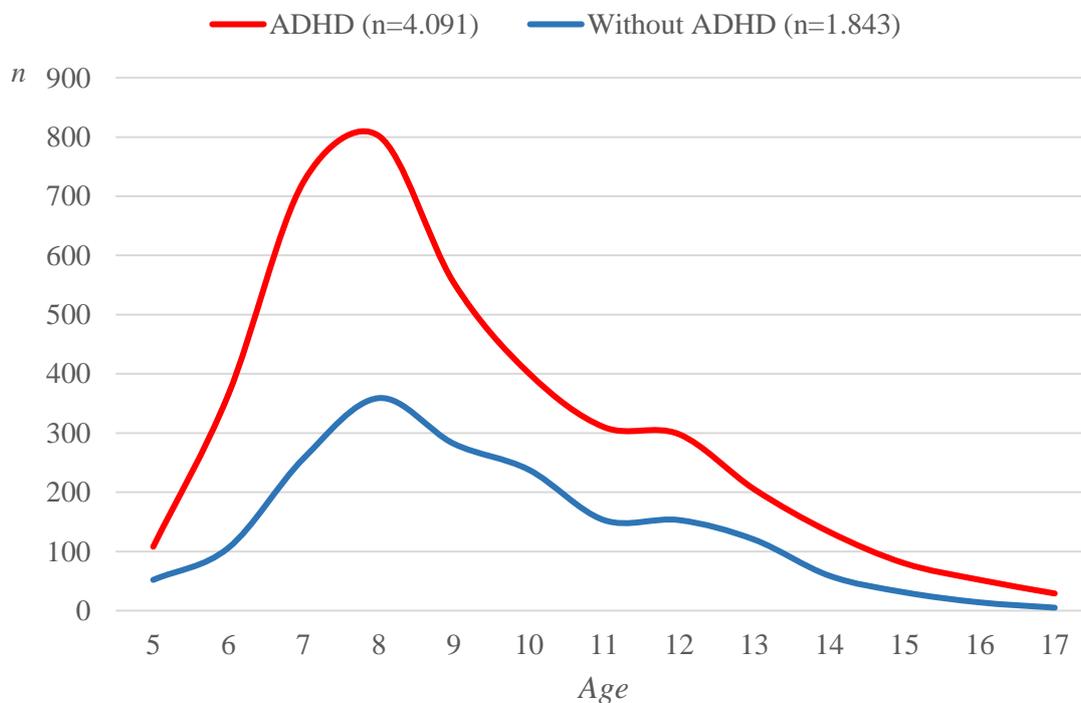
As shown in Table 1, the anamnestic characteristics strongly associated with ADHD by univariate analysis were lower age, male gender, only child, not born in Italy, adopted, support teacher, lower

educational level of parents, unemployed father, ADHD familiarity and psychiatric comorbidity. According to both univariate and multivariate analysis, only child (odds ratio [OR] = 1.22 95% CI = [1.07 – 1.41]) adopted (OR = 1.64 95% CI = [1.07 – 2.52]), primary school (OR = 1.15 95% CI = [1.00 – 1.31]), support teacher (OR = 2.82 95% CI = [2.19 – 3.64]), employed mother (OR = 1.14 95% CI = [1.01 – 1.20]) unemployed father (OR = 1.31 95% CI = [1.08 – 1.58]), and ADHD familiarity (OR = 2.21 95% CI = [1.86 – 2.63]) were higher in ADHD patients. In all, 2879 of 3956 (70.4%) had one or more psychiatric disorders (1079 without ADHD), whereas 387 (6.5%) had another concomitant chronic disease. Learning disorder (OR = 1.37 95% CI = [1.21 – 1.55]) , sleep disorder (OR = 1.83 95% CI = [1.50 – 2.23]), Oppositional Defiant Disorder (ODD) (OR = 2.87 95% CI = [2.27 – 3.64]), anxiety (OR = 0.70 95% CI = [0.56 – 0.87]), language disorder (OR = 1.36 95% CI = [1.05 – 1.77]), tic (OR = 1.87 95% CI = [1.16 – 3.03]), conduct disorder (OR = 0.49 95% CI = [0.32 – 0.76]), and motor coordination disorder (OR = 1.68 95% CI = [1.04 – 2.72]) were higher in ADHD patients. Among the medical conditions, neurological diseases were more frequent (n= 121, 2%)

Table 1. Demographic and Clinical Characteristics of the Sample Population.

