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Detection of autism in childhood

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Chapter 1
General introduction

As a child psychologist working at an expert center for autism I have had the opportunity to meet many children with Autism Spectrum Disorder (ASD) and their parents. Numerous parents have struggled for years in their search for the right help before ending up at the center. The confirmation of an ASD diagnosis is, for many parents, the end of a long quest and they are hugely relieved that they are finally going to receive the best possible help for their child. Simultaneously, I have met young children who have wondered for years why they are different to other children and at the center they finally find acknowledgement and recognition for their struggle. It is fantastic that we can help these children and their parents and siblings. However, the long and difficult quest could often have been shorter if the children's ASD signs had been detected earlier and they had been referred to the appropriate healthcare professional.

In this thesis I aim to explore the detection of Autism Spectrum Disorder in childhood, with emphasis on the current global age at diagnosis, early detection by preventive care physicians, and the possible role of eating behavior in the early detection of ASD.

AUTISM SPECTRUM DISORDER

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that is characterized by persistent impairments in social communication and social interaction, as well as by restricted, repetitive patterns of behavior, interests, or activities (see DSM-5¹). ASD has three severity levels based on the amount of support required (mild, moderate or severe, see Table 1.1).¹ See Box 1.1 for the full set of DSM-5 criteria. ASD is a multifunctional disorder with a genetic inheritance that can be explained up to 83%.² Although the exact numbers vary in different studies, there is a general consensus that ASD affects 1 in 68 children³, with boys overrepresented by a ratio of 4:1.⁴ ASD is a lifelong condition with different external signs at different life stages. It causes many challenges in a child's life, but these also affect the rest of the family. The mean age at diagnosis is believed to be 38–120 months, based on studies published between 1990 and 2012.⁵ However, the current age at ASD diagnosis is not known (chapter 2).

When evaluating the early detection of ASD it is important to keep the full spectrum of ASD in mind, with its wide variety of symptoms and range of severity, each presenting unique challenges and difficulties. This full ASD spectrum, with all its variation, is perfectly expressed by a widely known statement, *“When you have met one person with autism, you have met ONE person with autism”*.

Box 1.1 Full DSM-5 criteria for Autism Spectrum Disorders 299.00 (F84.0)¹

- A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive; see text):
1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
 2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
 3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.
- B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):
1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypes, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
 2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
 3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
 4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

Specify current severity: Severity is based on social communication impairments and restricted, repetitive patterns of behavior (see Appendix 1.1).

- C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).
- D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
- E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

Box 1.2 Case examples of problems at home and at school

Bram is a 6-year-old boy who loves being outdoors. Bram runs into multiple problems both at home and at school. The busy morning ritual in his home creates a lot of friction and Bram often gets angry, sometimes to the extent that he is so overwhelmed he refuses to go to school. Bram is easily distracted at school, finds it difficult to become involved in group activities, and has regularly issues with other children during play time.

Mara is a four-year-old girl and has a younger brother. She is cheerful but a little shy when with others. She loves watching cartoons and is doing well in her first few months in nursery school. Mara finds it difficult to try new types of vegetables – she only likes broccoli, which causes problems during family mealtimes.

EARLY DETECTION OF ASD

Early detection can prevent or restrict the full development of ASD and its related disabilities by offering early referral to effective treatment,⁶ which improves functioning in the long term.⁷

Although structured, long-term, early interventions are currently seen as the most beneficial ones to improve the level of functioning in children with ASD,⁶ it is also often possible to use small, non-intrusive, child or parent interventions at this early stage. Research shows that ASD often manifests before two years of age and that abnormalities can often be observed in the child as early as age 12–24 months.^{8,9}

Early signs of ASD that can be observed during (the start) of the second year are¹⁰:

- No babbling by 12 months
- No interest in other people by 12 months
- No smiling at others by 12 months
- No gesturing by 12 months (pointing, waving bye-bye)
- No functional use of single words by 18 months
- No 2-word spontaneous phrases (not echoic) by 24 months
- Any loss of any language or social skills at any age

