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Emotional problems in preschool and school-aged children with neurodevelopmental disorders in Spain: EPINED epidemiological project

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ABSTRACT

Background: Children with neurodevelopmental disorders (NDD) are often at risk of developing emotional problems.

Aims and methods: The co-occurrence of anxiety and depression with ASD and/or ADHD was determined by exploring the association with children's clinical and neuropsychological functioning and their parent's mental health. To this end, we assessed 295 preschoolers (PRE; 4-5 years old) and 486 school-aged children (SCH; 10-11 years old) in Tarragona, Spain. NDD diagnoses were based on DSM-5. Emotional problems were assessed using Achenbach's scales.

Results: Emotional problems (PRE: 36%-78%; SCH: 32%-81%) were more common and more severe in participants with NDD than in controls and children in the ASD + ADHD school-aged group were the most affected. In ADHD, emotional problems were associated with more severe symptoms of attention deficit (PRE) and hyperactivity/impulsivity (SCH). In ASD + ADHD, emotional problems showed a trend of association with more severe ASD repetitive behaviours and impaired working memory, whereas in ASD were associated with greater overall ASD severity.

Conclusions and implications: Children with NDD are vulnerable to emotional problems, which become more prevalent and interfering with age. Early detection and intervention aimed at tackling emotional problems can improve NDD prognosis.

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1. Introduction

Autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) are chronic and childhood-onset neurodevelopmental disorders (NDD). Global prevalence rates in children and adolescents stand at 1% for ASD (Zeidan et al., 2022) and 7% for ADHD (Thomas, Sanders, Doust, Beller, & Glasziou, 2015). Both conditions have shared risk factors in early development and subsequent common neurobiological alterations that affect cognitive abilities, behavioral and emotional regulation, and social development (Malone, 2012). Homotypic and heterotypic comorbidities are frequent in NDD, and particularly common in children, even at very young ages (Dewey, 2018; Hansen, Oerbeck, Skirbekk, Petrovski, & Kristensen, 2018). Previous studies have reported comorbidity rates of ASD and ADHD of 59% (Stevens, Peng, & Barnard-Brak, 2016). Anxiety and depression are also commonly associated with ASD or ADHD (Lai et al., 2019; Mohammadi et al., 2021; Mphahlele et al., 2020). Hence, in addition to the implicit impairment of NDD, concomitant psychopathological disorders or symptoms increase clinical heterogeneity and are associated with an even greater negative impact on functioning in familial, social and academic environments (Adams & Emerson, 2021; Cuffe et al., 2020; D'Agati, Curatolo, & Mazzone, 2019; Harkins, Handen, & Mazurek, 2021).

1.1. ASD and co-occurring emotional problems

In individuals with ASD, who have severely impaired social interactions and communication skills and restricted and repetitive interests or behaviours (American Psychiatric Association, 2013), psychiatric comorbidities are the norm rather than the exception, with rates as high as 90% (Brookman-Frazee, Stadnick, Chlebowski, Baker-Ericzén, & Ganger, 2018; Lecavalier et al., 2019). Studies reporting emotional symptoms in this population are highly heterogeneous because they use a variety of different assessment methods, informants, and age groups. In children and adolescents, anxiety symptoms have been reported at rates of between 11% and 84% (Strang et al., 2012; White, Oswald, Ollendick, & Scahill, 2009), while in children under seven years old the rates are between 2% and 62% (Vasa, Keefer, McDonald, Hunsche, & Kerns, 2020; Llanes, Blacher, Stavropoulos, & Eisenhower, 2020). The risk of developing depressive disorders is four times higher in people with ASD than in the general population (Hudson, Hall, & Harkness, 2019), with estimates of prevalence in children ranging from 11% to 12% (Lai et al., 2019) to 30% (Brookman-Frazee et al., 2018).

Prospective research has demonstrated that emotional symptoms are a persistent comorbidity throughout development in individuals with ASD (Kirsch et al., 2020). Emotional symptoms in ASD are associated with the impairment of social communication (Duvekot, van der Ende, Verhulst, & Greaves-Lord, 2018; Kim & Lecavalier, 2021), and repetitive and self-injurious behaviours (Muskett, Capriola-Hall, Radtke, Factor, & Scarpa, 2019; Russell, Frost & Ingersoll, 2019). McArthur, Lee, and Laycock (2022) also suggested that sleep disorders and anxiety, but not depression, may mediate the association between ASD and executive functioning. Research on school-related outcomes of emotional problems in autism (Adams et al., 2021) and even family-related outcomes is limited. Anxiety has been associated with school attendance and academic performance (Reyes et al., 2022). Parental emotional disturbances have been related to ASD symptoms (Chan, Lam, Law, & Cheung, 2018; Scherer, Verhey, & Kuper, 2019), but the specific role of ASD comorbidities is difficult to ascertain.

1.2. ADHD and co-occurring emotional problems

In individuals with ADHD, who have a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development (American Psychiatric Association, 2013), anxiety disorders can develop early in life and are one of the most prevalent comorbidities, reaching rates of 38% (D'Agati et al., 2019; Mohammadi et al., 2021; Shephard & Bedford, 2019). Also, children with ADHD display more symptoms of depression than controls without ADHD (Mitchison & Njardvik, 2019; Mphahlele et al., 2020).

Emotional problems can increase the severity of ADHD (Tsang et al., 2015) and change the evolution, prognosis and treatment of ADHD across the lifespan (D'Agati et al., 2019). These problems also mediate the greater risk of suicide and depression later in life (Levy, Kronenberg, Crosbie, & Schachar, 2020). When Reale et al. (2017) studied the efficacy of treatment in a large sample of children and adolescents with ADHD, they observed that those with ADHD and comorbid anxiety showed higher rates of worse outcomes after one year. Moreover, children with ADHD and co-occurring anxiety/depression presented a tenfold greater risk of poor academic performance than children with ADHD alone (Cuffe et al., 2020). Some authors have indicated that ADHD children with comorbid anxiety disorders performed worse in several domains of executive function when measured by the Continuous Performance Test (Ter-Stepanian et al., 2017) or working memory task (Jarrett, Wolff, Davis, Cowart, & Ollendick, 2016). However, a meta-regression analysis found that clinical anxiety may protect attention and working memory in boys with ADHD (Maric, Bexkens, & Bögels, 2018), especially in medication-naïve children. As far as family-related outcomes are concerned, parents of children with ADHD were found to have a 2.9 times higher risk of mental disorders than those without. Although externalized problems double the presence of that risk, little is known about the effect of internalized problems (Cheung & Theule, 2016). Therefore, it has been suggested that the severity of anxiety and depressive symptoms comorbid in children with ADHD reflect the severity found in their parents (Xia, Shen, & Zhang, 2015).