		ADHD yes	ADHD no	Total	p	OR (IC 95%)	Logistic
Children		4,091	1,843	5,934			
Age at diagnosis	median (q1 - q3)	9,0 (7,0 - 11,0)	9,0 (8,0 - 11,0)	9,0 (7,0 - 11,0)	<0.0001 *		
	media (ds)	9,2 (2,6)	9,4 (2,4)	9,2 (2,5)			
	(min - max)	(5,0 - 17,0)	(5,0 - 17,0)	(5,0 - 17,0)			
	Missing	30	14	44			
School age at diagnosis	5-11	3.264 (80.4)	1.447 (79.1)	4.711 (80.0)	0,2635	1.08 (0.94 - 1.24)	
	12-17	797 (19.6)	382 (20.9)	1.179 (20.0)		1.00 (Ref.)	
	Missing	30	14	44			
Gender	Female	607 (14.8)	367 (19.9)	974 (16.4)	<0.0001 *	1.00 (Ref.)	
	Male	3.484 (85.2)	1.476 (80.1)	4.960 (83.6)		1.43 (1.24 - 1.65) *	1.36 (1.17 - 1.58)
	Missing	-	-	-			
Only child	Yes	1.054 (25.8)	396 (21.5)	1.450 (24.5)	0,0004	1.27 (1.11 - 1.45)	1.22 (1.07 - 1.41)
	No	3.028 (74.2)	1.443 (78.5)	4.471 (75.5)		1.00 (Ref.)	
	Missing	9	4	13			
Born in Italy	Yes	3.869 (94.6)	1.774 (96.3)	5.643 (95.1)	0,0067	1.00 (Ref.)	
	No	220 (5.4)	69 (3.7)	289 (4.9)		1.46 (1.11 - 1.93)	
	Missing	2	-	2			
Adopted	Yes	149 (3.6)	34 (1.8)	183 (3.1)	0,0002	2.01 (1.38 - 2.93)	1.64 (1.07 - 2.52)
	No	3.938 (96.4)	1.807 (98.2)	5.745 (96.9)		1.00 (Ref.)	
	Missing	4	2	6			
School	Primary School	3.124 (76.4)	1.371 (74.5)	4.495 (75.8)	0,1124	1.11 (0.98 - 1.26)	1.15 (1.00 - 1.31)

5

	Middle/High School	964 (23.6)	469 (25.5)	1.433 (24.2)		1.00 (Ref.)	
	Missing	3	3	6			
Support teacher	Yes	514 (12.6)	79 (4.3)	593 (10.0)	<0.0001	3.21 (2.51 - 4.09)	2.82 (2.19 - 3.64)
	No	3.577 (87.4)	1.764 (95.7)	5.341 (90.0)		1.00 (Ref.)	
	Missing	-	-	-			
Educational level of mother	Yes	2.313 (56.5)	1.116 (60.6)	3.429 (57.8)	0,0038	0.85 (0.76 - 0.95)	
	No	1.778 (43.5)	727 (39.4)	2.505 (42.2)		1.00 (Ref.)	
	Missing	-	-	-			
Educational level of father	Yes	1.865 (45.6)	934 (50.7)	2.799 (47.2)	0,0003	1.00 (Ref.)	
	No	2.226 (54.4)	909 (49.3)	3.135 (52.8)		1.23 (1.10 - 1.37)	
	Missing	-	-	-			
Mother employed	Yes	2.729 (66.7)	1.227 (66.6)	3.956 (66.7)	0,9210	1.01 (0.90 - 1.13)	1.14 (1.01 - 1.30)
	No	1.362 (33.3)	616 (33.4)	1.978 (33.3)		1.00 (Ref.)	
	Missing	-	-	-			
Father employed	Yes	3.411 (83.4)	1.624 (88.1)	5.035 (84.9)	<0.0001	1.00 (Ref.)	
	No	680 (16.6)	219 (11.9)	899 (15.1)		1.48 (1.26 - 1.74)	1.31 (1.08 - 1.58)
	Missing	-	-	-			
ADHD familiarity	Yes	831 (20.3)	193 (10.5)	1.024 (17.3)	<0.0001	2.18 (1.84 - 2.58)	2.21 (1.86 - 2.63)
	No	3.260 (79.7)	1.650 (89.5)	4.910 (82.7)		1.00 (Ref.)	
	Missing	-	-	-			
Psychiatric comorbidity	Yes	2.879 (70.4)	1.079 (58.5)	3.958 (66.7)	<0.0001	1.68 (1.50 - 1.89)	
	No	1.212 (29.6)	764 (41.5)	1.976 (33.3)		1.00 (Ref.)	
	Missing	-	-	-			
Tyoe of comorbidity (flag)	Learning disorder	1.594 (39.0)	613 (33.3)	2.207 (37.2)	<0.0001	1.28 (1.14 - 1.44)	1.37 (1.21 - 1.55)
	Sleeping disorder	582 (14.2)	145 (7.9)	727 (12.3)	<0.0001	1.94 (1.60 - 2.35)	1.83 (1.50 - 2.23)
	ODD	569 (13.9)	93 (5.0)	662 (11.2)	<0.0001	3.04 (2.42 - 3.81)	2.87 (2.27 - 3.64)
	Anxiety	280 (6.8)	162 (8.8)	442 (7.4)	0,0083	0.76 (0.62 - 0.93)	0.70 (0.56 - 0.87)
	Language disorder	287 (7.0)	88 (4.8)	375 (6.3)	0,0010	1.50 (1.18 - 1.92)	1.36 (1.05 - 1.77)
	Tic	95 (2.3)	22 (1.2)	117 (2.0)	0,0038	1.97 (1.23 - 3.14)	1.87 (1.16 - 3.03)
	Conduct disorder	69 (1.7)	41 (2.2)	110 (1.9)	0,1551	0.75 (0.51 - 1.11)	0.49 (0.32 - 0.76)
	Coordination disorder	95 (2.3)	23 (1.2)	118 (2.0)	0,0061	1.88 (1.19 - 2.98)	1.68 (1.04 - 2.72)
Chronic disease	Yes	265 (6.5)	122 (6.6)	387 (6.5)	0,8376	0.98 (0.78 - 1.22)	Patologie croniche
	No Missing	3.826 (93.5) -	1.721 (93.4) -	5.547 (93.5) -		1.00 (Ref.)	
Type of chronic disease (flag)	Neurological	91 (2.2)	30 (1.6)	121 (2.0)	0,1324	1.37 (0.91 - 2.08)	Tipo di patologie croniche (flag)
	Breathing	60 (1.5)	32 (1.7)	92 (1.6)	0,4365	0.84 (0.55 - 1.30)	
	Gastrointestinal	18 (0.4)	11 (0.6)	29 (0.5)	0,4227	0.74 (0.35 - 1.56)	

