*Psychiatria Danubina, 2019; Vol. 31, No. 3, pp 333-339 https://doi.org/10.24869/psyd.2019.333* *Original paper*


# USING ESDM 12 HOURS PER WEEK IN CHILDREN WITH AUTISM SPECTRUM DISORDER: FEASIBILITY AND RESULTS OF AN OBSERVATIONAL STUDY

**Marie-Maude Geoffray[1,2], Angélique Denis[3], Flavia Mengarelli[1], Chloé Peter[1], Natacha Gallifet[1], Valentin Beaujeard[1], Céline Jacob Grosmaitre[4], Valéry Malo[4], Stephane Grisi[1], Nicolas Georgieff[1], Sabine Magnificat[4] & Sandrine Touzet[2,3]**

*[1]Department for Child and Adolescent Psychiatry, Centre Hospitalier le Vinatier, Bron, France*
*[2]Laboratory Health Services and Performance Research (HESPER), Lyon, France*
*[3]Hospices Civils de Lyon, Pôle de Santé Publique, Lyon, France*
*[4]Department for Child and Adolescent Psychiatry, Centre Hospitalier de Saint Jean de Dieu, Lyon, France*

received: 23.10.2018; revised: 19.8.2019; accepted: 27.8.2019

## *SUMMARY*

***Background:*** *Early intervention for Autism Spectrum Disorder (ASD) in France is heterogeneous and poorly evaluated to date. Early Start Denver Model (ESDM) is a developmental and behavioral model of intervention for toddlers with ASD which has already shown very interesting outcomes on the development of children with ASD in various studies with different settings. However, it is not possible with the current research to agree on the best setting. Thus, we implemented an ESDM program according to our context where children are often pre-schooling early from 30 months old. This therapy was applied by a multidisciplinary team working in close collaboration with parents and other partners.*

***Subjects and methods:*** *A prospective observational study including 19 toddlers with ASD was conducted. We evaluated improvement on the cognitive level of toddlers with ASD receiving therapist-delivered ESDM intervention for 12 hours per week.*

***Results:*** *Significant improvements in verbal and nonverbal cognitive skills at the Mullen Scale of Early Learning were obtained after 10 months of intervention in our sample. The largest improvement was in receptive language development quotient with a mean improvement of 19.6 points. We also observed promising outcomes in daily adaptive behavior, with a slight improvement in communication at the Vineland Adaptive Behavioral Scale. These outcomes, when compared to the conclusions of previous studies, are leading us to the need for a therapy duration beyond 10 months.*

***Conclusions:*** *Our outcomes were very encouraging even with low cognitive and nonverbal children. These outcomes may be confirmed in a multicenter randomized controlled trial that is ongoing.*

***Key words:*** *early intervention - autism spectrum disorder - behavioral therapy*

* * * * *

## INTRODUCTION

Autism Spectrum Disorder (ASD) is a heterogeneous developmental disorder with impairments in reciprocal socio-communicative interactions, a restricted repertoire of interests and behaviours and atypical sensory reactivity (American Psychiatric Association 2013). The prognosis is often a life-long disability and involves individuals, families and society (Howlin 1988, Ganz 2007, Hayes & Watson 2013). No curative treatment has been found yet, however there is some evidence that early comprehensive, developmental and behavioural intervention may improve children's developmental trajectory (Warren et al. 2011, Maglione et al. 2012).

Early intervention for ASD in European countries is heterogeneous and poorly evaluated to date (Salomone et al. 2016). In France, most children and their families have access to a public consultation center. Families and children have regular consultations with a public psychologist or a child and adolescent psychiatrist, but meeting schedules vary greatly (weekly, monthly or once a quarter). Moreover, children can also receive speech and language therapy and/or occupational therapy and/or individual or group psychotherapy. Occupational therapy and individual or group psychotherapy are frequently based on psychoanalytic or psychodynamic traditions (Evans 2013). Group psychotherapy is a relationship-based intervention in small groups (3 to 4 children for 2 therapists), generally conducted in sessions of 1hr30, once or twice a week. Of all interventions, speech and language therapies are those most frequently reported in Europe (Salomone et al. 2016). These therapies can vary in frequency (usually one or two 30-minute session(s) per week and rarely, up to 3-4 times weekly). With regards to schooling, children have access to regular pre-school from 30 months with an optional special-needs assistant or they may attend special pre-schools for children with more severe disabilities.