1.3. ASD + ADHD and co-occurring emotional problems

The comorbidity between ASD and ADHD (hereinafter, ASD + ADHD) has been reported at rates between 50% and 70% (Rong, Yang, Jin, & Wang, 2021). Children with this dual condition have more severe ASD symptoms and more impaired adaptative

behaviour than children with ASD alone. Likewise, they do not respond as well as to pharmacological treatment for ADHD symptoms as children with ADHD alone (Antshel, Zhang-James, Wagner, Ledesma, & Faraone, 2016; Hours, Recasens, & Baleyte, 2022). The findings on the prevalence of co-occurring emotional problems in this population are mixed. Some studies in clinical-based



Fig. 1. Study design and participants flow chart.

PRE: Preschool-aged children, SCH: Primary school-aged children. Sub: Subclinical.

populations of 5-to-12-year-old children with ASD + ADHD, report a prevalence of emotional symptoms similar to that in children with ASD or ADHD alone (Carta et al., 2020; Craig et al., 2015; Dellapiazza, Audras-Torrent, Michelon, & Baghdadli, 2021). Other studies, however, have reported a higher prevalence of emotional symptoms (Thomas, Sciberras, Lycett, Papadopoulos, & Rinehart, 2018; Yamawaki et al., 2020) and an even greater risk of anxiety and mood disorders (Avni, Ben-Itzchak, & Zachor, 2018; Gordon-Lipkin, Marvin, Law, & Lipkin, 2018; Lecavalier et al., 2019). And while externalizing problems have been associated with ADHD severity, internalizing problems appear to be associated with ASD severity (Dellapiazza et al., 2021).

The co-occurrence of emotional problems may further increase impairment in children with ASD + ADHD, and numerous authors have reported poorer adaptative daily-living skills, a lower quality of life and lack of response to social skills training (Antshel et al., 2016; Avni et al., 2018; Thomas et al., 2018). However, the impact of triple comorbidity on cognitive and academic performance and how this can influence the family's mental health has been understudied. Further information on the clinical characteristics of this population will be useful for improving the design of effective treatments (Antshel & Russo, 2019).

Table 1 Sociodemographic and clinical characterization of the sample by diagnostic group and age.

	$ASD_{a} ADHD_{b} ASD + ADHD_{c}$ $N = 44 N = 32 N = 12$		AS	D ADHD -	CO	CONTROL d		Group comparisons									
Preschool-age children			= 12	N = 187		Model parameters		ab	ac	ad	bc	bd	cd				
Gender, male (%)	33 (75.00)	19 (59.38)	10	(83.33)	102 (54.55)		.02	.8									
Age (M, SD)	5.14 (1.14)	5.15 (.43)	5.2	3 (.31)	5.0	5 (.52)	.29	2									
Ethnicity, autochthonous (%)	36 (81.82)	30 (93.75)	12 (10	14		16 (78.08) .06		01									
Socioeconomic status (%), Low	10 (22.73)	9 (28.12) 1(1 (8.33)		28 (14.97)											
Medium	25 (56.82)	21 (65.63)	7 (7 (58.34)		121 (64.71)		5									
High	9 (20.45)	2 (6.25)	4 (4 (33.33)		38 (20.32)											
ASD severity score	4.64	1.04	4.0	4.00 (1.95) 46.67 (6.44) 88.08 (16.91)		1.42 (1.04) 27.65 (7.69)		001	< .001	.992	< .001	.002	.009	.005			
(M, SD)	(2.26)	(.44)															
ADHD severity score	29.14	46.19	46.					001	.001	< .001	.846	.999	< .001	< .001			
(M, SD)	(9.97)	(5.50)	(6.4			101.74			.999	.999			< .001	.103			
(M SD)	91.17	90.34	00. (16					001			.002	.999					
Academic	(19.13)	(14.20)	(10	.91)	(12.43)												
achievement (M.	3.00	3.33	3.33 2.7		4.1	4.11 (.75)		001	.490	.989	< .001	.509	< .001	.012			
SD)	(.93)	(.72)		- ()		- (
School-age children	N=29	$\mathbf{N} =$	126	N=22		N=282											
Gender, male (%)	24 (82.76	5) 88 (59.84)	19 (86.3	6)	165 (58.51	l)	.002	.161	.726	.011	.110	.029	.010			
Age (M, SD)	11.05 (.66)	11.1	1 (.51)	51) 11.02 (.60)		11.04 (.48)		.633									
Ethnicity, autochthonous (%)	24 (82.76	24 (82.76) 106 (84.13) 6 (20.69) 31 (24.13)		17 (77.27) 50) 5 (22.73)		 7) 252 (89.36 39 (13.83) 		.205									
Socioeconomic status (%), Low	6 (20.69)																
Medium	17 (58.62) 79 (52.70)	.70) 13 (59.0		9) 180 (63.83		.100									
High	6 (20.69) 16		2.70)	.70) 4 (18.18) 63 (22.34)											
ASD severity score (M, SD)	4.48 (2.20)	1.27	(.77)	.77) 4.77 (2.14)		1.28 (.81)		< .001	< .001	.998	< .001	< .001	.999	< .001			
ADHD severity score	27.97	44.4	44.46 45.9		27.74			< 001	< .001	< .001	000	880	< 001	< .001			
(M, SD)	(8.32)	(6.2-	(6.24) ((7.69)			< .001			.,,,,	.000	<.001				
Intelligence quotient	96.58	96.58 95.65 (17.82) (12.61)		93.45		104.84		< .001	.999	.986	.121	.991	< .001	.121			
(M, SD)	(17.82)			(17.69)		(13.22)											
Academic achievement (M, SD)	3.08 (1.13) 2.		(.89)	89) 2.73 (1.00)		3.33 (1.03)	< .001	.019	.845	.881	.531	< .001	.109			

The ASD groups included children with ASD and subclinical ASD.

ASD severity was based on total ADOS-2 standardized scores ranging from 1 to 10 as follows: a score of < 3 was 'non-ASD', a score of 4–5 was 'ASD' and a score of 6–10 was 'autism'.