From 4 years of age, ASD early detection focuses on deficiencies in social interaction, communication, stereotypical behavior, and sensory processing.¹¹ Although early signs of ASD can often be observed before 24 months of age, the global average age at diagnosis ranges from 38–120 months.⁵ In addition, delays of up to 4.5 years were found in the process from first parental concern to first contact with a healthcare professional to receiving an ASD diagnosis.¹²

The early detection of ASD is a collaboration between many people and professionals looking at multiple levels and moments in a child's life. ASD can be detected by preventive care (e.g. well-baby clinics), primary care (e.g. general practitioners), and/or secondary care (e.g. psychologists, psychiatrists, physiotherapist and pediatricians). However, non-healthcare professionals like nursery/pre-school staff and school teachers can also play a significant role in the early detection of ASD. And last but not least, parents and the social environment (e.g. family, neighbors) have a crucial role in early detection. Although it is not discussed further in this dissertation, the field of clinical genetics of neurology is also contributing to ASD detection by identifying genes and biomarkers that may be associated with the development of ASD.¹³

Box 1.3 Case examples of well-child visits to Youth and Family Centers (YFC)

Bram: The well-child screening indicates no physical deficiencies, but the YFC physician notices limited social interaction and abnormal motor skills. Results from a questionnaire indicate multiple problems at home and school. The mother explains that she has higher levels of stress due to Bram's problems and wonders how long they can keep this up.

Mara: The screening indicates no physical deficiencies, but the YFC physician notices that Mara has a slight delay in vocal skills for her age. The mother mentions Mara's eating problems. As there are no other abnormalities (at home nor at the nursery), the physician asks the mother to return in 6 months.

This thesis aims to improve the detection of ASD by increasing knowledge about its early detection, expanding skills in preventive care physicians (chapters 3 and 4), and by introducing problems in early eating behavior as a possible early sign of ASD (chapters 5 and 6).

PREVENTIVE CARE PHYSICIANS

Preventive care physicians in well-baby and primary well-child and youth care clinics play a vital role in the Dutch national screening program for developmental delays and mental health issues.¹⁴ In the Dutch healthcare system, the Youth and Family Centers (YFC) provide free prenatal and preventive child healthcare for all parents and their children. All children are invited for 13 individual, 6 collective, and 3 optional individual consultations during their first 18 years. In the Rotterdam area, these centers reach 98.9% of the 0-4 year-olds and 97.9% of the 4-19 year-olds.¹⁵ The 13 individual consultations focus on the medical and developmental screening of the child, while the collective program conducts vaccinations and offers information.¹⁶ This large outreach into the general population of children means that YFC nurses and physicians are the primary healthcare

professionals conducting screening for developmental delays and mental health issues in the Netherlands. YFC staff screen almost all Dutch children preventively and are thus particularly well-placed to detect subtler developmental changes in development and/or to help hesitant or anxious parents. It was, however, essential to gain more insight into the YFC physicians' level of ASD knowledge and beliefs about mental illness (chapter 3). We also wanted to assess the effect of an ASD detection educational program provided to promote physicians' ASD knowledge, beliefs towards mental illness, self-confidence, and potential ASD referrals (chapter 4).

Box 1.4 Case examples: school observation/follow-up and referral

Bram: School observation reveals that Bram is easily distracted by noises from children walking past him. He also has difficulties with the unclear school schedule and does not like to play with other children. The YFC physician finds enough indication from the well-child visit, school observation, and screening questionnaires to refer Bram to an ASD expertise center. Extensive diagnostic research reveals that Bram has ASD.

Mara: A 6-month follow-up visit indicates no improvement in Mara's eating behavior. Staff at the nursery indicate no significant abnormalities, but do notice that Mara loves to play alone, especially liking 'butterfly' in the school yard (running from one side of the yard to another), during play breaks. In recent weeks, however, the mother has become more worried as Mara sometimes gets so upset when she tries to introduce a new vegetable that Mara does not eat at all. The YFC physician refers Mara to a child dietician to help with her eating problems.

