Genes or environment? Assessing and lessening the impact of the main drivers of ASD.

The Lauriston Centre

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Smart Kids Conference 24th April 2025

FOOD FOR THE BRAIN FOUNDATION

The Lauriston Centre

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AGENDA

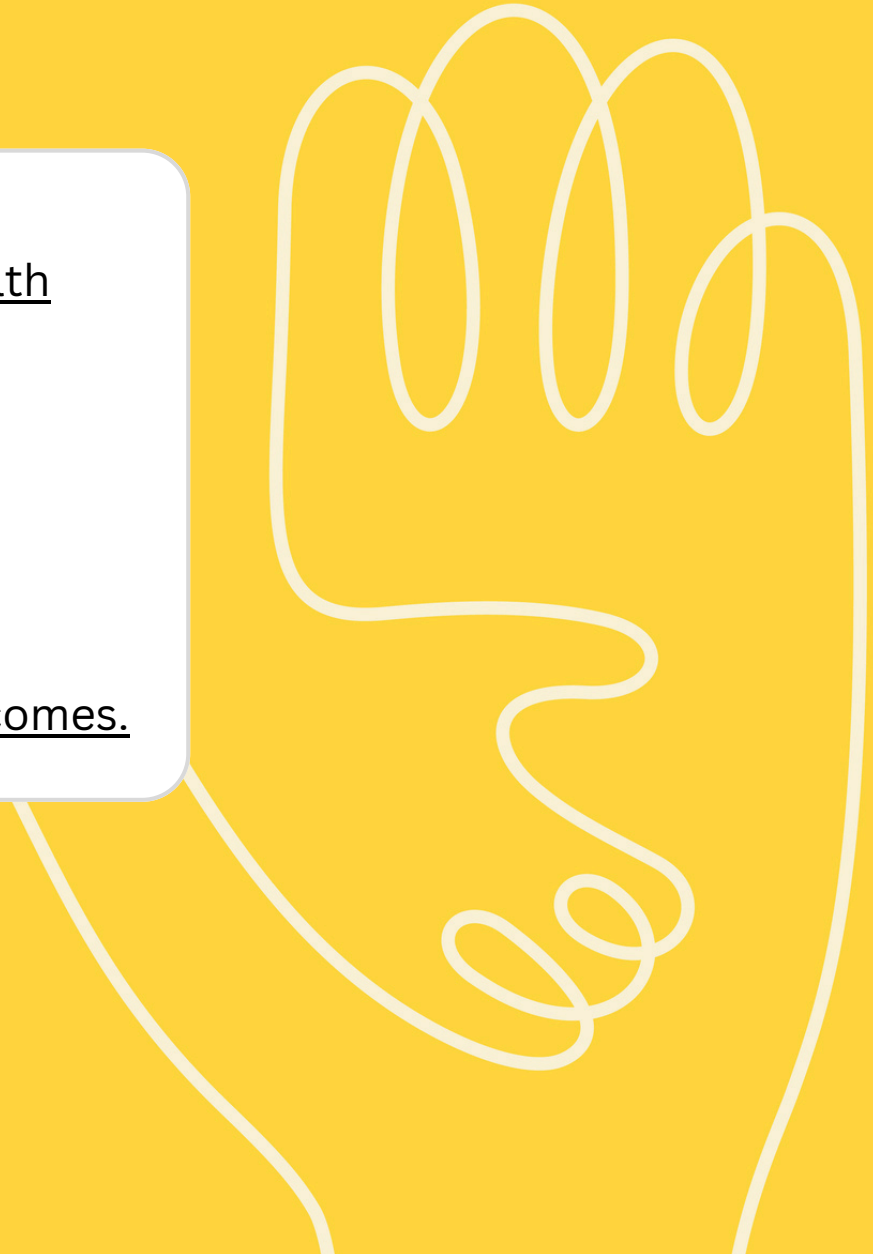
ASD Challenges and Considerations

- Increasing rates of ASD and related health comorbidities are a concern.

- Genes and environmental factors both influence ASD.