In France, the majority of children with ASD below the age of four have on average less than 2-3 hours special interventions per week and often go to preschool with a special-needs assistant. Educational professionals

are connected with healthcare professionals (once per year and sometimes more). Additional interventions may include, very rarely at this age, low-intensity behavioral therapies.

Among early behavioral and developmental models of intervention most evaluated in the literature, there is the Early Start Denver Model (ESDM) (Dawson et al. 2010, Rogers and Dawson 2012, Estes et al. 2015). ESDM guides professionals or parents to implement a comprehensive intervention for 12-60 months children with ASD (Rogers and Dawson 2012, Rogers et al. 2012). It has been developed by Sally Rogers, Geraldine Dawson and her colleagues for the past 30 years. It aims to promote optimal social interactions between the child and his/her environment to enable the child to learn. It integrates applied behavior analysis with developmental and relationship-based approaches. The ESDM involves a therapist who interacts with the child. Parents or other childcare professionals (e.g. nursery/pre-school) can also be taught to apply ESDM techniques in daily life and thereby improve the generalization of the children's skills. In addition to a certified training, the ESDM methodology is detailed in a manual, which includes a fidelity rating scale (Rogers and Dawson 2012).

Among the various ESDM studies, we can highlight one randomized control trial that evaluated 20-hours per week ESDM therapist-delivered intervention on a 2-year period in 2-3 years old children with ASD. They compared the interventional group to a control group receiving an equivalent amount of intervention and showed a significant improvement in the overall cognitive level (difference of 10 points in standard score at the Mullen Scale of early learning between the 2 groups) in the short term and they also significantly improve adaptive behavior and autism symptoms long term (Dawson et al. 2010, Estes et al. 2015). One pre-post design study evaluated an ESDM group setting and showed also significantly better outcomes in the cognitive level in ESDM group versus the control group receiving similar amount of other therapy (Vivanti et al. 2014). Others setting in observational studies showed promising outcomes (Eapen et al. 2013, Devescovi et al. 2016). There is still no proof of the efficacy of the ESDM parent-delivered intervention on the cognitive improvement of children (Rogers et al. 2012). However, the hypothesis is that parent using the model daily in an ecological way could improve cognitive skills of children and facilitate generalization of their skills (Oono et al. 2013). Moreover, as concluded by Estes and her colleagues, it diminishes parental stress (Estes et al. 2014).

Thus, ESDM showed already very interesting outcomes on the development of children with ASD. However, that is not possible from the current literature to know what the best design will be to implement (optimal intensity, duration, individual versus group and parents or professionals-delivered therapy). We chose to implement 12 hours (semi-intensive) ESDM therapy which can complement an early inclusion at the nursery or in preschool. This therapy will be applied by a multi-disciplinary team working in close collaboration with parents and other partners (professionals of nursery, teachers and other professionals like speech therapists).

The aim of this study was to evaluate improvement of children with ASD in cognitive skills when Early Start Denver Model (ESDM) is applied 12 hours per week, by a trained therapist, over a 10 months period.

## SUBJECTS AND METHODS

### Study design and participants

We conducted a prospective observational study from September 2014 to July 2015. The trial was performed in 2 early-intervention units from 2 different hospitals in Lyon, France using ESDM. We included children 18-50 months old, meeting the criteria for a diagnostic of ASD according to the DSM-5 from a multidisciplinary team and child psychiatrists on the affiliated autism diagnostic unit. All the children had a positive score to the international standard diagnostic test the ADOS-2 (Autism Diagnosis Observation Schedule version 2) (Lord et al. 2000, Gotham et al. 2009). We excluded children and their families who could not come regularly to the center or with severe medical conditions (e.g. instable epilepsy). There were no exclusion/inclusion criteria based on the child's behavioral characteristics (e.g. low IQ, challenging behaviors). Hearing and visual impairments were systematically checked and corrected if necessary.