ADHD = Attention Deficit Hyperactivity Disorder, OR = odds ratio, CI = confidence interval.

Treatment

Overall, 4016 patients with ADHD (98.2%) received at least one prescription: 640 patients (15.6%) received a combination of pharmacological and psychological treatment, 94 (2.3%) received pharmacotherapy alone, and 3282 (80.2%) received a psychological treatment alone. Of the 734 patients treated with a psychoactive drug, 679 (16.6%) received methylphenidate (0.5 – 80 mg daily), 21 (0.5%) of whom in combination with an additional drug (Risperidone, aripiprazole, haloperidol, lorazepam, sertraline, alprazolam, fluvoxamine, clomipramine, delorazepam), 23 (0.6%) atomoxetine (10 – 60 mg daily), and 53 (1.3%) other psychotropic drugs. Among the 3922 (95.9%) patients prescribed a psychoeducational intervention, 2631 (64.3%) received at least one type of training intervention (parents, teacher or child), whereas 2820 (68.9%) received other psychological treatment. The most commonly prescribed intervention was parent training (n = 2311, 56.5%), followed by the child training (n= 1556, 38%) and teacher training (n= 870, 21.3%). A total of 519 (12.7%) patients received a prescription for all training types. In all 2485 (61.9%) patients had an ADHD Combined subtype (ADHD-C) whereas 1218 (30.3%) were diagnosed with Inattentive Type (ADHD-I) and 313 (7.8%) Hyperactive Type (ADHD-HI) subtypes. Of all 4091 patients diagnosed with ADHD, 4016 patients received a prescription (Table 2).

Table 2. Clinical Characteristics of the ADHD Patients by Treatment Prescription

		Pharmacological Treatment	Psychological Treatment	Total	p	OR (IC 95%)	Logistic
		734	3,282	4,016			
ADHD Subtype	Combined	586 (79.8)	1.899 (57.9)	2.485 (61.9)	<0.0001 *	3.41 (2.26 - 5.14)	* 3.48 (1.84 - 6.59)
	Inattentive	122 (16.6)	1.096 (33.4)	1.218 (30.3)		1.23 (0.79 - 1.91)	2.34 (1.19 - 4.62)
	Hyperactive	26 (3.5)	287 (8.7)	313 (7.8)		1.00 (Ref.)	
	Missing	-	-	-			
QI pathologic	Yes	82 (11.4)	79 (2.4)	161 (4.1)	<0.0001 *	5.18 (3.76 - 7.13)	
	No	635 (88.6)	3.166 (97.6)	3.801 (95.9)		1.00 (Ref.)	
	Missing	17	37	54			
CPRS-O	Pathological	384 (63.6)	1.305 (42.6)	1.689 (46.0)	<0.0001 *	2.36 (1.97 - 2.82)	
	Normal	220 (36.4)	1.761 (57.4)	1.981 (54.0)		1.00 (Ref.)	
	Missing	130	216	346			
CTRS-O	Pathological	310 (59.0)	1.219 (41.7)	1.529 (44.3)	<0.0001 *	2.02 (1.67 - 2.44)	
	Normal	215 (41.0)	1.707 (58.3)	1.922 (55.7)		1.00 (Ref.)	
	Missing	209	356	565			
CPRS-I	Pathological	515 (85.3)	2.176 (70.9)	2.691 (73.3)	<0.0001 *	2.37 (1.87 - 3.01)	
	Normal	89 (14.7)	892 (29.1)	981 (26.7)		1.00 (Ref.)	
	Missing	130	214	344			