EATING BEHAVIOR AND ASD

Eating problems, like emotional undereating, satiety responsiveness, picky eating, and related under- or overweight are very common in pre-school children (4 years); 13% are underweight, 8% are overweight, and 2% are obese.¹⁷ Children undergo an extraordinary transition in digestive behavior during the early years of life; this becomes more stable by the end of the pre-school period.¹⁸ Although almost half (46%) of children are picky eaters at some point during early childhood, remittance is very high, which suggests that picky eating is usually a transient behavior and part of normal development in pre-school children.¹⁹

Eating problems like severe or prolonged picky eating and neophobia (fear of anything new) are seen in 46-89% of children with ASD²⁰ compared to 6-50% of children in the general population.²¹

Research findings indicate that the probability of eating problems is five times higher in children with ASD than for their more normally developing peers.²² Food neophobia is two to three times more common in children with ASD than in non-ASD children.²³ Common problems among children with autism are aversive eating behaviors, such as food refusal, choking, gagging, and expulsion with no

medical basis. They may also have sensory-based feeding problems, include aversion to specific kinds of food textures.²⁴ These eating problems are most likely due to their restricted interests combined with the sensory over-sensitivity to texture, taste and smell associated with ASD.^{25–27} Eating difficulties in ASD may lead to various health consequences, including a 40% higher chance of being obese than developing peers.²⁸

Eating behavior is currently not included in popular ASD screenings instruments like The Modified Checklist for Autism in Toddlers (M-CHAT)(R/F),^{29,30} Social Communication Questionnaire (SCQ)³¹ or the Early Screening of Autistic Traits Questionnaire (ESAT).³² However, a study in the Dutch general population provided the first indication that picky eating is a possible early sign of ASD.³³ And, due to the overrepresentation of boys in the ASD population (at a 4:1 ratio),³⁴ most of what we know about the relationship between autism and eating behaviors is based on male study samples.

There is now a growing debate regarding sex differences in the prevalence of ASD symptomology, with recent literature suggesting a possible girl-specific phenotype,³⁵ complicating the detection of ASD in girls.^{35,36} Multiple studies found higher levels of autistic traits among girls with anorexia nervosa,^{37,38} suggesting that dietary restraint and other food control behaviors may co-occur with ASD symptomatology. However, anorexia nervosa is seen almost solely in girls, making it difficult to study sex-specific associations between anorexia nervosa and autism. General population studies evaluating clinical and subclinical traits may help elucidate sex differences in the association between the full spectrum of ASD and eating behaviors as these studies include both boys and girls.

We need further studies and more information on the association between infant eating behavior and later autistic traits (chapter 5) and on the sex-specific association between autistic traits and eating behavior in middle childhood (chapter 6).

Box 1.5 Case examples: 1 year after referral

Bram and his family received treatment at an ASD expert center and they have adjusted some of their daily routines. The morning ritual now follows a strict schedule using pictograms for visual support. To reduce distractions in the classroom Bram now has a quiet place at the back of the room and can use a headphone when needed. The teacher now also provides an overview of upcoming class activities each week. These first adjustments have had a positive effect on Bram and his family. He is still receiving mental healthcare.

Mara was treated by a dietician but showed little progress. After three years and several referrals to different healthcare professionals, she was diagnosed with ASD.

The case examples (described in the boxes) provide a glimpse into the wide range of symptoms and challenges that children with ASD and their families encounter. Although in Bram’s case the signs of ASD were noticed and he was referred to the proper healthcare professional, it is possible that the diagnosis could have been made earlier, which would have spared Bram and his family a difficult period with many concerns. In Mara’s case the more general signs of ASD—like limited social interaction—were more subtle and were therefore not noticed in this young girl. As eating problems are often seen in young children, they are not generally associated with ASD and, in this case, possibly affected the choice for referral, thereby delaying the age at ASD diagnosis. The objective of this thesis is to identify factors to enhance the detection of ASD in childhood. Three aspects of the detection of ASD are addressed:

- Age at ASD diagnosis; *what is the current global age at ASD diagnosis?*
- Early detection of ASD by preventive care physicians; *can we improve early detection by healthcare professionals?*
- Eating problems and ASD; *can the assessment of eating behavior potentially be useful in the (early) detection of ASD?*