ADHD severity was based on K-SADS-PL scores ranging from 19 to 57, where higher scores indicated greater severity and the presence of symptoms. Academic achievement ranged from 1 (fail or low achievement) tefore be a key factor in the treatment o 5 (excellent or high achievement). M: Mean, SD: Standard Deviation.

Differences between continuous variables have been analysed through ANOVA and differences between categorical variables have been analysed through chi square. Post-hoc comparisons have been performed using Bonferroni and Z test, respectively. Differences p < .005 are shown in bold.

1.4. Study aims and hypothesis

In view of the above research, the main purpose of this study is to examine the prevalence of emotional symptoms in a communitybased sample of children with ASD and/or ADHD. Emotional problems have most frequently been studied in clinical-based samples rather than in community-based samples in which the severity profile of children with NDD is different and some individuals are left undetected and untreated. For this reason, we considered a four-sample design consisting of preschool and school-aged children diagnosed with ASD, ADHD, ASD + ADHD, and children without NDD. The specific objectives are 1) To describe the prevalence and severity of the co-occurrence of emotional problems in children diagnosed with ASD, ADHD, ASD + ADHD and in children without NDD, and 2) To explore how the co-occurrence of emotional symptoms and the severity of ASD and ADHD symptoms are associated with the need for support, neuropsychological and academic performance, and the psychological health status of the family. On the basis of the above objectives, we formulated the following hypotheses: 1) Children diagnosed with ASD or ADHD may present a high co-occurrence of emotional symptoms and, due to double vulnerability, those with ASD + ADHD may show an even higher and more severe co-occurrence, 2) The co-occurrence of emotional symptoms may be associated with ASD and ADHD severity and the need for support, and 3) Emotional problems might be associated with neuropsychological and academic performance and family psychological health status in children with NDD, especially in those with a diagnosis of ASD + ADHD.

2. Method

2.1. Study design

The Neurodevelopmental Disorders Epidemiological Research Project (EPINED) is a cross-sectional two-phase study that applies screening and diagnostic procedures in a school population in Tarragona, Spain, between 2014 and 2019. Its main aim is to describe the epidemiology of ASD and ADHD at two developmental stages: preschoolers aged 4–5 years old (PRE) and primary schoolchildren aged 10–11 years old (SCH). Fig. 1 shows the flow chart of the study design, the distribution of participants and the characteristics of the analysis groups. The details of sample-size estimation, procedure and assessment methods have been extensively described in Morales-Hidalgo, Roigé-Castellví, Hernández-Martínez, Voltas, and Canals (2018) and Canals, Morales-Hidalgo, Roigé-Castellví, Voltas & Hernández (2021). The EPINED protocol was validated by the Ethics Committee of the Sant Joan University Hospital in Reus, Spain (13–10–31/10proj5).

2.2. Participants

The participants consisted of two age groups: 4–5 year-old preschool children (PRE) and 10–11 year-old primary school children (SCH).

During the screening phase, 6894 children (PRE: 3374; SCH: 3520) were assessed for ASD and/or ADHD symptoms. A total of 54% (PRE: 53.4%; SCH: 54.7%) obtained informed consent from their families to participate in the second phase of the study. Differences between participants and non-participants, and between geographical areas, are described in Morales-Hidalgo, Voltas, & Canals, 2021. In the diagnostic phase, which is the focus of this study, we assessed 781 children (PRE: 295; SCH: 486) with risk symptoms of ASD/ADHD and a control group with no risk symptoms. The assessment procedure for each phase is described in the section below.

Using DSM-5 criteria and without considering comorbidities, we divided the children into several diagnostic groups: ASD (N = 57), ADHD (N = 192), and no neurodevelopmental or psychopathological disorders (N = 469). We also detected a group of children with subclinical ASD traits (N = 50). Previous findings with the EPINED sample suggested that the needs and characteristics of ASD and subclinical ASD were similar. For this present study, therefore, the following groups were created: 1) any ASD condition (i.e., ASD and subclinical ASD) without comorbid ADHD (N = 73); 2) any ASD condition with comorbid ADHD (N = 34); 3) ADHD without any comorbid ASD condition (N = 158); and 4) a comparison group with no NDD or other psychopathological disorders (N = 469) (See Fig. 1). The sociodemographic and clinical characteristics of the sample are presented in greater detail in Table 1.

2.3. Measures and procedure

2.3.1. ASD/ADHD symptoms and diagnoses

ASD and ADHD screening was completed by parents and teachers, while children and their parents were individually assessed to make a diagnosis.

ASD screening was performed using the Childhood Autism Spectrum Test (CAST; Scott, Baron-Cohen, Bolton, & Brayne, 2002) and the EDUTEA questionnaire (Morales-Hidalgo, Hernández-Martínez, Voltas, & Canals, 2017). When either of the two questionnaires gave a positive outcome, it was considered that there was a risk or likelihood of ASD. For ADHD, the 10-item Conners' indexes were used with preschool (Conners ECGI; Conners and Goldstein, 2009) and school-aged children (Conners 3 ADHD Index; Conners, 2008). ADHD was considered to be likely when scores were high or very high ($T \ge 65$) in both the parent and teacher indexes.

Diagnoses were based on DSM-5 criteria and clinical consensus among the researchers, who considered the information from a standardized assessment protocol including the Autism Diagnostic Interview-Revised (ADI-R; Rutter, Le Couteur, & Lord, 2003), the Autism Diagnostic Observation Schedule, Second Version (ADOS-2; Lord et al., 2012), and the ADHD scale of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-PL; Kaufman et al., 1997). When the information provided was unclear or inconsistent, it was supported by qualitative information obtained from teachers and observations in the children's natural

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surroundings. The severity of total ASD symptoms, social communication symptoms and repetitive behaviours was determined using the standardized ADOS-2 scores by Gotham, Pickles, and Lord (2009) and Hus et al. (2014), where a score of < 3 was 'non-ASD', a score of 4–5 was 'ASD' and a score of 6–10 was 'autism'. ADHD severity was calculated using the scores in the ADHD section of the K-SADS-PL for each ADHD presentation, where higher scores indicated greater severity and the presence of symptoms. The reliability of the ADHD section of the K-SADS-PL is very high (Cronbach's $\alpha = 0.94$ in the present sample) and the scores range from 19 to 57.