CTRS-I	Pathological	362 (69.0)	1.717 (58.6)	2.079 (60.2)	<0.0001 *	1.57 (1.28 - 1.91)	
	Normal	163 (31.0)	1.211 (41.4)	1.374 (39.8)		1.00 (Ref.)	
	Missing	209	354	563			
CPRS-H	Pathological	477 (79.0)	1.840 (60.0)	2.317 (63.1)	<0.0001 *	2.51 (2.03 - 3.09)	* 1.48 (1.10 - 1.99)
	Normal	127 (21.0)	1.228 (40.0)	1.355 (36.9)		1.00 (Ref.)	
	Missing	130	214	344			
CTRS-H	Pathological	403 (76.6)	1.893 (64.7)	2.296 (66.5)	<0.0001 *	1.79 (1.44 - 2.22)	
	Normal	123 (23.4)	1.035 (35.3)	1.158 (33.5)		1.00 (Ref.)	
	Missing	208	354	562			
CPRS-ADHD	Pathological	557 (92.2)	2.371 (77.3)	2.928 (79.7)	<0.0001 *	3.48 (2.56 - 4.75)	* 2.79 (1.82 - 4.28)
	Normal	47 (7.8)	697 (22.7)	744 (20.3)		1.00 (Ref.)	
	Missing	130	214	344			
CTRS-ADHD	Pathological	459 (87.3)	2.285 (78.1)	2.744 (79.5)	<0.0001 *	1.92 (1.47 - 2.52)	
	Normal	67 (12.7)	642 (21.9)	709 (20.5)		1.00 (Ref.)	
	Missing	208	355	563			
CGI-S	5-7	516 (71.9)	597 (18.8)	1.113 (28.6)	<0.0001 *	11.02 (9.15 - 13.26) *	8.04 (6.35 - 10.19)
	1-4	202 (28.1)	2.575 (81.2)	2.777 (71.4)		1.00 (Ref.)	
	Missing	16	110	126			
Psychiatric comorbidity	Yes	612 (83.4)	2.215 (67.5)	2.827 (70.4)	<0.0001 *	2.42 (1.96 - 2.97) *	
	No	122 (16.6)	1.067 (32.5)	1.189 (29.6)		1.00 (Ref.)	
	Missing	-	-	-			
Type of comorbidity (flag)	Learning Disorder	265 (36.1)	1.296 (39.5)	1.561 (38.9)	0,0890	0.87 (0.73 - 1.02)	
	Sleeping disorder	130 (17.7)	443 (13.5)	573 (14.3)	0.0032 *	1.38 (1.11 - 1.71)	
	ODD	209 (28.5)	356 (10.8)	565 (14.1)	<0.0001 *	3.27 (2.69 - 3.97)	1.64 (1.25 - 2.15)
	Anxiety	70 (9.5)	208 (6.3)	278 (6.9)	0.0020 *	1.56 (1.17 - 2.07)	
	Intellectual disability	94 (12.8)	150 (4.6)	244 (6.1)	<0.0001 *	3.07 (2.34 - 4.02)	2.47 (1.65 - 3.69)
	Mood disorder	57 (7.8)	170 (5.2)	227 (5.7)	0.0061 *	1.54 (1.13 - 2.11)	
	Language disorder	61 (8.3)	221 (6.7)	282 (7.0)	0,1307	1.26 (0.93 - 1.69)	
	Tic	40 (5.4)	54 (1.6)	94 (2.3)	<0.0001 *	3.45 (2.27 - 5.23)	3.60 (2.02 - 6.43)
	Conduct disorder	29 (4.0)	39 (1.2)	68 (1.7)	<0.0001 *	3.42 (2.10 - 5.57)	
	Autism	60 (8.2)	65 (2.0)	125 (3.1)	<0.0001 *	4.41 (3.07 - 6.32)	
	Coordination disorder	28 (3.8)	63 (1.9)	91 (2.3)	0.0018 *	2.03 (1.29 - 3.19)	3.67 (2.02 - 6.67)
	Other	17 (2.3)	66 (2.0)	83 (2.1)	0,5994	1.16 (0.67 - 1.98)	