### Intervention

Each Team was composed of 12-14 professionals including speech language therapists, occupational therapists, clinical nurses, educators and psychologists. They received formal ESDM training prior to the intervention with official trainers certified by the University of California, Davis. To ensure treatment adherence, all therapists had to have a score above 80% on the ESDM fidelity scale. Half of the team had more than 3 years' experience in autism fields.

Therapists applied the ESDM principles outlined in the manual (Rogers and Dawson 2012). According to the ESDM manual, 20 to 25 behavioural and developmental objectives were set every 12 weeks based on observations made by therapists and parents. ESDM techniques were adapted depending on the child's improvement monitored during every session with a data sheet checking the progress in the objectives. ESDM was applied in an individualized Intervention, i.e one child for one therapist. However, depending on the child's objectives, 2 children and 2 therapists could work together to promote social interaction. Therapy ESDM was provided 10 hours per

week at the ESDM intervention unit and 2 hours per week in the child's natural environment (home, nursery, preschool).

When delivered in the child's natural environment, mostly at home, ESDM was alternatively performed by the therapist and the parent in presence of the therapist. Parents were coached applying ESDM by therapists. Therapists gave them information on their child's functioning and ESDM techniques and guided them with constructive feedback to practice ESDM with their child. Parents were encouraged to use ESDM in daily activities and for periods of ESDM play sessions (about 30 minutes per day in addition to the 2 hours weekly intervention).

Once every 2 months, i.e about 5 times during the study, time was spent by the therapist to convey information about autism and ESDM techniques and to share the child's developmental objectives with childcare professionals of the nurseries and preschools.

In addition to the direct intervention at the child level, once a month, i.e about 10 times during the study, parents had an additional consultation in the unit, with the child's psychologist or psychiatrist, in order to assist the family further in the understanding of ASD, coping and to reinforce support for parents and siblings.

Four family workshops (2 hours each) per year, i.e 10 during the study, were also proposed to parents by professionals in order to share general information about autism, rights and social aids, and to solve problems related to challenging behaviour, food selectivity and disorders, together with other parents of children with ASD.

Parents were free to seek other care available in the community (e.g: speech pathologist, occupational therapist etc.).

### Outcome measures and tools

The primary outcome was the overall Developmental Quotient (DQ) measured with the Mullen Scale of Early Learning (MSEL) after 10-month follow-up (T1). The MSEL is a direct-observation tool measuring cognitive levels of children with four subscales (fine motor, visual reception i.e. assessing nonverbal skills such as object tracking and categorization, expressive language and receptive language). According to the test manual, you can measure an Early Learning Composite Score (ELCS, standardized score with mean at 100 and SD at 15) derived from the four subscales T-Score (mean at 50 and SD at 10) (Mullen 1995). It is also possible to calculate an MSEL age-equivalent to generate Developmental Quotient (DQ) score (i.e. developmental age equivalent divided by chronological age) for each subscale using MSEL age-equivalents, which is useful in population with low IQ (Lord et al. 2012, Anderson et al. 2014, Pickles et al. 2014, Vivanti et al. 2014). It is a reliable, validated test widely used to evaluate the pediatric ASD population (Bishop et al. 2011, Swineford et al. 2015). It has been translated into French, a process that includes translation, back translation and harmonization.

The secondary outcome was the Second Version of the Vineland Adaptive Behaviour Scales (VABS-2) standard scores after 10-month follow-up (Sparrow et al. 2005). VABS-2 measures personal and social skills needed for everyday living. It assesses socialization, communication, motor and daily living skills, based on interviews with the parents. Standard scores for each of the four studied domains are provided and a composite standard score is derived from the four domains. VABS-2 was already translated and back-translated into French and validated. We used American norms in order to be comparable with previous studies.

The assessments were conducted by an independent clinician not involved in ESDM intervention.

### Statistical analyses

Quantitative data were expressed by the mean value, the median, their quartiles and 95% confidence intervals. Qualitative data were expressed by frequency and percentage. The DQ and VABS-2 scores were compared between inclusion (T0) and 10-month follow-up (T1) using the Wilcoxon signed rank test. The size of effect between the measures T0 and T1 was considered by Cohen's d, which expresses a difference of average in numbers of standard deviation. An effect is considered small for values between 0.2 and 0.49; medium for values between 0.5 and 0.79 and large for values >0.80. A linear model was used to model overall DQ at T1 after controlling for T0 values and the following baseline variables: age at T0, ADOS comparative standard score (CSS) at T0, previous ESDM intervention and number of ESDM intervention hours between T0 and T1. All tests were two-sided and carried out at the 5% level of significance. Statistical analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC, US) by the teaching hospital of Lyon (Hospices Civils de Lyon, France).