Participants were diagnosed with ADHD when information in the K-SADS-PL interview met the DSM-5 criteria for any of the three presentations of ADHD (inattentive, hyperactive-impulsive, and combined). Participants were diagnosed with ASD when their scores reached or exceeded the threshold in all the ADI-R diagnostic algorithm domains and in the ADOS-2 calibrated score of severity (score \geq 4). Participants were diagnosed with subclinical ASD when the scores on the ADI-R and ADOS-2 diagnostic algorithms were slightly below the ADI-R and ADOS-2 cut-off scores, the screening questionnaires were positive in both family and school settings and two professionals agreed that not all DSM-5 diagnostic criteria were met. These children exhibited both socio-communicative problems and repetitive behaviour patterns and, according to the K-SADS-PL interview, did not qualify for other diagnostic categories. In this regard, the diagnoses of tic disorder, obsessive-compulsive disorder and conduct disorders were evaluated in all the children using the specific scales of the K-SADS-PL. Information on language problems was provided by the families and by the school psychological services.

2.3.2. Co-occurring emotional problems

During the second phase of the study, emotional, behavioural, attentional and social problems were reported by parents through Achenbach's behaviour checklists for preschool-aged children (CBCL1 $\frac{1}{2}$ -5; Achenbach & Rescorla, 2000) and school-aged children (CBCL6–18, Achenbach & Rescorla, 2001). Both checklists included empirically based syndrome scales and DSM-oriented scales. A quantitative T-score was obtained for each scale in accordance with Spanish population scores. The DSM scales of anxiety problems and depressive problems were used to estimate the co-occurrence of these symptoms. Following the score classification provided by the CBCL, co-occurring clinical emotional problems were considered when the T-score was \geq 70, while co-occurring subclinical emotional problems were score was 65–69.

2.3.3. Cognitive and academic performance

Child neuropsychological functioning was assessed using the Spanish version of the Wechsler scales (WPPSI-IV, Wechsler Preschool and Primary Scales of Intelligence; WISC-IV, Wechsler Intelligence Scales for Children; Wechsler et al., 2005, 2014). The working-memory (WM) and speed-processing (SP) indexes were used to assess the children's neuropsychological functioning. The full-scale intelligence quotient (IQ) was also obtained so that the analysis could be adjusted. A diagnosis of intellectual disability (ID) was based on cognitive performance (IQ \leq 75) and DSM-5 criteria for adaptive skills.

Academic performance was ascertained from school grade reports provided by teachers on a 5-point Likert scale. We classified the achievement of preschoolers from low to high in language, maths, science, music and arts, psychomotricity, social interaction, and school habits. We classified the achievement of school-aged children from fail to excellent in language, maths, history and science but not in music/arts or physical education.

2.3.4. Sociodemographic information and psychological health status of the family

The families completed an ad-hoc questionnaire during the first and second phases to provide sociodemographic data and clinical information about previous psychopathological or medical diagnoses and service use. Socioeconomic levels were estimated in accordance with Hollingshead (2011).

Maternal and paternal psychological problems were assessed using the 12-item General Health Questionnaire (GHQ-12; Goldberg & Williams, 1988), where the scores of which range from 0 to 36 and higher scores indicate worse psychological health.

2.4. Data analytic strategy

Statistical analyses were performed using IBM SPSS 27 and EPIDAT 4.2. Descriptive analyses of the general characteristics of the sample were performed and differences between diagnostic groups were assessed using the Z test for categorical variables and the T-test/analysis of variance (ANOVA) with Bonferroni post-hoc analysis for continuous parametric variables. To test differences in the severity of emotional problems between diagnostic groups, analysis of covariance (ANCOVA) was used with adjustments for ethnicity, socioeconomic status, gender, age and intelligence quotient. We thus obtained the adjusted mean T-scores and computed post-hoc group comparisons using the Sidak test.

To test whether the co-occurrence of emotional problems is related to ASD/ADHD severity, neuropsychological functioning (working memory and speed processing), academic performance and family mental health, multiple linear regression models with the *enter* and *stepwise* methods were used. A regression model was performed for every dependent variable: ASD severity, ASD social communication severity, ASD repetitive behaviour severity, ADHD severity, ADHD attention deficit severity, ADHD hyperactivity/ impulsivity severity, working memory, speed processing, academic performance of the child, psychological problems of the mother and father. The independent variables used to adjust these relationships were gradually incorporated into the models in four steps. In the first step, the model was adjusted for sociodemographic data (ethnicity, socioeconomic status, gender, age) and intelligence quotient using the *enter* method (in regression models for working memory and speed processing, perceptive reasoning was used instead of intelligence quotient). In the second step, the NDD groups (ASD, ADHD, ASD + ADHD) were added to the previous adjustment using the *enter* method. In the third step, the variables of the emotional problem (anxiety and depression) were added using the *stepwise* method, and in the fourth step, the co-occurrence of NDD with emotional problems (ASD and depression, ASD and anxiety,

Table 2 Prevalence and severity of co-occurrent emotional symptoms by diagnostic group and age.

