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Age at initial diagnosis of autism spectrum disorders: a retrospective comparison of screening techniques between the southern and northwestern regions of Switzerland

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Summary

AIMS: Early diagnosis of autism spectrum disorders (ASD) offers the possibility of early intervention and, in turn, gains in adaptive behaviour, language and cognition. The aim of the present study was to analyse whether age at diagnosis of autism spectrum disorders decreased in two regions of Switzerland from 2006 to 2016 following the implementation of different screening and referral techniques. In southern Switzerland, systematic paediatric screening using the Modified Checklist for Autism (M-CHAT) in toddlers was implemented in 2013, whereas in northwestern Switzerland, periodic trainings were used to increase paediatrician awareness of ASD. We investigated which method was associated with a younger average age at diagnosis.

METHODS: We conducted a retrospective, two-centre study searching clinical records of children and adolescents (aged 0–16 years) diagnosed with ASD in two neuropaediatric departments at Swiss hospitals between January 2006 and December 2016. All patients were diagnosed via a standardised evaluation based on two approved diagnostic tests: the Autism Diagnostic Observation Schedule–Second Edition (ADOS-2) and the Autism Diagnostic Interview–Revised (ADI-R).

RESULTS: In southern Switzerland, training and subsequent widespread use of the M-CHAT among paediatricians appeared to contribute to a significantly younger age at diagnosis. Age at diagnosis did not significantly decrease during the same period in northwestern Switzerland.

CONCLUSION: Our results point to the possibility of successfully reducing age at diagnosis in specific geographic areas through the implementation of screening questionnaires, such as the M-CHAT, at year 2 well-baby visits.

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Introduction

Early diagnosis of autism spectrum disorders

Autism spectrum disorders (ASD) are pervasive developmental disorders with a heterogeneous phenotype and mixed patient outcomes.

The prevalence of autism has risen worldwide [1], particularly in Switzerland. Epidemiological research shows a prevalence of 1% in the general population [2]. In Switzerland, ASD is diagnosed at a mean age of 5.4 years [3], though it can be reliably diagnosed at 24 months of age or younger [3–5]. To our knowledge, there are no epidemiological studies looking at age of diagnosis in Switzerland.

Despite compulsory health insurance for all Swiss residents, ASD is diagnosed relatively late, often precluding the possibility of early preschool intervention [2, 6]. One reason for the persistence of late diagnosis could be the inconsistent use of screening tools such as the Modified Checklist for Autism in Toddlers (M-CHAT) [7], in addition to a lack of knowledge of early signs of autism among paediatricians [3]. The M-CHAT questionnaire is an easy-to-use and effective screening tool with good specificity in children aged 18 months or older [8–10].

Standard autism diagnostic practices are based on a structured parent interview and an observational assessment, frequently the Autism Diagnostic Interview–Revised (ADI-R) [11] and the Autism Diagnostic Observation Schedule–Second Edition (ADOS-2) [12]. Both tests re-

LIST OF ABBREVIATIONS

ASD	Autism spectrum disorder
SD	Standard deviation
UCHB	University Children's Hospital Basel
IPSI	Pediatric Institute of Southern Switzerland, EOC, Bellinzona
ADOS	Autism Diagnostic Observation Schedule
ADI-R	Autism Diagnostic Interview – Revised
M-CHAT	Modified Checklist for Autism in toddlers

quire specific training for administration and provide complementary information necessary for an ASD diagnosis, either documentation of autistic behaviours present before age 5 as reported by the parent or caregiver (ADI-R) or observation of current autistic behaviours (ADOS-2) by a trained clinician in accordance with the latest version of the ICD-10 and DSM-5 diagnostic manuals.

Benefits of early diagnosis

Early diagnosis is crucial for improving outcomes in children and toddlers with ASD [13–16]. Studies show that early diagnosis facilitates gains in adaptive behaviour and IQ through timely intervention [13, 17]. For example, a recent randomised controlled trial showed important differences in the gains of children who started early intervention at 18 months of age versus 27 months of age [16]. Language abilities, including expressive language, receptive language and daily communication skills can improve through early treatment [18]. If early intervention is practiced with patients younger than 4 years, there is a good chance of decreasing ASD severity and of increasing cognitive and behavioural skills [19], as well as both social and daily living skills [20]. However, the gains available through early intervention appear to be accessible only if a child is diagnosed during preschool years. Later treatment may be less effective [21, 22].

A late diagnosis of ASD can lead to parental stress, delayed intervention and less optimal school placement [23]. However, despite these risks, there are many barriers that delay diagnosis of ASD. Isolating behaviours or slow language development can be falsely interpreted as sluggish development or shyness [24]. Parents often recognise delayed speech development or other non-specific signs of ASD, such as atypical sleep and aspects attributed to temperament, that do not differ from what is seen in other children with delayed development [25].