## RESULTS

A total of 19 children (15 males/4 females) were included. They were aged 34.7±7.3 months (min-max: 21.7-49.2 months) with an ADOS CSS equal to 7.6±1.8 (min-max: 5-10). Among them, 37% (7/19) had previously followed 10-hour weekly behavioral and developmental interventions over a 10-month period in the same center. The children had no signs of epilepsy and took no medication for autism or other behavioral disorders during the ESDM intervention year.

Between T0 and T1, children received ESDM intervention on average 8.3±1.2 hours a week (median: 8.7; min-max: 4.2-9.7). This value takes into account absences of the children or the professionals.

Outcomes measured at T1 were collected on average 9.8±1.2 months after the baseline measure T0 (min-max: 7.4-12.4 months).

**Table 1.** Comparison outcomes of the MSEL and VABS-2 scores before (T0) and after (T1) 10-month ESDM intervention

| | T0 mean (SD) N=19 | T1 mean (SD) N=19 | Mean Difference (SD) | Effect size[#] | p-value[##] |
|---|---|---|---|---|---|
| MSEL | | | | | |
| Overall DQ | 44.8 (17.7) | 56 (25.5) | 11.2 (11.5) | 0.51 | 0.0003*** |
| Nonverbal DQ | 55.3 (16.7) | 64.1 (23.9) | 8.8 (11.3) | 0.43 | 0.0046** |
| Visual reception DQ | 52.8 (20.9) | 63.1 (27.1) | 10.3 (12.9) | 0.43 | 0.0062** |
| Fine motor DQ | 58 (14.8) | 65.2 (22.3) | 7.1 (12.6) | 0.38 | 0.0602 |
| Verbal DQ | 33.9 (20.7) | 47.9 (28.9) | 13.9 (17.1) | 0.56 | 0.0012** |
| Receptive language DQ | 36.8 (22.2) | 56.4 (31.4) | 19.6 (20.2) | 0.72 | 0.0006*** |
| Expressive language DQ | 33.8 (20.6) | 43.7 (28.1) | 9.9 (17.1) | 0.40 | 0.0323* |
| VABS | | | | | |
| Composite score | 71.5 (7.3) | 70.6 (9.8) | -0.9 (5.4) | -0.10 | 0.4001 |
| Communication | 64.7 (7.3) | 69.7(14.7) | 5.0 (11.4) | 0.43 | 0.1261 |
| Daily living skills | 80.3 (11.8) | 74.9 (13.5) | -5.4 (7.8) | -0.43 | 0.0131* |
| Socialization | 73.8 (6.9) | 70.9 (7.2) | -2.9 (4.8) | -0.41 | 0.0200* |
| Motor skills | 80.2 (8.8) | 79.3 (10.5) | -0.8 (6.7) | -0.09 | 0.2110 |

[#] Cohen's d score, values of 0.2-0.49 denote small sized effects; 0.5-0.79 medium sized effects; >0.8 large sized effects;
[##] Wilcoxon signed-rank test; * p<0.05, ** p<0.01, *** p<0.001

Table 1 displays the MSEL and VABS-2 results between T0 and T1. A large and significant difference was observed between nonverbal DQ (mean=55.3; SD=16.7) and verbal DQ (mean= 33.9; SD=20.7) (P<10-3). There was a significant improvement of the overall DQ between T0 and T1 (11.2 points, SD=11.5, IC95%=(5.7-16.7), p=0.0003). Cohen's d effect size was 0.51 and was thus medium. In the subscales, the largest improvement was in receptive language DQ with an effect size at 0.72 and a mean difference of 19.6 points (SD=20.2, IC95%=(9.8-29.3)). There was a small effect size in expressive language DQ. There was no significant improvement in fine motor.