CPRS = Conners Parents Rating Scale (CPRS-O = Oppositive Scale; CPRS-I = Inattention Scale; CPRS-H = Hyperactivity Scale; CPRS-ADHD = ADHD Index; CPRS-E = Emotion Lability Scale); CTRS= Conners Teachers Rating Scale (CTRS-O = Oppositive Scale; CTRS-I = Inattention Scale; CTRS-H = Hyperactivity Scale; CTRS-ADHD = ADHD Index; CTRS-E = Emotion Lability Scale); CGI-S = Clinical Global Impressions Severity Scale

Those with an ADHD-C diagnosis were treated more commonly with drug therapy (79.8%) than withpsychological treatment (57.9%) p< 0.0001. Otherwise, ADHD-I patients were more treated with psychological treatment (33.4%) than drug therapy (16.6%) p < 0.0001. Univariate analysis between patients treated with pharmacological and psychological treatment highlighted several significant differences, as reported in Table 2. Multivariate analysis showed that an ADHD-C diagnosis (OR = 3.48 95% CI = [1.84 – 6.59]) a pathological score on the Conner's Parent Rating Scale – Hyperactivity Scales (CPRS-H) (OR= 1.48 95% CI [1.10 – 1.99]) and CPRS-ADHD Index (OR = 2.79 95% CI = [1.82 – 4.28]), and a Clinical Global Impressions – Severity Scale (CGI-S) score of 5 or above (OR= 8.04 95% CI = [6.35 – 10.19]) were associated with a higher probability of receiving drug therapy in addition to psychological treatment, as well as the presence of a concomitant psychiatric disorder as ODD (OR = 1.64 95% CI = [1.25 – 2.15]), cognitive delay (OR = 2.47 95% CI = [1.65 – 3.69]), tic (OR = 3.60 95% CI = [2.02 – 6.43]) and coordination disorder (OR = 3.67 95% CI = [2.02 – 6.67]).

Parents and Teachers Rating Scales

In order to evaluate parents' and teachers' perceptions about symptoms and behaviour of ADHD children, a comparison of the Conner's' Rating Scales and the Child Behaviour Checklist (CBCL) was performed (Table 3).

Table 3. Rate of participants with scores within the pathological range on the Conners' and CBCL Scales

| Conners' Rating Scales	Score	CPRS	CTRS	p	K (IC 95%)	Agreement %
Subscales		4,909	4,909			
O	Pathological	1.938 (39.5)	1.884 (38.4)	0,2637	0.32 (0.29 - 0.35)	68
	Normal	2.971 (60.5)	3.025 (61.6)			
I	Pathological	3.270 (66.6)	2.682 (54.6)	<0.0001 *	0.25 (0.22 - 0.28)	64
	Normal	1.639 (33.4)	2.227 (45.4)			
H	Pathological	2.646 (53.9)	2.846 (58.0)	<0.0001 *	0.31 (0.28 - 0.34)	66
	Normal	2.263 (46.1)	2.063 (42.0)			
ADHD Index	Pathological	3.530 (71.9)	3.478 (70.8)	0,2456	0.26 (0.23 - 0.29)	70
	Normal	1.379 (28.1)	1.431 (29.2)			
E	Pathological	1.645 (33.5)	1.942 (39.6)	<0.0001 *	0.26 (0.23 - 0.29)	65
	Normal	3.264 (66.5)	2.967 (60.4)			
CBCL	Score	Mother	Father	p	K (IC 95%)	Agreement %
		1,082	1,082			
I	Pathological	223 (20.6)	159 (14.7)	0.0003	0.64 (0.58 - 0.70)	89
	Normal	859 (79.4)	923 (85.3)			
E	Pathological	254 (23.5)	204 (18.9)	0.0085	0.69 (0.63 - 0.74)	89
	Normal	828 (76.5)	878 (81.1)			
T	Pathological	349 (32.3)	255 (23.6)	< 0.0001	0.66 (0.61 - 0.71	86
	Normal	733 (67.7)	827 (76.4)			

CBCL = Child Behaviour Checklist (CBCL-I = Internalizing problems; CBCL-E = Externalizing problems; CBCL-T =Total).

Parents consistently rated their children higher than teachers on the Cognitive Problems/Inattention subscale (CPRS-I = 3270, 66.6%; CTRS-I =2682, 54.6%; p < 0.0001). On the other hand, teachers consistently rated children higher than parents on the Hyperactivity subscale (CTRS-H =2848, 58%; CPRS-H = 2646, 53.9%; p < 0.0001) and Emotional Lability subscale (CTRS-E =1942, 39.6%; CPRS-E = 1645, 33.5%; p < 0.0001). On the CBCL questionnaire, pathological mothers' ratings were significantly higher than those of fathers on both CBCL Subscales (CBCL-I =223, 20.6%; CBC-I father = 159, 14.7%; p= 0.0003) (CBCL-E = 254, 23.5%; CBCL- E father = 204, 18.9%; p = 0.0085) and on the CBCL-Total score (CBCL-T = 349, 32.3%; CBCL-T father = 255, 23.6%; p< 0.0001). Kappa values showed "substantial" agreement between parents and teachers (>60%) and "excellent" agreement between mothers and fathers (>85%).