OUTLINE AND SCOPE OF THIS THESIS

Because the current global age at diagnosis was not known when I started this project, I first performed a comprehensive, systematic review and meta-analysis on the age at ASD diagnosis. The review was based on literature published between 2012–2019 and is reproduced here in chapter 2. Chapters 3 and 4 examine the early detection of ASD among of 93 Dutch Youth and Family Center (YFC) physicians, using data from a Live Online intervention developed for this study. The development of this intervention was part of Project 4: Transitions in education, part of the Reach-Aut Academic Centre for Autism. Chapter 3 reports an evaluation of the level of autism knowledge and stigmatizing attitudes toward mental illness in Youth and Family Center physicians before the start of our intervention. Chapter 4 reports an evaluation of the effect of the intervention on their level of ASD knowledge, psychiatric stigma, self-confidence, and potential ASD referrals. Chapters 5 and 6 examine the association between autism and eating problems in childhood using data from the Generation R cohort study.³⁹ Chapter 5 evaluates whether early life eating habits can predict later autistic traits in 3,546 mother-child dyads. Chapter 6 reports on an evaluation of the sex-specific association between autistic traits and eating behavior in childhood using 3,559 mother-child dyads. Chapter 7 offers a general discussion on the main findings of this thesis.

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)*. Arlington, VA: American Psychiatric Association; 2013. doi:10.1176/appi.books.9780890425596
2. Sandin S, Lichtenstein P, Kuja-Halkola R, Hultman C, Larsson H, Reichenberg A. The heritability of autism spectrum disorder. *JAMA*. 2017;318(12):1182-1184. doi:10.1001/jama.2017.12141
3. Christensen DL, Baio J, Braun KVN, et al. Prevalence and characteristics of autism spectrum disorder among children aged 8 years - Autism and developmental disabilities monitoring network, 11 sites, United States, 2012. *MMWR Surveill Summ*. 2016;65(3):1-23. doi:10.15585/mmwr.ss6503a1
4. Fombonne E. Epidemiological surveys of autism and other pervasive developmental disorders: An update. *J Autism Dev Disord*. 2003;33(4):365-382. doi:10.1023/a:1025054610557
5. Daniels AM, Mandell DS. Explaining differences in age at autism spectrum disorder diagnosis: A critical review. *Autism*. 2014;18(5):583-597. doi:10.1177/1362361313480277
6. Rogers SJ, Vismara L, Wagner AL, McCormick C, Young G, Ozonoff S. Autism treatment in the first year of life: A pilot study of infant start, a parent-implemented intervention for symptomatic infants. *J Autism Dev Disord*. 2014;44(12):2981-2995. doi:10.1007/s10803-014-2202-y
7. Dawson G, Burner K. Behavioral interventions in children and adolescents with autism spectrum disorder. *Curr Opin Pediatr*. 2011;23(6):616-620. doi:10.1097/MOP.0b013e32834cf082
8. Johnson CP, Myers SM, Lipkin PH, et al. Identification and evaluation of children with autism spectrum disorders. *Pediatrics*. 2007;120(5):1183-1215. doi:10.1542/peds.2007-2361
9. Filipek PA, Accardo PJ, Baranek GT, et al. The screening and diagnosis of autistic spectrum disorders. *J Autism Dev Disord*. 1999;29(6):439-484. doi:10.1023/A:1021943802493
10. Dietz C. *The Early Screening of Autistic Spectrum Disorders [Dissertation]*. Enschede: Gildeprint; 2007.
11. Van Berckelaer-Onnes IA, van de Glind G, Anzion P, Werkgroep Richtlijnen ASS-JGZ. *JGZ-Richtlijn Autismespectrumstoornissen: Signalering, begeleiding en toeleiding naar diagnostiek*. Utrecht: Nederlands Centrum Jeugdgezondheid; 2015. <https://assets.ncj.nl/docs/bc756f24-ff04-45f3-b0fd-3756dec2cabb.pdf>
12. Crane L, Chester JW, Goddard L, Henry LA, Hill E. Experiences of autism diagnosis: A survey of over 1000 parents in the United Kingdom. *Autism*. 2016;20(2):153-162. doi:10.1177/1362361315573636
13. Frye RE, Vassall S, Kaur G, Lewis C, Karim M, Rossignol D. Emerging biomarkers in autism spectrum disorder: A systematic review. *Ann Transl Med*. 2019;7(23):792-792. doi:10.21037/atm.2019.11.53
14. Pijl MKJ, Buitelaar JK, Korte MWP de, Rommelse NNJ, Oosterling IJ. Sustainability of an early detection program for autism spectrum disorder over the course of 8 years. *Autism*. 2017;22(8):1018-1024. doi:10.1177/1362361317717977
15. Centrum voor Jeugd en Gezin Rijnmond. *Financieel Jaarverslag 2016*. Rotterdam; 2016. <https://cjgrijnmond.nl/online-jaarverslag-2016/>
16. Centrum voor Jeugd en Gezin Rijnmond. *Alles voor een gezonde jeugd: Productenboek*. Rotterdam; 2016. <https://cjgrijnmond.nl/wp-content/uploads/Productenboek-CJGRijnmond-2016.pdf>
17. Jansen PW, Roza SJ, Jaddoe VW, et al. Children's eating behavior, feeding practices of parents and weight problems in early childhood: Results from the population-based Generation R Study. *Int J Behav Nutr Phys Act*. 2012;9(1):130. doi:10.1186/1479-5868-9-130
18. Ashcroft J, Semmler C, Carnell S, van Jaarsveld CHM, Wardle J. Continuity and stability of eating behaviour traits in children. *Eur J Clin Nutr*. 2008;62(8):985-990.