There was no significant difference in the mean of the VABS-2 composite standard score between measures at T0 and T1 (p=0.4001). There was a slight non-significant improvement in communication. There was a slight significant decrease between T0 and T1 in social (effect size= -0.43; p=0.0131) and daily living skills scores (Effect size=0.41; p=0.0200). Similarly, to the MSEL outcomes, there was an important variability in the outcomes. For example, the median of the difference in communication was 1 with a minimum of -12 and a maximum of 32.

After adjustment in linear models, overall DQ at T1 was associated with fine motor DQ at T0 (p=0.0052) and visual reception DQ at T0 (p=0.0378). Baseline Fine motor DQ and baseline Visual reception DQ were positively correlated to the overall DQ at T1. Variation in this model accounted for 82% of the overall variance. It was not associated to age at T0, ADOS CSS at T0, previous ESDM intervention and number of ESDM intervention hours between T0 and T1.

## DISCUSSION

The primary outcome of this current study showed a significant improvement in overall cognitive level at endpoint compared to the baseline value previously found in different ESDM studies (Dawson et al. 2010, Eapen et al. 2013, Vivanti et al. 2014, 2016, Devescovi et al. 2016). As other studies' short-term outcomes, the largest improvement was observed in receptive language (Dawson et al. 2010, Vivanti et al. 2014). However, we also observed a significant improvement in nonverbal and other verbal cognitive skills. Moreover, to correctly analyze our results, it is important to note that our sample had a very low cognitive level at baseline. NVDQ and VDQ are often accepted as equivalent to Nonverbal IQ (NVIQ) and Verbal IQ (VIQ) because of their convergence with IQ measurements (Bishop et al. 2011). Andrew Pickles and his colleagues published outcome measures with MSEL in a large population (N=192) of young children with ASD and found NVIQ of 66.9 (21.8). Our sample had a nonverbal IQ 10 points lower, which is an important clinical difference. Verbal IQ of this current study was equivalent to the population of Andrew Pickles and his colleagues who had a VIQ at 35.8 (21.9) (Pickles et al. 2014). Moreover, if we use standardized scores, 84.2% of our sample had an early learning composite score (mean=100; min-max=49-155; SD=15) in a range of 49-54 or below; that is equal or below -3 SD. Then, even with a low IQ, we obtained significant improvements in verbal and nonverbal cognitive skills. ESDM aims to stimulate communication and language but also nonverbal skills compared to some models that focus mainly on core autism symptoms, i.e. socio-communicative deficit (Green et al. 2010, Wetherby et al. 2014, Thomas et al. 2016). The literature highlights that a "multiple interacting system" is implicated in the development (Hellendoorn et al. 2015); therefore, stimulation of different domains is necessary to improve verbal and nonverbal skills, in particular for children with intellectual disabilities. Nevertheless, the most relevant

techniques in the ESDM have not yet been determined. It could be interesting to look for mediators of the ESDM effect and determine the ESDM active components (Dunn et al. 2015).

Other important outcome is the adaptive behavior. We found similar profiles of gain compare to the outcomes of two previous studies except in fine motricity (Dawson et al. 2010, Vivanti et al. 2014). Like them, we had a slight non-significant improvement in communication and a slight decrease in daily living skills and socialization as measured by the T-score at the VABS. We gained 5 points in communication similar to the 20 hours per week ESDM intervention group of Dawson and his colleagues after 1 year (Dawson et al. 2010). Vivanti and his colleagues had a gain of 7. 38 points in communication which was significantly higher compared to their control group (Vivanti et al. 2014). We had a similar decrease in social and daily living skills compared to Dawson and his colleagues (Dawson et al. 2010). What is important in this study is that after 2 years, communication scores showed significantly better outcomes compared to their control group (13 points more) (Dawson et al. 2010). Moreover, social skills in the ESDM group of Dawson and his colleagues (2010), after 2 years, showed also a decrease but lesser than in their control group (-4.6 points in ESDM group versus -8.9 points in control group). There were similar results for daily skills. Importantly, in the follow-up study, gains in their ESDM group compared to their control group were maintained (Estes et al. 2015). Thus, we can also expect significant improvements with a longer duration of the ESDM therapy.

Our results also highlighted that it was not easy to maintain a rate of 12 hours of intervention per week because of vacation and absences of professionals and children. We didn't monitor the other therapies received by the children neither the number of schooling or nursery hours, which could have been interesting.