In Switzerland, services for children with disabilities are attributed differently in each of the 26 cantons, making it difficult to track and compare similar treatments. Outside of Switzerland, therapy and early intervention programmes are implemented with varying outcomes. While some children show great signs of improvement from early intervention, others benefit minimally, if at all [26]. The reasons for these differences in outcome are not yet understood [27]. One possible explanation is the variability inherent in the ASD phenotype, as well as differential cognitive functioning. Children with higher cognitive functioning and less severe symptoms may improve the most from early intervention [28]. However, they are also frequently diagnosed at a later age [28, 29]. More severe autistic disorders tend to be diagnosed earlier.

Study objectives

The objectives of this study were twofold: (1.) to measure age at diagnosis in two major diagnostic centres in Switzerland; (2.) to determine whether age at diagnosis decreased over a specific period during which a specific measure was implemented: an M-CHAT-based screening model in southern Switzerland or sporadic paediatrician training in northwestern Switzerland.

Materials and methods

We conducted a retrospective, two-centre study using past clinical records from children and toddlers (aged 0–16 years) diagnosed with ASD in the neuropaediatric departments of two Swiss children's hospitals between January 2006 and December 2016. We first searched the records of all patients diagnosed with ASD in both hospitals in early 2017. Nineteen different variables were extracted from the clinical records. The study was approved by the local ethics committees from the northwestern and central Swiss university hospitals (EKNZ BASEC 2016-01063) and Ticino (EK TI BASEC 2016-01063) and performed in accordance with the ethical standards defined in the Declaration of Helsinki.

Participants were children and toddlers diagnosed with ASD between January 2006 and December 2016 at the Neuropaediatric Department of University Children's Hospital of Basel (UCHB) or the Neuropaediatric Unit of the Paediatric Institute of Southern Switzerland (IPSI), San Giovanni Hospital, Bellinzona. Patients diagnosed with an Asperger-like profile due to an absence of language delays, a risk for higher age at diagnosis [29], as well as diagnoses made before 2006 or after 2016 were excluded from the cohort. All diagnoses were coded according to the International Classification of Diseases, 10th edition. Children and toddlers were diagnosed using the ADOS-2 [12] and ADI-R [11] instruments, which were administered by trained professionals.

Both hospitals are reference centres for autism diagnosis made in their respective areas of Switzerland. The UCHB Neuropaediatric Department covers children living in the northwest of Switzerland. Most ASD diagnoses in this region are made at UCHB directly, which serves a region of approximately 650,000 people (approximately 8% of the total Swiss population). From 2006 to 2016, UCHB organised occasional trainings for regional paediatricians in collaboration with an outpatient clinic (in cooperation with local child psychiatric services) specialised in detecting and diagnosing autism spectrum disorders. The systematic use of screening tools was not part of the referral system in the northwestern region of Switzerland.

In southern Switzerland, use of M-CHAT was strongly encouraged by IPSI at the 2-year developmental health check between 2009 and 2012. By 2013, paediatricians were systematically using this checklist at well-baby appointments [30]. Ramelli et al. previously showed a significant decrease in age at diagnosis using this screening tool [30]. At-risk cases were subsequently referred for evaluation by regional paediatricians to a specialised outpatient clinic in IPSI. IPSI diagnoses most cases of ASD in children in the southern Italian-speaking part of Switzerland serving an area of approximately 350,000 people.

Clinical records for 258 ASD diagnoses were consulted; 112 cases were excluded for the above-mentioned reasons (an Asperger-like profile or missing data), leaving 146 records for analysis. Information on sex, nationality, native language, other languages spoken at home, presence of comorbid cerebral pathology and presence of comorbid epilepsy were available both in the IPSI and the UCHB datasets and were therefore used in the analysis (see table 1).