- doi:10.1038/sj.ejcn.1602855
19. Cardona Cano S, Tiemeier H, Van Hoeken D, et al. Trajectories of picky eating during childhood: A general population study. *Int J Eat Disord*. 2015;48(6):570-579. doi:10.1002/eat.22384
 20. Ledford JR, Gast DL. Feeding problems in children with autism spectrum disorders : A review. *Focus Autism Other Dev Disabl*. 2006;21(3):153-166. doi:10.1177/10883576060210030401
 21. Taylor CM, Wernimont SM, Northstone K, Emmett PM. Picky / fussy eating in children : Review of de fi nitions, assessment, prevalence and dietary intakes. *Appetite*. 2015;95:349-359. doi:10.1016/j.appet.2015.07.026
 22. Sharp WG, Berry RC, McCracken C, et al. Feeding problems and nutrient intake in children with autism spectrum disorders: A meta-analysis and comprehensive review of the literature. *J Autism Dev Disord*. 2013;43(9):2159-2173. doi:10.1007/s10803-013-1771-5
 23. Wallace GL, Llewellyn C, Fildes A, Ronald A. Autism spectrum disorder and food neophobia: Clinical and subclinical links. *Am J Clin Nutr*. 2018;108(4):701-707. doi:10.1093/ajcn/nqy163
 24. Schwarz SM. Feeding disorders in children with developmental disabilities. *Infants Young Child*. 2003;16(4):317-330. doi:10.1097/00001163-200310000-00005
 25. Ahearn WH, Castine T, Nault K, Green G. An assessment of food acceptance in children with autism or pervasive developmental disorder not otherwise specified. *J Autism Dev Disord*. 2001;31(5):505-511. doi:10.1023/a:1012221026124
 26. Cermak S, Curtin C, Bandini L. Food selectivity and oral sensitivity in children with autism spectrum disorders. *J Am Diet Assoc*. 2010;110(2):238-246. doi:10.1016/j.jada.2009.10.032
 27. Chistol LT, Bandini LG, Must A, Phillips S, Cermak SA, Curtin C. Sensory sensitivity and food selectivity in children with autism spectrum disorder. *J Autism Dev Disord*. 2018;48(2):583-591. doi:10.1007/s10803-017-3340-9
 28. Curtin C, Anderson SE, Must A, Bandini LG. The prevalence of obesity in children with autism: A secondary data analysis using nationally representative data from the National Survey of Children's Health. *BMC Pediatr*. 2010;10:11. doi:10.1186/1471-2431-10-11
 29. Robins DL, Casagrande K, Barton M, Chen C-MA, Dumont-Mathieu T, Fein D. Validation of the modified checklist for autism in toddlers, revised with follow-up (M-CHAT-R/F). *Pediatrics*. 2014;133(1):37-45. doi:10.1542/peds.2013-1813
 30. Robins DL, Fein D, Barton ML, Green JA. The modified checklist for autism in toddlers: An initial study investigating the early detection of autism and pervasive developmental disorders. *J Autism Dev Disord*. 2001;31(2):131-144. doi:10.1023/A:1010738829569
 31. Rutter M, Bailey A, Lord C. *The Social Communication Questionnaire*. Torrance, CA: Western Psychological Services; 2003.
 32. Swinkels SHN, Dietz C, Daalen E Van, Kerkhof IHGM, Engeland H Van, Buitelaar JK. Screening for autistic spectrum in children aged 14 to 15 months. I : The development of the early screening of autistic traits questionnaire (ESAT). *J Autism Dev Disord*. 2006;36:723-732. doi:10.1007/s10803-006-0115-0
 33. Cardona Cano S, Hoek HW, van Hoeken D, et al. Behavioral outcomes of picky eating in childhood: A prospective study in the general population. *J Child Psychol Psychiatry*. 2016;57(11):1239-1246. doi:10.1111/jcpp.12530
 34. Baio J, Wiggins L, Christensen DL, et al. Prevalence of autism spectrum disorder among children aged 8 years - Autism and developmental disabilities monitoring network, 11 sites, United States, 2014. *MMWR Surveill Summ*. 2018;67(6):1-23. doi:10.15585/mmwr.ss6706a1
 35. Van Wijngaarden-Cremers PJM, Van Eeten E, Groen WB, Van Deurzen PA, Oosterling IJ, Van Der Gaag RJ. Gender and age differences in the core triad of impairments in autism spectrum disorders: A systematic review and meta-analysis. *J Autism Dev Disord*. 2014;44(3):627-635. doi:10.1007/s10803-013-1913-9
 36. Ratto AB, Kenworthy L, Yerys BE, et al. What about the girls? Sex-based differences in autistic traits and adaptive skills. *J Autism Dev Disord*. 2018;48(5):1698-1711. doi:10.1007/s10803-017-3413-9