		ASD a	ADHD b	$ASD + ADHD_{c}$	CONTROL d	Group comparisons							
Preschool-age children: Achenbach's	$N=41 \qquad \qquad N=32 \qquad \qquad N=11$		N=182	Model parameters	ab	ac	ad	bc	bd	cd			
DSM Depression problems scale	Clinical prevalence	12 (29.27)	10 (31.25)	3 (27.27)	12 (6.59)	< .001	.855	.897	< .001	.804	< .001	.013	
	Subclinical prevalence	26 (63.42)	16 (50.00)	5 (45.46)	45 (24.73)	< .001	.250	.509	< .001	.795	.003	.128	
	Mean T score	65.41 (7.45)	63.38 (8.83)	63.64 (6.87)	57.91 (7.77)	11 202 (< 001)	000	000	- 001	000	006	050	
	Estimated mean T score	65.34	63.15	64.42	57.92	11.203 (<.001)		.999	< .001	.998	.006	.058	
DSM Anxiety problems scale	Clinical prevalence	12 (29.27)	8 (25.00)	3 (27.27)	16 (8.79)	.001	.685	.897	< .001	.882	.007	.046	
	Subclinical prevalence	20 (48.78)	12 (37.50)	7 (63.64)	27 (14.84)	< .001	.335	.174	< .001	.132	.002	< .001	
	Mean T score	63.46 (8.30)	62.44 (9.21)	63.27 (9.26)	57.59 (7.45)	(7.45)		000	. 001	0(0	000	. 001	
	Estimated mean T score	63.42	62.15	64.33	57.59	8.014 (<.001)	.982	.999	< .001	.963	.022	< .001	
Anxiety AND Depression problems	Clinical prevalence	7 (17.07)	6 (18.75)	2 (18.18)	6 (3.30)	< .001	.853	.931	.001	.967	< .001	.016	
	Subclinical prevalence	14 (34.15)	12 (37.50)	5 (45.46)	17 (9.34)	< .001	.767	.489	< .001	.642	< .001	< .001	
Anxiety OR Depression problems	Clinical prevalence	17 (41.46)	12 (37.50)	4 (36.36)	22 (12.09)	< .001	.731	.760	< .001	.943	< .001	.022	
	Subclinical prevalence	32 (78.05)	16 (50.00)	6 (54.55)	55 (30.22)	< .001	.012	.119	< .001	.795	.028	.092	
School-age children: Achenbach's	N = 28	N = 118	N = 21	N = 273									
DSM Depression problems scale	Clinical prevalence	6 (21.43)	31 (26.27)	9 (42.86)	21 (7.69)	< .001	.596	.107	.015	.122	< .001	< .001	
	Subclinical prevalence	10 (35.71)	52 (44.07)	14 (66.67)	40 (14.65)	< .001	.421	.032	.004	.056	< .001	< .001	
	Mean T score	61.54 (8.77)	63.03 (8.69)	67.67 (9.45)	56.02 (6.95)	(6.95) 28 133 (< 001)		025	003	023	< 001	< 001	
	Estimated mean T score	61.54	62.59	67.81	56.15	20.133 (<.001)	.900	.025	.003	.025	< .001	< .001	
DSM Anxiety problems scale	Clinical prevalence	6 (21.43)	29 (24.58)	10 (47.62)	13 (4.76)	< .001	.726	.053	.001	.030	< .001	< .001	
	Subclinical prevalence	7 (25.00)	47 (39.83)	15 (71.43)	42 (15.39)	< .001	.144	.001	.189	.007	< .001	< .001	
	Mean T score	58.82 (7.82)	62.00 (9.84)	67.43 (10.02)	55.67 (6.7)	55.67 (6.7)		. 001	014	017	< 001	< 001	
	Estimated mean T score	58.75	61.83	67.44	55.75	23.031 (<.001)	.324	< .001	.314	.017	< .001	< .001	
Anxiety AND Depression problems	Clinical prevalence	3 (10.71)	15 (12.71)	9 (42.86)	6 (2.20)	< .001	.773	.010	.012	.001	< .001	< .001	
	Subclinical prevalence	6 (21.43)	19 (16.10)	12 (57.14)	18 (6.59)	< .001	.501	.010	.006	< .001	.003	< .001	
Anxiety OR Depression problems	Clinical prevalence	9 (32.14)	45 (38.14)	12 (57.14)	28 (10.26)	< .001	.555	.080	.001	.103	< .001	< .001	
	Subclinical prevalence	11 (39.29)	66 (55.93)	17 (80.95)	64 (23.44)	< .001	.113	.004	.065	.031	< .001	< .001	

The ASD groups include children with ASD and subclinical ASD.

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Prevalence is presented as n (%) and is calculated through T scores \geq 70 (clinical level) and \geq 65 (subclinical level). Differences in ratios of symptoms are calculated using the Z test. Severity is presented as T mean score (standard deviation) and estimated severity is presented as an estimated mean. Mean differences in severity are calculated using ANCOVA test adjusting by ethnicity, socioeconomic status, gender, age and IQ. Post-hoc group comparisons are calculated by Sidak's method. The model parameters correspond to F test and model signification. Differences p < .005 are shown in bold. ADHD and depression; ADHD and anxiety; ASD + ADHD and depression, and ASD + ADHD and anxiety) were added using the *stepwise* method.

To control the increase in type-I error due to multiple comparisons regression models, a *p* correction was applied with 0.005 as the minimum level of significance.

3. Results

3.1. Sociodemographic characteristics of the sample

Table 1 shows the sociodemographic and clinical characterization of the sample by diagnostic group and age. No differences were found between groups in terms of age, ethnicity, or socioeconomic status. No differences were found between the ADOS-2 or K-SADS-PL severity scores of children with ASD or ADHD and those with ADHD + ASD, respectively.

Age differences in socio-demographic and clinical characteristics were also analysed for each diagnostic group. No sociodemographic differences were found by age in ASD, ADHD or ASD + ADHD groups. The groups were also clinically equivalent. Only for ADHD, was the intelligence quotient (QI) higher in school-aged children.

3.2. Prevalence of emotional problems in neurodevelopmental disorders

Table 2 shows the prevalence of co-occurring emotional problems at the clinical and subclinical levels and the CBCL severity scores (mean T-scores and adjusted mean T-scores) by diagnostic group and age. The ASD and subclinical ASD groups were analysed together as no statistically significant differences in the co-occurrence of emotional problems were observed between the two groups. Neither were any significant differences found in the rates of emotional problems at the clinical and subclinical levels between the two age groups within each diagnostic group. Only preschoolers with ASD showed a significantly higher prevalence of any emotional problems at the subclinical level ($T \ge 65$: 78%) than school-aged children (39.3%). However, for ASD + ADHD, the prevalence of emotional problems was higher in school-aged children than in preschool children. Regarding the mean T-scores, no age differences were found between the ASD, ADHD and comorbid ASD and ADHD groups.

Preschool participants with ASD, ADHD and comorbid ASD + ADHD presented higher rates and severity scores than the comparison control group for co-occurring emotional problems (see Table 2). Children with ASD + ADHD did not have more emotional problems than those with ASD or ADHD alone. The prevalence of anxiety or depression at the clinical level ($T \ge 70$) was 41.5%, 37.5% and 36.4% for ASD, ADHD and ASD + ADHD, respectively, compared to 12.1% for the control group. Rates were also very high at the subclinical level ($T \ge 65$), with values of 78%, 50% and 54% for ASD, ADHD and ASD + ADHD, respectively, compared to 30.2% for the control group.