The dataset was created using SPSS (version 24) and Excel software applications, and was characterised by full information for all variables (no missing data). Descriptive statistics were used to illustrate the variables considered. Categorical variables were presented as percentages, whereas continuous variables were presented using either mean and standard deviation or median and interquartile range according to the distribution type (evaluated through a skewness-kurtosis normality test). Differences between hospitals were tested using the chi-square test (or Fisher's exact test, where appropriate) and the Mann-Whitney test for categorical and continuous variables, respectively. Period-specific differences in age at ASD diagnosis between hospitals, as well as hospital-specific differences, were also assessed using the Mann-Whitney test. We used linear regression for assessing the relationship between age at ASD diagnosis and a four-category variable of interest created to account for hospital- and period-specific conditions (i.e. category 1 = UCHB, 2006–2012; category 2 = IPSI, 2006–2012; category 3 = UCHB, 2013–2016; category 4 = IPSI, 2013–2016), while controlling for a set of covariates. We fitted three versions of the model with a different reference category for the variable of interest, for the purpose of assessing whether age at ASD diagnosis was lower for category 4 (IPSI, 2013–2016) regardless of the reference category considered. Model 1 (M1) had category 1 (UCHB, 2006–2012) as its reference, while model 2 (M2) had category 2 (IPSI, 2006–2012) and model 3 (M3) had category 3 (UCHB, 2013–2016). We calculated the Variance Influence Factor (VIF) for each model to check for multicollinearity, while we used the Breusch-Pagan and Cook-Weisberg test to check for model heteroskedasticity. The statistical significance threshold was set at $p < 0.05$. All statistical analyses were conducted with Stata/IC 16.0 (StataCorp, 4905 Lakeway Drive, College Station, Texas, USA).

Results

The overall sample was composed of 70 children assessed at UCHB and 76 assessed at IPSI; table 1 gives their sociodemographic and clinical characteristics. These children did not differ between hospital sites by sex (approximately 80% males), presence of epilepsy (affecting 3–4% of the children) and period of diagnosis (slightly more than half were diagnosed with ASD between 2013 and 2016). Instead, children assessed at UCHB were more likely to be foreign (57% vs 42% at IPSI, $p = 0.049$), have a mother tongue different to the regional language (27% vs 4% at IPSI, $p < 0.001$), speak more than one language (56% vs 30% at IPSI, $p = 0.002$) and suffer from cerebral pathology (13% vs 1% at IPSI, $p = 0.006$). Overall, the median age at ASD diagnosis was significantly higher at UCHB (44 months vs 36 months at IPSI, $p < 0.001$).

The detailed analysis of the differences in age at ASD diagnosis between hospitals and periods is presented in table 2. Considering the differences between hospitals, the median age at ASD diagnosis was significantly lower at IPSI both for the period 2006–2012 (39 months vs 47 months at UCHB, $p = 0.038$) and the period 2013–2016 (30 months vs 43 months at UCHB, $p < 0.001$). If we consider the differences between periods within the same hospital, at UCHB the median age at ASD diagnosis did not change significantly (47 months for the period 2006–2012 vs 43 months for the period 2013–2016, $p = 0.680$), while it decreased significantly at IPSI (39 months for the period 2006–2012 vs 30 months for the period 2013–2016, $p = 0.003$).

The results of the estimated linear regression models are in table 3. The VIF (maximum mean value of 1.53) did not point to multicollinearity problems, but the Breusch-Pagan and Cook-Weisberg test indicated clear model heteroskedasticity ($p = 0.000$). To fix this problem, we calculated robust standard errors for assessment of statistical significance.

Table 1:
Sociodemographic and clinical characteristics of study participants.

		Regional hospital		p-value of the statistical test
		UCHB (n = 70)	IPSI (n = 76)	
Sex	Male	81.4%	81.6%	0.981
	Female	18.6%	18.4%	
Nationality	Swiss	42.9%	57.9%	0.049*
	Foreign	57.1%	42.1%	
Mother tongue	Matching regional language	72.0%	96.0%	<0.001***
	Different to regional language	27.1%	4.0%	
Languages spoken	One	44.3%	69.7%	0.002**
	Two or more	55.7%	30.3%	
Organic cerebral pathology?	No	87.1%	98.7%	0.006**
	Yes	12.9%	1.3%	
Epilepsy?	No	97.1%	96.1%	0.539
	Yes	2.9%	3.9%	
Period of ASD diagnosis	2006–2012	41.4%	48.7%	0.379
	2013–2016	58.6%	51.3%	
Age in months at ASD diagnosis: median (IQR)		44.0 (18.5)	36.0 (16.0)	<0.001***

ASD: autism spectrum disorders; IQR: interquartile range; UCHB: University Children's Hospital of Basel; IPSI: Paediatric Institute of Southern Switzerland.

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

The three models indicated that, when controlling for sociodemographic and clinical covariates included in the model, age at ASD diagnosis was significantly lower at IPSI for the period 2013–2016 compared to all the reference categories considered. More specifically, we found greater differences compared to the UCHB reference categories, with an average reduction in age at ASD diagnosis at IPSI of 13–15 months, regardless of the period considered (p <0.01). The IPSI difference between periods was smaller, but still significant, with an average reduction in age at ASD diagnosis of approximately 6 months between the two periods (p <0.05).

Discussion

We observed that systematic implementation of the M-CHAT screening questionnaire at the year 2 well-baby visit

Table 2:
Differences in months at ASD diagnosis between hospitals and between periods.