No correlation between age at baseline and DQ outcomes was found in our sample. Vivanty and his colleagues showed better results with children beginning the intervention up to 4 years old (Vivanti et al. 2016). In the current study, most of the children began intervention up to 3 years old. Moreover, the few children over 3 years old were coming for their second year of intervention in the center. Interestingly, these children improved as much as the children who were in their first year of intervention.

We observed few differences between our outcomes and others studies with different settings and intensity (Eapen et al. 2013, Vivanti et al. 2014). It would be interesting to develop studies which compare settings and discussed which setting may be more efficient, less costly and give more free time to the families (Hoefman et al. 2014).

The needs of children with ASD are complex. A diversity of outcome measurement tools is often used to collect evidence about the child's progresses (McConachie et al. 2015). The use of MSEL DQ, as primary outcome, could be criticized because it does not measure the core autism symptoms. However, we knew that ADOS could not measure a change after 10 months and no other direct-observation published tools were available at that time. Follow-up study of the randomized controlled trial of Dawson and his colleagues found about 1 point in reduction of the autism severity score (scale from 1 to 10) between interventional and control group 5 years after the inclusion (Estes et al. 2015). Moreover, the cognitive skills play a central role in the expression of core and associated symptoms in ASD (Bishop et al., 2011). Finally, MSEL DQ has also been used in previous studies and allows comparisons (Bishop et al. 2011, Pickles et al. 2014, Rogers et al. 2012).

Pickles and his colleagues examined the development of language in ASD children and showed that variation in trajectory of language development was evident up to 6 years old (Pickles et al. 2014). This diversity of development patterns up to 6 years old is also reflected in increases of SDs in our current study. This could be due to differences in biological and genetic characteristics and also to a greater sensitivity to environment that supports more or less cognitive and language skills development, highlighting the importance of early intervention and the choice of intervention and techniques.

## CONCLUSIONS

To the best of our knowledge, this is the first study to have evaluated an ESDM intervention with an intensity of 12 hours per week, over a 10 months period. It showed improvement in verbal and nonverbal cognitive skills of young children in this setting.

In addition, this paper highlights that ESDM can also improve cognitive skills even for low IQ, nonverbal children. However, stronger evidence of efficacy of such setting are still required to justify costs, opening of more centers and to promote reorganization of current centers available for families in the French public health system. Thus, a multicenter randomized control trial is been run to evaluate further these results (Touzet et al. 2017).

***Acknowledgements:***

Paul Belhouchat of CRA Lyon for bibliography ressources; Jeanne Fettet, Audrey Richier, Coline Dambrin, Vanessa Magne, Caroline Giulianotti, Gaelle Borron, Patricia Ricq, Lorene Hamon, Noémie Fanget, Geraldine Malpesa, Marie-Dominique Verpoix, Sonia Kouyate, Claire Gerin Denis, Juliette Cosnier, Ariane Toselli, Audrey Renaudineau, Eleonore Simon, Eva Laccarière,Séverine Lachèvre for their implication in the implementation of this model and work with children and families. Emilie Boyer and Saadia Soualah for administration helps. Marc and Joseph Chevalier for English review.

**Funding:**
This study was supported by a grant from hospital and promotor from 2012: Le Vinatier, Bron, France.

**Ethics approvals:**
The study protocol was approved by the French Ethics Committee Sud-Est 6 (reference AU 1047) and the French National Data Protection Agency (ANSM) (reference B130758-31)

**Avaibility of data:**
The datasets used in the current study are available from the corresponding author on reasonable request.

***Conflict of interest:*** None to declare.

***Contribution of individual authors:***

Marie-Maude Geoffray, Sabine Magnificat & Sandrine Touzet conceived and designed the project.

Marie-Maude Geoffray & Sandrine Touzet drafted the protocol and procured the project funding.

Marie-Maude Geoffray was responsible for study implementation, staff training and supervision.

Angélique Denis was responsible for statistical analysis.

Chloé Peter, Natacha Gallifet, Valentin Beaujeard, Céline Jacob Grosmaitre, Valéry Malo & Nicolas Georgieff worked on implementing and maintaining the model.

Flavia Mengarelli & Stephane Grisi were responsible for recruitment and evaluation of children.