School-aged participants with NDD also had higher rates and severity of co-occurring emotional problems than participants without NDD (see Table 2). Greater differences between diagnostic groups were found in school-aged participants than in preschoolers. In this regard, children diagnosed with ASD + ADHD had significantly higher severity scores for depression and anxiety than children with ASD or ADHD. They also exhibited significantly higher rates of depression and anxiety (42.7% and 57.1% at the clinical and subclinical levels, respectively) than children with ASD (10.7% and 21.4%), ADHD (12.7% and 16.1%) and controls (2.2% and 6.6%). Moreover, the presence of at least one of these emotional problems rose to 57-81% in children with ASD + ADHD, 32-39%



Emotional problems: C = Clinical level (T ≥ 70) and S = Subclinical level (T ≥ 65) in Achenbach's DSM scales



in children with ASD, 38–56% in children with ADHD, and 10–23% in controls at the clinical and subclinical levels for each diagnostic group.

Information on the co-occurrence of any emotional problems in children with NDD is graphically summarized in Fig. 2.

3.3. Co-occurring emotional problems and level of support required

The clinical impairment associated with the co-occurrence of emotional problems was assessed by examining the level of support needed by the child and the severity of the underlying ASD or ADHD symptomatology. In terms of support, children with ASD and clinical-level emotional problems ($T \ge 70$) received a higher proportion of psychological (58% versus 34%; p = .050) and pharmacological (85% versus 0%; p = .001) intervention than children with ASD but without emotional problems. On the other hand, we found no significant differences between children with and children without emotional problems in the ADHD and ASD + ADHD groups. In general, no group differences were found at lower severities ($T \ge 65$), with the exception of those children with ASD + ADHD and emotional problems, who presented higher rates of pharmacological treatment than those without these problems (52% versus 11%). No differences were observed in the level of educational support.

3.4. Clinical, neuropsychological, educational, and family psychological health status associated with emotional problems: Multivariate analyses

The association between co-occurring emotional problems and ASD/ADHD severity, neuropsychological functioning, academic performance and parents' psychological problems was explored using multiple linear regression models.

3.4.1. Association with ASD/ADHD symptom severity

Our results indicated that the co-occurrence of emotional problems was not significantly associated with the severity of ASD among preschoolers. For school-aged children, although not statistically significant, the severity of repetitive behaviours was associated with the diagnosis of ASD + ADHD and co-occurring anxiety ($\beta = 1.443$; CI: .336–2.549; p = .011) or depression ($\beta = 1.526$; CI: .179–2.873; p = .027; Adjusted $R^2_{100} = 43.7$, $F_{8435} = 43.204$, p < .001). In children with ASD alone, was co-occurrence with anxiety positively associated with overall ASD severity ($\beta = .636$; CI: .048–1.224; p = .034; adjusted $R^2_{100} = 51.3$, $F_{6435} = 77.30$; p < .001). The effect of emotional problems on ADHD severity depended on symptom presentation and age, and associations were found only in children with ADHD alone but not in the ASD + ADHD group. Co-occurring depression among preschoolers was associated with an increase in the severity of attentional problems ($\beta = 3.631$, CI: 1.367-5.895; p = .002; adjusted $R^2_{100} = 42.2$, $F_{7265} = 28.661$, p < .001) and total problems ($\beta = 5.855$; CI: 1.484; 10.225; p = .009; adjusted $R^2_{100} = 47.7$, $F_{6265} = 41.293$; p < .001), whereas co-occurring anxiety in schoolchildren was related only to an increase in hyperactivity and impulsivity symptoms ($\beta = 3.217$, CI: 1.271-5.160; p < .001; Adjusted $R^2_{100} = 34.5$, $F_{7437} = 33.917$, p < .001). (See supplementary Table S1).

3.4.2. Association with educational and neuropsychological performance

In terms of neuropsychological functioning, the co-occurrence of ASD or ADHD with emotional symptoms was not significant in explaining variation in the performance of working memory or speed of processing tasks in preschool children. In school-aged children, the diagnosis of ASD + ADHD and depressive symptoms was negatively associated with working memory performance (β = -14.689; CI: -26.605 to -2.772; *p* < .016; Adjusted R²_{*100} = 27.4, F₈₄₃₆ = 21.573; *p* < .001). Speed processing and academic achievement were not associated with the co-existence of emotional problems in either age group of children with NDD. Despite this, academic performance was significantly lower in preschoolers with NDD and school-aged children with ADHD (see Table 1).

3.4.3. Association with family psychological health status

In terms of mental health status of the mother and father, only the mother's GHQ score was related to the co-occurrence of emotional problems with ASD or ADHD in both age groups. In the preschool sample, the co-occurrence of ASD with anxiety (β = 3.591; CI: .930–6.252; p = .008) and the co-occurrence of ADHD with depression (β = .242; CI: 1.340–7.814; p = .006) were associated with more maternal psychopathological symptoms (adjusted R^2_{*100} = 16.9, F_{7261} = 6.292; p < .001). In school-aged children, only a trend was found for the co-occurrence of ADHD with anxiety (β = 2.493; CI: .613–4.374; p = .009; adjusted R^2_{*100} = 11.7, $F_{10,432}$ = 6.724; p < .001).

4. Discussion

As stated in the study hypotheses, children with ASD and/or ADHD had a high co-occurrence of emotional problems (32–81%) and a considerable coexistence of anxiety and depression. No significant differences were found between age groups. This supports data on the early onset of this comorbidity (Gair, Brown, Kang, Grabell, & Harvey, 2021) and on stability through childhood and pre-adolescence (Strang et al., 2012). The comorbid condition of ASD + ADHD presented even higher rates of emotional problems in school-aged children. The high levels of anxiety and depression in individuals with ASD or ADHD have been widely reported in childhood and adolescence (Hudson et al., 2019; Mphahlele, Pillay, & Meyer, 2020; Meinzer, Pettit, & Viswesvaran, 2014; Van Steensel and Heeman, 2017), as has persistence into adulthood (D'Agati et al., 2019; Hollocks, Lerh, Magiati, Meiser-Stedman, & Brugha, 2019). The presence of emotional dysregulation as a core underlying dimension among NDD conditions may mediate comorbidity with emotional disorders (England-Mason, 2020) and lead to changes in clinical manifestations and prognosis as well as

functional impairments in different areas of daily life, thus becoming an important feature of psychological intervention.