Continuity of Care and Management

Throughout the regional database system, data on patient care from the first request to the diagnosis, and data on treatment prescriptions and follow-up visits were systematically collected. High level of completeness and accuracy was found. The rate of completion of the diagnostic evaluation was reported in Figure 2: each axis has a range of 0% to 100% and represents one of the seven areas of the shared evaluation pathway, while the three sets of data represent the performance scores of the most (average = 100%) and least compliant (average = 91,01%) ADHD centre, as well as the total completeness (average =97,86%) estimated by the analysis of data recorded by all 18 ADHD centres. Overall 320 of 4091 patients with a diagnosis of ADHD were discharged during the first 3 months; 1468 patients with ADHD had been monitored for more than 1 year after the diagnosis, half of whom had a significant improvement with CGI-I scores of 1-3, and the majority of these (89%) were in a stable condition with 4 scores on the CGI-I. In all, 755 patients reached the legal age (range 18-27 years), 31.3% of whom just turned 18 years old.

Figure 2. Rate of completeness levels based on data inputted in the registry.
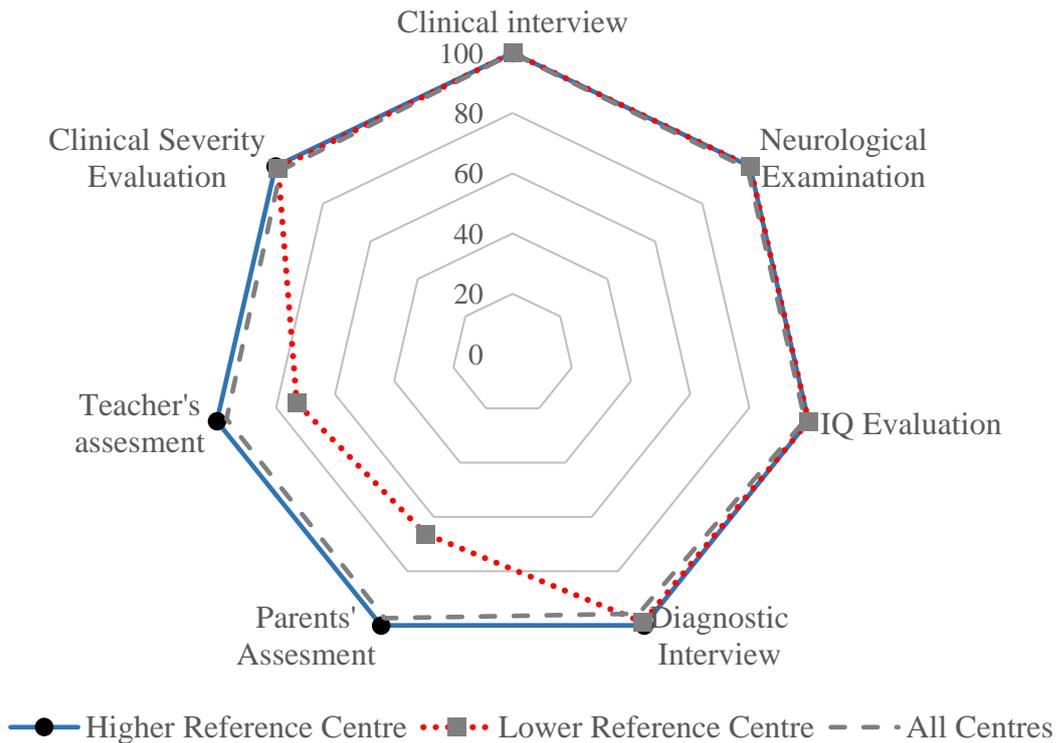
Discussion

After ten years of the creation of the Lombardy Registry Project, clinical and service assessment data revealed the effectiveness and usefulness of this regional project in providing assistance and continuity of care to ADHD patients and their families. Over the years, the registry was monitored to achieve clinical improvement, using systematic activities and an interactive system evaluation to test the change, according to the main clinical quality improvement features [23]. Clinical characteristics of the ADHD patients of the Lombardy Registry Project were in line with the literature; the peak age of diagnosis was in primary school children aged 5–10 years [6], LD was the main psychiatric comorbidity followed by ODD, anxiety, and sleeping disorders [1,12]. The most associated chronic disease was a neurological condition. Concerning treatment, data extracted from the registry highlighted a relation between some clinical characteristics and the type of prescription at diagnosis; according to the literature the symptom severity increased the likelihood of being prescribed ADHD medication [24]. The higher the score CGI-S was the higher the probability of receiving a medical prescription was, in particular for patients with ODD, intellectual disability, tic or coordination disorder. Differently from what we expected, learning problems were not associated with being prescribed a medication, suggesting that learning problems may not be pertinent to pharmacological treatment decisions for children with ADHD. Pharmacological prescription was infrequent (18%), and nearly all of the patients (96%) received a psychological prescription such as child, parent or teacher training. Comparing data with higher rates reported in other countries [25],