		Regional hospital		p-value of the statistical test
		UCHB (n = 70)	IPSI (n = 76)	
Difference in the age in months at ASD diagnosis between hospitals for the period 2006–2012	Age: median (IQR)	47.0 (20.0)	39.0 (12.0)	0.038*
Difference in the age in months at ASD diagnosis between hospitals for the period 2013–2016	Age: median (IQR)	43.0 (15.5)	30.0 (14.0)	<0.001***
Difference in the age in months at ASD diagnosis between periods for UCHB	Age, 2006–2012: median (IQR) [n = 29]	47.0 (20.0)	–	0.680
	Age, 2013–2016: median (IQR) [n = 41]	43.0 (15.5)	–	
Difference in the age in months at ASD diagnosis between periods for IPSI	Age, 2006–2012: median (IQR) [n = 37]	–	39.0 (12.0)	
	Age, 2013–2016: median (IQR) [n = 39]	–	30.0 (14.0)	0.003**

ASD: autism spectrum disorders; IQR: interquartile range; UCHB: University Children's Hospital of Basel; IPSI: Paediatric Institute of Southern Switzerland.

* p <0.05

** p <0.01

*** p <0.001

Table 3:
Results from the linear regression models. Robust standard errors in brackets.

Variables	Dependent variable: age in months at ASD diagnosis		
	Coefficient (robust std. error)	95% confidence interval	
		Lower	Upper
Model 1 (reference category: UCHB 2006–2012)			
IPSI 2006–2012	–7.356	–14.810	0.097
	(3.769)		
UCHB 2013–2016	1.756	–7.092	10.604
	(4.474)		
IPSI 2013–2016	**–13.102****	**–20.827**	**–5.376**
	(3.907)		
Model 2 (reference category: IPSI 2006–2012)			
UCHB 2006–2012	7.356	–0.097	14.810
	(3.769)		
UCHB 2013–2016	9.112*	1.809	16.416
	(3.693)		
IPSI 2013–2016	**–5.746***	**–10.311**	**–1.180**
	(2.308)		
Model 3 (reference category: UCHB 2013–2016)			
UCHB 2006–2012	–1.756	–10.604	7.092
	(4.474)		
IPSI 2006–2012	–9.112*	–16.416	–1.809
	(3.693)		
IPSI 2013–2016	**–14.86*****	**–22.662**	**–7.054**
	(3.946)		
Observations[b]	146		
R-squared	0.191		

* p <0.05

** p <0.01

*** p <0.001

[a] All models include the following control variables: sex (male vs female), nationality (Swiss vs foreign), native language (commensurate with regional language vs different to regional language), languages spoken (one vs two or more), organic cerebral palsy (absence vs presence) and epilepsy (absence vs presence).

[b] All models had the same number of observations and R-squared.

was associated with a decrease in age at diagnosis in southern Switzerland (from 39 to 30 months). In northwestern Switzerland, we did not observe a significant decrease in age during the same period, despite comparable diagnostic methods and an effort to include infantile autism as a subject in trainings and continued education for paediatricians. Moreover, in southern Switzerland, more children and toddlers were diagnosed with ASD, even though IPSI serves a much smaller portion of the population than northwestern Switzerland.

In Switzerland, everyone has compulsory healthcare insurance and access to healthcare. Therefore, both cohorts should have had access to healthcare providers, such as paediatricians, child psychiatrists and neuropaediatricians (developmental paediatricians). A difference in healthcare resources in the regions would most likely not explain the difference in age at diagnosis. In Switzerland, a lower age at diagnosis facilitates preschool access to therapeutic intervention programmes that can improve patient functioning and school placement [31].

There presently exists a wide choice of screening questionnaires that assess autism risk in young children [5, 10, 32]. In addition to good sensitivity and specificity, M-CHAT has the distinct advantage of being simple for parents to complete and simple for the clinician to score, allowing for quick and efficient administration during the short time that parents are waiting for an appointment [9]. The simplicity of the M-CHAT questionnaire surely contributed to the ease of implementation of the project, allowing for widespread adherence by paediatricians and a possible relationship with the decrease in age at diagnosis.

While further investigation is needed, our retrospective study supports the idea that implementation of M-CHAT at paediatrician well-baby visits may be a promising approach to lowering age at diagnosis in other geographic regions where paediatricians are the main source of referrals for specialised evaluations. During the period we studied, mean age at diagnosis in southern Switzerland fell from 39 months to 30 months, making some participants eligible for early intervention when they otherwise would not have been. The demonstration of such a decrease is encouraging, but not yet optimal. It will be important to continue to decrease the age at which autism is diagnosed in southern Switzerland to take full advantage of the neurological plasticity associated with the toddler years [16].

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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