4.1. ASD or ADHD and co-occurring emotional problems

In this study we found that anxiety and depression problems increased about threefold in children with ASD or ADHD alone compared to a population without NDD.

Anxiety symptoms were present in 21.4–48.8% of the children, which is within the range described by other authors in ASD populations: for example, Strang et al. (2012) reported 35%, Lai et al. (2019) 20%, Brookman-Frazee et al. (2018) 56%, Llanes et al. (2020) 31–50% and van Steensel et al. (2011) 40%. For the ADHD population, co-occurrence with clinical anxiety was roughly 25% for both age groups, which is in line with the rates of 25–30% described by Reimherr, Marchant, Gift, and Steans (2017), Shea, Lee, Lai, Luk, and Leung (2018), and Maric et al. (2018). Likewise, the prevalence of anxiety in the subclinical level was similar to the rates of symptoms (38–40%) found by other authors (D'Agati et al., 2019; Mitchison & Njardvik, 2019; Mohammadi et al., 2021). Depressive symptoms at the clinical level were present in 29% of preschoolers and 21% of school-aged children with ASD. These figures are close to the 30% found in children aged between 6 and 18 years old (Strang et al., 2012) and even to the 12–26% rate of depression diagnosis reported by Hudson et al. (2019). The prevalence of depressive symptoms in ADHD was higher than the 21% reported by Mitchison and Njardvik (2019).

As outlined in the introduction, detecting depression and anxiety in children with NDD is extremely important because cooccurring symptoms may worsen clinical severity and prognosis in both conditions and mediate the greater risk of negative schoolrelated and family mental health outcomes. The high prevalence of anxiety or depression problems found in preschool children with ADHD or ASD suggests that there are common factors for this association. In this regard, a genetic liability could explain the relationship between childhood ADHD and subsequent depression when the onset of depression is very early (Rice et al., 2019; Riglin et al., 2020). In ASD, the presence of common developmental pathways in early symptoms of autism and anxiety suggests an overlap between these two disorders (Shephard & Bedford, 2019).

4.2. ASD + ADHD and co-occurring emotional problems

In children with comorbid ASD + ADHD, we observed a 4–5-fold greater risk of emotional problems than in the neurotypical population, and similar prevalences of anxiety and depression. Our results are consistent with our hypothesis, with the greater prevalence of comorbid psychiatric symptomatology reported by Mansour, Dovi, Lane, Loveland, and Pearson (2017) and with the data reported by Gordon-Lipkin et al. (2018), who stated that ASD + ADHD leads to even greater vulnerability to anxiety and depression (relative risks of 2.20 and 2.72, respectively) than ASD alone. In agreement with Thomas et al. (2018) and Yamawaki et al. (2020), in this group, we found the greatest coexistence between anxiety and depression symptoms and the highest prevalence and severity scores for these problems. This was particularly the case in the school-aged group, which suggests that comorbidity may increases as children get older, thus worsening their prognosis. In fact, emotional disorders have their onset mostly in puberty (Rapee et al., 2019; Solmi et al., 2022). However, we only observed this trend in the NDD groups. This may be because our sample comprises mainly prepubertal children or because children with NDD start to show emotional problems even at younger ages.

The comorbidity of ADHD + ASD together with the presence of emotional problems was associated with more severe ASD repetitive behaviour. This tendency in our results emphasizes the need for clinicians to assess both ADHD and emotional symptomatology in ASD children in order to plan better treatments. Antshel and Russo (2019) state that there is an increasing trend to consider comorbid ASD + ADHD as representing a distinct subtype within a heterogeneous disorder. However, although the resulting impairment is recognised, little is known about effective interventions. Our results suggest the need to prevent and address emotional problems as a basic goal of any intervention programme from early ages.

4.3. Association between co-occurring emotional problems and need for support

As expected, children with ASD and clinical emotional problems as well as those with ASD + ADHD and clinical emotional problems received more psychological and pharmacological treatment. No differences were found in educational support, which is surprising since emotional symptoms have a negative effect on daily living adaptive skills Avni et al. (2018), school participation, performance, risk of school non-attendance, and subsequent disengagement from formal learning in this population (Preece & Howley, 2018; Reaven, Reyes, Pickard, Tanda, & Morris, 2020).

No differences in service use were observed in children with ADHD whether or not they also had co-occurring emotional problems, though it is already known that comorbidity worsens prognosis and the effectiveness of treatment (Levy et al., 2020; D'Agati et al., 2019; Reale et al., 2017; Riglin et al., 2020). This raises questions about unmet needs and the presence of barriers to accessing services. Emotional difficulties are often not identified by families or the school. As a result, specialised services are not provided until behavioural disturbances appear, or emotional problems become too severe. Some authors point out that ADHD and comorbid symptoms did not predict service use. More significant predictors were parental mental health, socio-demographic factors and access to services information (Sayal, Mills, White, Merrel, & Tymms, 2015; Sayal, Prasad, Daley, Ford, & Coghill, 2018).

4.4. Clinical, neuropsychological, educational, and family psychological health status associated with emotional problems

Clinical, neuropsychological, educational, and family psychological health status outcomes related to co-occurrence with

emotional problems differed according to age group. The differences do not seem to be related to the socio-demographic and clinical characteristics of the age groups, since they were observed to be equivalent. The associations found were clinically suggestive but not completely statistically consistent, probably due to the small sample size of the subgroups analysed.

4.4.1. Association with ASD/ADHD symptom severity

In preschoolers with ASD + ADHD or ASD alone, the presence of emotional problems did not show a significant association with core ASD severity. Only in preschoolers with ADHD, depression problems were associated the overall severity of ADHD and inattention symptoms. It seems that both anxiety (Tsang et al., 2015; Overgaard, Aase, Torgersen, & Zeiner, 2016) and depression are related to the increased severity of these symptoms, and some authors identify poor frustration tolerance as an underlying mechanism (Seymour & Miller, 2017).