All authors critically reviewed and approved the final version of the manuscript.

## References

1. *American Psychiatric Association AP: Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub, 2013*
2. *Anderson DK, Liang JW, Lord C: Predicting young adult outcome among more and less cognitively able individuals with autism spectrum disorders. Journal of Child Psychology and Psychiatry 2014; 55:485-494*
3. *Bishop SL, Guthrie W, Coffing M, Lord C: Convergent validity of the Mullen Scales of Early Learning and the differential ability scales in children with autism spectrum disorders. American journal on intellectual and developmental disabilities 2011; 116:331-343*
4. *Dawson G, Rogers S, Munson J, Smith M, Winter J, Greenson J, Donaldson A, Varley J: Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. Pediatrics 2010; 125:e17*
5. *Devescovi R, Monasta L, Mancini A, Bin M, Vellante V, Carrozzi M, Colombi C: Early diagnosis and Early Start Denver Model intervention in autism spectrum disorders delivered in an Italian Public Health System service. Neuropsychiatr Dis Treat 2016; 12:1379-84*
6. *Dunn G, Emsley R, Liu H, Landau S, Green J, White L, Pickles A: Evaluation and validation of social and psychological markers in randomised trials of complex interventions in mental health: a methodological research programme. Health Technology Assessment 2015; 19*
7. *Eapen V, Črnčec R, Walter A: Clinical outcomes of an early intervention program for preschool children with autism spectrum disorder in a community group setting. BMC pediatrics 2013; 13:3*
8. *Estes A, Munson J, Rogers SJ, Greenson J, Winter J, Dawson G: Long-Term Outcomes of Early Intervention in 6-Year-Old Children With Autism Spectrum Disorder. J Am Acad Child Adolesc Psychiatry 2015; 54:580–7*
9. *Estes A, Vismara L, Mercado C, Fitzpatrick A, Elder L, Greenson J et al.: The impact of parent-delivered intervention on parents of very young children with autism. J Autism Dev Disord 2014; 44:353–65*
10. *Evans B: How autism became autism: The radical transformation of a central concept of child development in Britain. History of the Human Sciences 2013; 26:3–31*
11. *Ganz ML: The lifetime distribution of the incremental societal costs of autism. Archives of pediatrics & adolescent medicine 2007; 161:343–349*
12. *Gotham K, Pickles A, Lord C: Standardizing ADOS scores for a measure of severity in autism spectrum disorders. Journal of autism and developmental disorders 2009; 39:693–705*
13. *Green J, Charman T, McConachie H, Aldred C, Slonims V, Howlin P, Le Couteur A, Leadbitter K, Hudry K, Byford S: Parent-mediated communication-focused treatment in children with autism (PACT): a randomised controlled trial. The Lancet 2010; 375:2152–2160*
14. *Green J, Garg S: Annual Research Review: The state of autism intervention science: progress, target psychological and biological mechanisms and future prospects. Journal of Child Psychology and Psychiatry 2018; 424–43*
15. *Hayes SA, Watson SL: The impact of parenting stress: A meta-analysis of studies comparing the experience of parenting stress in parents of children with and without autism spectrum disorder. Journal of autism and developmental disorders 2013; 43:629–642*
16. *Hellendoorn A, Wijnroks L, van Daalen E, Dietz C, Buitelaar JK, Leseman P: Motor functioning, exploration, visuospatial cognition and language development in preschool children with autism. Research in Developmental Disabilities 2015; 39:32–42*
17. *Hoefman R, Payakachat N, van Exel J, Kuhlthau K, Kovacs E, Pyne J, Tilford JM: Caring for a Child with Autism Spectrum Disorder and Parents' Quality of Life: Application of the CarerQol. J Autism Dev Disord 2014; 44:1933–45*
18. *Howlin P: Living with impairment: The effects on children of having an autistic sibling. Child: care, health and development 1988; 14:395–408*
19. *Lord C, Petkova E, Hus V, Gan W, Lu F, Martin DM et al.: A multisite study of the clinical diagnosis of different autism spectrum disorders. Arch Gen Psychiatry 2012; 69:306–13*
20. *Lord C, Risi S, Lambrecht L, Cook EH, Leventhal BL, DiLavore PC et al.: The Autism Diagnostic Observation Schedule - Generic: A Standard Measure of Social and Communication Deficits Associated with the Spectrum of Autism. J Autism Dev Disord 2000; 30:205–23*
21. *Maglione MA, Gans D, Das L, Timbie J, Kasari C: Technical Expert Panel, HRSA Autism Intervention Research – Behavioral (AIR-B) Network. Nonmedical interventions for children with ASD: recommended guidelines and further research needs. Pediatrics 2012; 130(Suppl 2):S169-178*