Approaches and Solutions

- Personalised assessments to guide outcomes.



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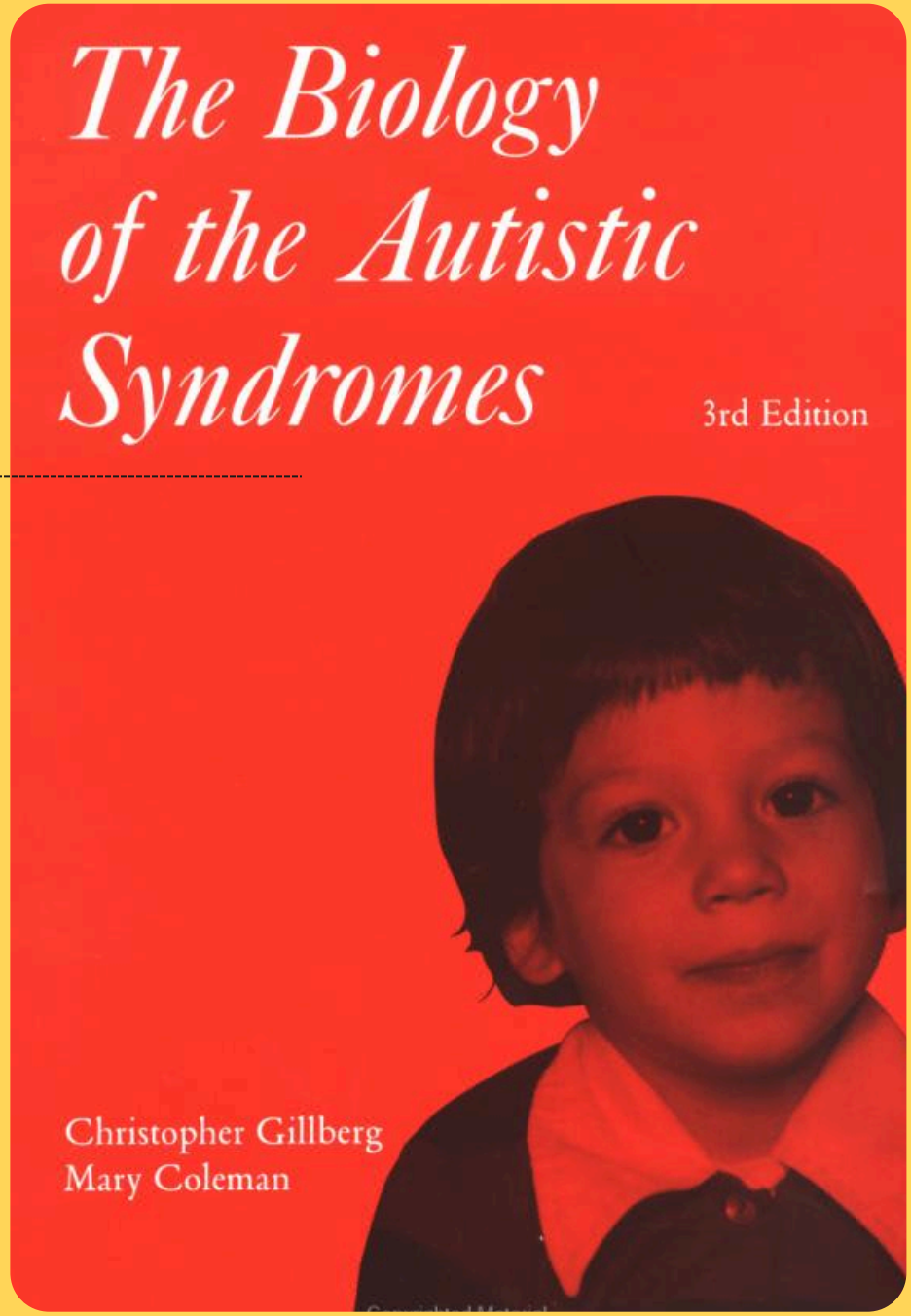
INTRODUCTION