In school-aged children, anxiety or depression symptoms showed a tendency of association with impairments in the clinical severity of NDD. In children with ASD + ADHD, emotional problems were related to more severe repetitive and restricted behaviours, whereas in children with ASD or ADHD alone they were related to the severity of total ASD symptoms and hyperactive-impulsive symptoms, respectively. Our results differ from those of Strang et al. (2012), who found no differences in ADOS scores when emotional symptoms were present in children with ASD and a mean age of 11. On the other hand, Duvekot, van der Ende, Verhulst, and Greaves-Lord (2018) suggested there was a strong association with social communication impairments, perhaps because these difficulties become more evident when social relations become complex in adolescents with less severe profiles of ASD and emotional problems. Our results are also in line with those that suggest an association with both areas of impairment (Factor, Ryan, Farley, Ollendich & Scarpa, 2017) or with repetitiveness, sameness and self-injurious behaviours (Muskett et al., 2019; Russell et al., 2019). The underlying mechanisms of this association may be related to the role of repetitive behaviours as coping strategies for dealing with emotional problems (Joyce, Honey, Leekam, Barrett, & Rodgers, 2017). As far as ADHD is concerned, there is considerable debate on how anxiety affects symptoms of attention or impulsivity. In some cases, anxiety has been found to behave in the same way as in children without ADHD; in others, however, if there is a good response to stimulant treatment, anxiety has been considered secondary to stress due to ADHD (Pliszka, 2019). To provide the best therapeutic approach, it is therefore important to correctly identify the symptoms of anxiety in clinical settings.

4.4.2. Association with educational and neuropsychological performance

Emotional problems were not observed to be associated with neuropsychological functioning in the preschool-aged group. In school-aged children, the comorbidity of ASD + ADHD with depressive problems was related to decreased working memory. This tendency is not consistent with neuropsychological findings in either ASD or ADHD populations, in which only anxiety has been associated with executive functioning (Gnanavel, Sharma, Kaushal, & Hussain, 2019; Jarrett et al., 2016; McArthur et al., 2022; Ter-Stepanian et al., 2017). As far as age differences are concerned, it should be noted that working memory assessment in school-aged children includes both visuospatial and auditory memory, whereas in preschoolers it only includes visuospatial. Besides the neuropsychological impairments described in ASD (Habib, Harris, Pollick, & Melville, 2019), comorbidity with ADHD affects both the presence of anxiety symptoms and working memory performance (Colombi & Ghaziuddin, 2017). Since working memory deficits have been reported to improve with age, emotional problems could therefore be a key factor in the treatment of ADHD (Ramos, Hamdan & Machado, 2020).

Despite our hypothesis that children with NDD and emotional problems would have worse academic performance, we found no such association. In contrast, Cuffe et al. (2020) found a tenfold greater risk of poor academic performance in children with ADHD + anxiety/depression. They also studied a community population but focused on emotional disorders, not just symptoms. In the ASD population, Kim and Lecavalier (2021) suggested considerable variability in academic performance and a strong association with cognitive skills. Our sample was characterised by average cognitive performance.

4.4.3. Association with family psychological health status

In both age groups, emotional problems were associated with maternal mental health but not with paternal mental health. Our findings do not coincide with some studies which suggest that parents of children with ASD and ADHD are also prone to emotional disturbances (Cohrs & Leslie, 2017; Cheung & Theule, 2016), but they are in line with the findings of others (Scherer et al., 2019; Xia et al., 2015). Similarly, Scherer et al. (2019) suggested that the higher levels of emotional problems found in mothers of children with developmental disabilities are associated with greater caregiving responsibilities or with under-reported symptoms among fathers. Cheung and Theule (2016) also state that few studies have focused solely on fathers.

4.5. Study strengths and limitations, and future research directions

One of the strengths of this study is that the sample is a representative community-based population sample so that children with NDD can be compared with their neurotypical peers in the same school and social context. Previous research on ASD/ADHD has mainly focused on clinical samples, which makes it difficult to generalise the results, as cases tend to be more severe and the participants mainly male.

However, our methodological approach made it more difficult to reach a large diagnostic sample. The low participation rate and possible biases between participants and non-participants must also be considered. Our use of a cross-sectional design was also a limitation because we were unable to establish the direction of effects between neurodevelopmental and emotional disorders. Nor could we confirm the presence of emotional disorders through interviews, as we did for NDD, and had to rely on information provided

by parents. Although the CBCL is a screening test, its scales show excellent convergence with the DSM-based diagnoses provided from structured interviews, including anxiety and depressive disorders. It is also regarded as very useful tool for identifying comorbid psychopathology in children and adolescents with ADHD (Biederman et al., 2021).

We believe that evaluating how emotional symptoms on a dimensional basis or at different levels of severity (clinical and subclinical) affect children's functioning is important for improving clinical management. Also, future research should look more closely at the needs of the population with NDD at both the community and clinical levels so that the necessary educational and family supports can be planned. It is also important to improve the detection of emotional problems in this population and to study how these emotional problems evolve and impact later stages of development, since the impairment found in our sample varied according with age and was especially pronounced in school-aged children.

5. Conclusions

The co-occurrence of anxiety and depression in children with ASD, ADHD and ASD + ADHD from a community population was very high from the early ages of development. This co-occurrence was associated with ADHD severity and to a lesser extent with ASD severity. School-aged children with ASD + ADHD showed the highest prevalence and severity of emotional problems, which was associated with severe repetitive behaviour and a poorer working memory.

What this paper adds?

Findings on the prevalence of emotional problems in children with comorbid ASD + ADHD are mixed. Some authors point out that these children present more common and more severe emotional problems than children with ASD or ADHD alone, while others suggest that there are no differences. The implications of the triple comorbidity at the individual and family levels have not been fully studied. In this study, we explore the co-occurrence of emotional symptoms in children with ASD, ADHD, ASD + ADHD and a control group from a school community population. Rather than focus on severe cases, as clinical samples often do, we describe the clinical characteristics of a heterogeneous subgroup of children, with low, moderate, and high severity profiles of ASD and/or ADHD. Both anxiety and depression problems were significantly more prevalent in the school-aged children with ASD + ADHD than in those with ASD and AHDH alone, but this was not the case in preschoolers. Importantly, the results have the potential to provide greater insight into comorbidity patterns at different ages and in different populations.

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CRediT authorship contribution statement

Conception and design of study to Canals, J. (JC) and Morales, P. (PM), acquisition of data, JC, PM, Voltas, N. (NV) and Hernández, C. (CH); analysis and/or interpretation of data: JC, PM, NV, CH. Drafting the manuscript: PM, NV and JC; revising the manuscript critically for important intellectual content: JC and PM. Approval of the version of the manuscript to be published: JC, PM, NV and CH.

Data Availability

The authors do not have permission to share data.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ridd.2023.104454.

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