22. McConachie H, Parr JR, Glod M, Hanratty J, Livingstone N, Oono IP et al.: Systematic review of tools to measure outcomes for young children with autism spectrum disorder. NIHR Journals Library, 2015
23. Mullen EM: Mullen scales of early learning. AGS Circle Pines, MN, 1995
24. Oono IP, Honey EJ, McConachie H: Parent-mediated early intervention for young children with autism spectrum disorders (ASD). Evidence-Based Child Health: A Cochrane Review Journal 2013; 8:2380–2479
25. Pickles A, Anderson DK, Lord C: Heterogeneity and plasticity in the development of language: a 17-year follow-up of children referred early for possible autism. J Child Psychol Psychiatr 2014; 55:1354–62
26. Rogers S, Dawson G: Early start Denver Model for Young children with Autism. promoting Language, learning, and Engagement. Guilford, 2012
27. Rogers SJ, Dawson G, Vismara LA: An Early Start for Your Child with Autism: Using Everyday Activities to Help Kids Connect, Communicate, and Learn. Guilford Press, 2012
28. Rogers SJ, Estes A, Lord C, Vismara L, Winter J, Fitzpatrick A et al.: Effects of a brief Early Start Denver model (ESDM)-based parent intervention on toddlers at risk for autism spectrum disorders: a randomized controlled trial. J Am Acad Child Adolesc Psychiatry 2012; 51:1052-65
29. Salomone E, Beranová Š, Bonnet-Brilhault F, Briciet Lauritsen M, Budisteanu M, Buitelaar J et al.: Use of early intervention for young children with autism spectrum disorder across Europe. Autism 2016; 20:233–249
30. Sparrow SS, Cicchetti DV, Balla DA: Vineland Adaptive Behavior Scales:(VABS). NCS Pearson, 2005
31. Swineford LB, Guthrie W, Thurm A: Convergent and divergent validity of the Mullen Scales of Early Learning in young children with and without autism spectrum disorder. Psychol Assess 2015; 27:1364–78
32. Thomas MSC, Davis R, Karmiloff-Smith A, Knowland VCP, Charman T: The over-pruning hypothesis of autism. Dev Sci 2016; 19:284–305
33. Touzet S, Occelli P, Schröder C, Manificat S, Gicquel L, Stanciu R et al.: Impact of the Early Start Denver Model on the cognitive level of children with autism spectrum disorder: study protocol for a randomised controlled trial using a two-stage Zelen design. BMJ open 2017; 7:e014730
34. Vivanti G, Dissanayake C, Team VA: Outcome for children receiving the Early Start Denver Model before and after 48 months. Journal of autism and developmental disorders 2016; 46:2441–2449
35. Vivanti G, Paynter J, Duncan E, Fothergill H, Dissanayake C, Rogers SJ, Team VA: Effectiveness and feasibility of the Early Start Denver Model implemented in a group-based community childcare setting. Journal of autism and developmental disorders 2014; 44:3140–3153
36. Warren Z, McPheeters ML, Sathe N, Foss-Feig JH, Glasser A, Veenstra-VanderWeele J: A systematic review of early intensive intervention for autism spectrum disorders. Pediatrics-English Edition 2011; 127:e1303
37. Wetherby AM, Guthrie W, Woods J, Schatschneider C, Holland RD, Morgan L, Lord C: Parent-implemented social intervention for toddlers with autism: an RCT. Pediatrics 2014; 134:1084

*Correspondence:*

*Marie-Maude Geoffray, MD*
*Department of Child and Adolescent Psychiatry*
*CH le Vinatier, 95 Boulevard Pinel, 69 Bron, France*
*E-mail: marie-maude.geoffray@ch-le-vinatier.fr*