in Italy child psychiatrists' professional attitude leaned more toward behavioural treatments than to the use of drugs [26]. In general, half of the patients with a diagnosis of ADHD and in treatment almost for one year (follow up between 12 and 18 months) reported an improvement in their level of symptom severity on the CGI-I score. These data were comforting, suggesting the clinical care utility of a continuously monitored, standardised system. The collaborative aspects and the chosen approaches of the project created opportunities for continuous improvement in shared processes of care in all of the 18 ADHD centres. This represented an important value for the project; the endorsement of continuous quality improvement is an essential approach in order to guarantee the quality of care. The experience acquired with the ADHD project could be useful if applied to other chronic conditions and psychiatric disorders in childhood, in order to improve care. A lot of work is still necessary for the best management of ADHD across the lifespan, in particular during transition periods, such as school entry, comprehensive or high school entry, transition to adult services, and transition to parenthood.

Conclusion

The regional ADHD Registry represents a distinctive tool, a unique experience in the international context, to help guarantee a shared pathway of care in ADHD children. The continuous, systematic monitoring allows resources to be invested appropriately, such as in promoting progressive and significant improvement in clinical practice, ensuring a shared and efficient quality of care. Training initiatives involving clinicians, patients, parents and teachers may be useful in order to raise awareness about the disorder in clinical practice.

Acknowledgments

Author contributions

MB had the idea for the study and designed it, FS drafted the initial version. MC and MZ managed and analysed the data. All collected data were analysed monthly, and the findings were reported and periodically discussed with all 18 ADHD centres belonging to the Lombardy ADHD Group. All authors participated in study design, contributed to interpretation of data, critical review and revision of the report, and approved the final report as submitted. MB is guarantor for the study. The views expressed are those of the authors and not necessarily those of Regional Healthcare Directorate.

Conflict of interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article. All authors declare no financial relationships with any organizations that might have an interest in the submitted work; no other relationships or activities that could appear have influenced the submitted work.

References

1.   Faraone, S.V.; Banaschewski, T.; Coghill, D.; Zheng, Y.; Biederman, J.; Bellgrove, M.A.; Newcorn, J.H.; Gignac, M.; Al Saud, N.M.; Manor, I.; et al. The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder. *Neurosci. Biobehav. Rev.* **2021**, S0149-7634(21)00049-X. doi: 10.1016/j.neubiorev.2021.01.022.

2.   Bonati, M.; Reale, L.; Zanetti, M.; Cartabia, M.; Fortinguerra, F.; Capovilla, G.; Chiappedi, M.; Costantino, A.; Effedri, P.; Luoni, C.; et al; Lombardy ADHD Group. A Regional ADHD Center-Based Network Project for the Diagnosis and Treatment of Children and Adolescents With ADHD. *J. Atten. Disord.* **2018**, 22, 1173-1184.

3.   Caye, A.; Rocha, T.B.; Anselmi, L.; Murray, J.; Menezes, A.M.; Barros, F.C.; Gonçalves, H.; Wehrmeister, F.; Jensen, C.M.; Steinhausen H.C.; et al. Attention-Deficit/Hyperactivity Disorder Trajectories From Childhood to Young Adulthood: Evidence   From   a   Birth Cohort Supporting a Late-Onset Syndrome. *JAMA Psychiatry* **2016**, 73, 705-712.

4.   Reale, L.; Bonati, M. ADHD prevalence estimates in Italian children and adolescents: a methodological issue. *Ital. J. Pediatr.* **2018**, 44, 108.

5.   Austerman J. ADHD and behavioral disorders: Assessment, management, and an update from DSM-5. *Cleve Clin J Med.* **2015**, 82, S2–S7.

6.   Eysbouts, Y.; Poulton, A.; Salmelainen, P. Stimulant medication in preschool children in New South Wales. *J. Paediatr. Child. Health.* **2011**, 47, 870–874.

7.   Bonati, M.; Cartabia, M.; Zanetti, M.; Reale, L.; Didoni, A.; Costantino, M.A.; Lombardy ADHD Group. Age level vs grade level for the diagnosis of ADHD and neurodevelopmental disorders. *Eur. Child. Adolesc. Psychiatry.* **2018**, 27, 1171-1180.

8.   National Guideline Centre (UK). Attention deficit hyperactivity disorder: diagnosis and management. London: National Institute for Health and Care Excellence (UK); **2018** Mar. PMID: 29634174.