37. Wentz E, Lacey JH, Waller G, Rastam M, Turk J, Gillberg C. Childhood onset neuropsychiatric disorders in adult eating disorder patients: A pilot study. *Eur Child Adolescent Psychiatry*. 2005;14(8):431-437. doi:10.1007/s00787-005-0494-3
38. Westwood H, Eisler I, Mandy W, Leppanen J, Treasure J, Tchanturia K. Using the autism-spectrum quotient to measure autistic traits in anorexia nervosa: A systematic review and meta-analysis. *J Autism Dev Disord*. 2016;46(3):964-977. doi:10.1007/s10803-015-2641-0
39. Erasmus Medical Center. Generation R. <https://generationr.nl/>. Accessed April 18, 2020.

Appendix 1.1

Table 1.1 Severity levels for autism spectrum disorder, from DSM-5¹

Severity level	Social communication	Restricted, repetitive behaviors
<p>Level 3 “Requiring very substantial support”</p>	<p>Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. For example, a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and responds to only very direct social approaches.</p>	<p>Inflexibility of behavior, extreme difficulty coping with change, or other restricted/repetitive behaviors markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action.</p>
<p>Level 2 “Requiring substantial support”</p>	<p>Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal responses to social overtures from others. For example, a person who speaks simple sentences, whose interaction is limited to narrow special interests, and who has markedly odd nonverbal communication.</p>	<p>Inflexibility of behavior, difficulty coping with change, or other restricted/repetitive behaviors appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action.</p>
<p>Level 1 “Requiring support”</p>	<p>Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful responses to social overtures of others. May appear to have decreased interest in social interactions. For example, a person who is able to speak in full sentences and engages in communication but whose to-and-fro conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful.</p>	<p>Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence.</p>