- *"Autism is not a single disease entity, but features as part of a series of syndromes with different aetiologies"*- Gillberg and Coleman 1992, 2002

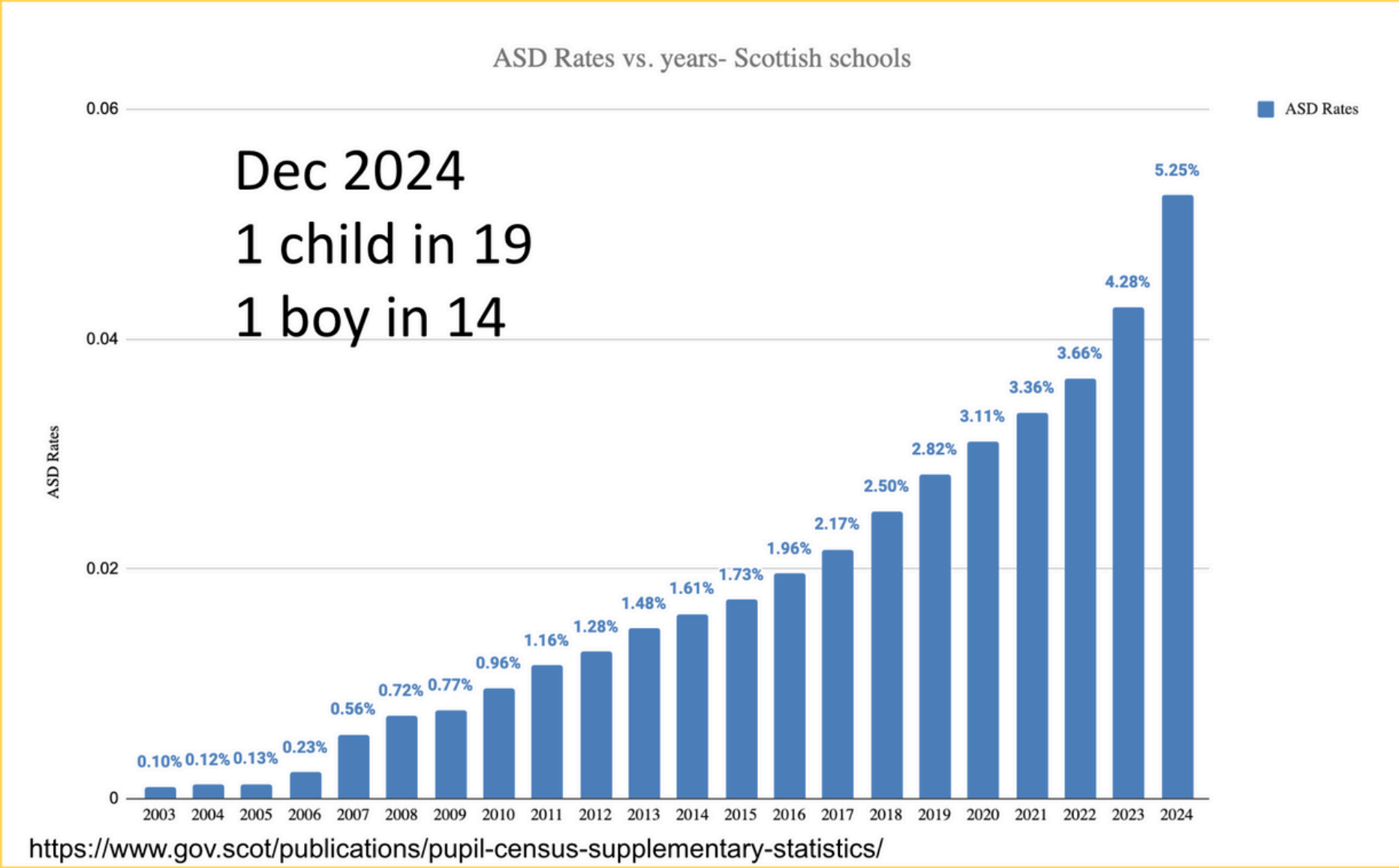
- Autism is associated with a range of health comobidities