9.   Chiarenza GA, Bianchi E, Marzocchi MM. Linee guida del trattamento cognitivo comportamentale deidisturbi da deficit dell'attenzione con iperattività (adhd) – Linee guida SINPIA **2003**. https://www.sinpia.eu/wp-   content/uploads/atom/allegato/147.pdf (Accessed 21 May 2021)

10.   Harpin, V.; Mazzone, L.; Raynaud, J.P.; Kahle, J.; Hodgkins, P. Long-Term Outcomes of ADHD: A Systematic Review of Self-Esteem and Social Function. *J. Atten. Disord.* **2016,** 20, 295-305.

11.   Faraone, S.V.; Asherson, P.; Banaschewski, T.; Biederman, J.; Buitelaar, J.K.; Ramos-Quiroga, J.A.; Rohde, L.A.; Sonuga-Barke, E.J.; Tannock, R.; Franke, B. Attention-deficit/hyperactivity disorder. *Nat. Rev. Dis. Primers.* **2015**, 1, 15020.

12.   Jensen, C.M.; Steinhausen, H.C. Comorbid mental disorders in children and adolescents with attention-deficit/hyperactivity disorder in a large nationwide study. *Atten. Defic. Hyperact. Disord.* **2015**, 7, 27-38.

13.   Wilens TE, Adler LA, Adams J, Sgambati S, Rotrosen J, Sawtelle R, Utzinger L, Fusillo S. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature. *J Am Acad Child Adolesc Psychiatry*. **2008** 47, 21-31.

14.   Clemow, D.B.; Walker, D.J. The potential for misuse and abuse of medications in ADHD: a review. *Postgrad. Med.* **2014,** 126, 64-81.

15.   Lambez, B.; Harwood-Gross, A.; Golumbic, E.Z.; Rassovsky, Y. Non-pharmacological interventions for cognitive difficulties in ADHD: A systematic review and meta-analysis. *J. Psychiatr. Res.* **2020,** 120, 40-55.

16. Clavenna, A.; Cartabia, M.; Sequi, M.; Costantino, M.A.; Bortolotti, A.; Fortino, I.; Merlino, L.; Bonati, M. Burden of psychiatric disorders in the pediatric population. *Eur. Neuropsychopharmacol.* **2013**, 23, 98-106.

17. Coghill, D.R. Organisation of services for managing ADHD. *Epidemiol. Psychiatr. Sci.* **2017**, 26, 453-458.

18. Bonati, M.; Cartabia, M.; Zanetti, M.; Lombardy ADHD Group. Waiting times for diagnosis of attention-deficit hyperactivity disorder in children and adolescents referred to Italian ADHD centers must be reduced. *BMC Health. Serv. Res.* **2019**, 19, 673.

19. Reale, L.; Bartoli, B.; Cartabia, M.; Zanetti, M.; Costantino, M.A.; Canevini, M.P.; Termine, C.; Bonati, M.; Lombardy ADHD Group. Comorbidity prevalence and treatment outcome in children and adolescents with ADHD. *Eur. Child. Adolesc. Psychiatry.* **2017,** 26, 1443-1457.

20. Didoni, A.; Sequi, M.; Panei, P.; Bonati, M.; Lombardy ADHD Registry Group. One-year prospective follow-up of pharmacological treatment in children with attention-deficit/hyperactivity disorder. *Eur. J. Clin. Pharmacol.* **2011**, 67, 1061-1067.

21. Zanetti, M.; Cartabia, M.; Didoni, A.; Fortinguerra, F.; Reale, L.; Mondini, M.; Bonati, M. The impact of a model-based clinical regional registry for attention-deficit hyperactivity disorder. *Health. Informatics. J.* **2017**, 23, 159-169.

22. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; American Psychiatric Publishing: Arlington, VA, USA, 2013.

23. Rubenstein, L.; Khodyakov, D.; Hempel, S.; Danz, M.; Salem-Schatz, S.; Foy, R.; O'Neill, S.; Dalal, S.; Shekelle, P. How can we recognize continuous quality improvement? *Int. J. Qual. Health. Care.* **2014**, 26, 6-15.

24. Mowlem, F.D.; Rosenqvist, M.A.; Martin, J.; Lichtenstein, P.; Asherson, P.; Larsson, H. Sex differences in predicting ADHD clinical diagnosis and pharmacological treatment. *Eur. Child. Adolesc. Psychiatry.* **2019**, 28, 481-489.

25.   Scheffler, R.M.; Hinshaw, S.P.; Modrek, S.; Levine, P. The global market for ADHD medications. *Health. Aff.* (Millwood). **2007**, 26, 450-457.

26.   Clavenna, A.; Rossi, E.; Derosa, M.; Bonati, M. Use of psychotropic medications in Italian children and adolescents. *Eur. J. Pediatr.* **2007**, 166, 339-347.