- Autism is associated with increased risk of early mortality

- Autism rates are increasing yearly

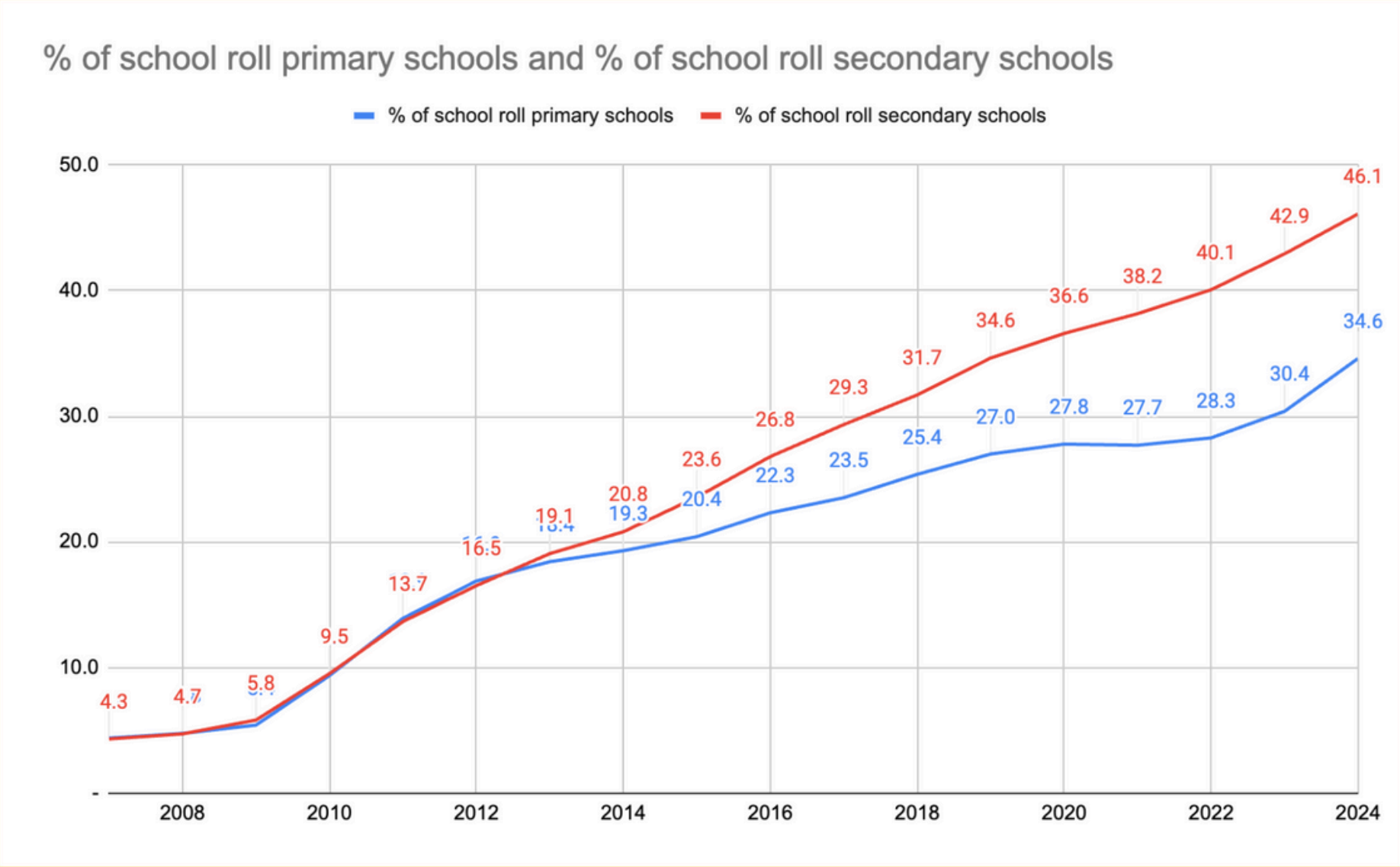


PROBLEMS: AUTISM RATES



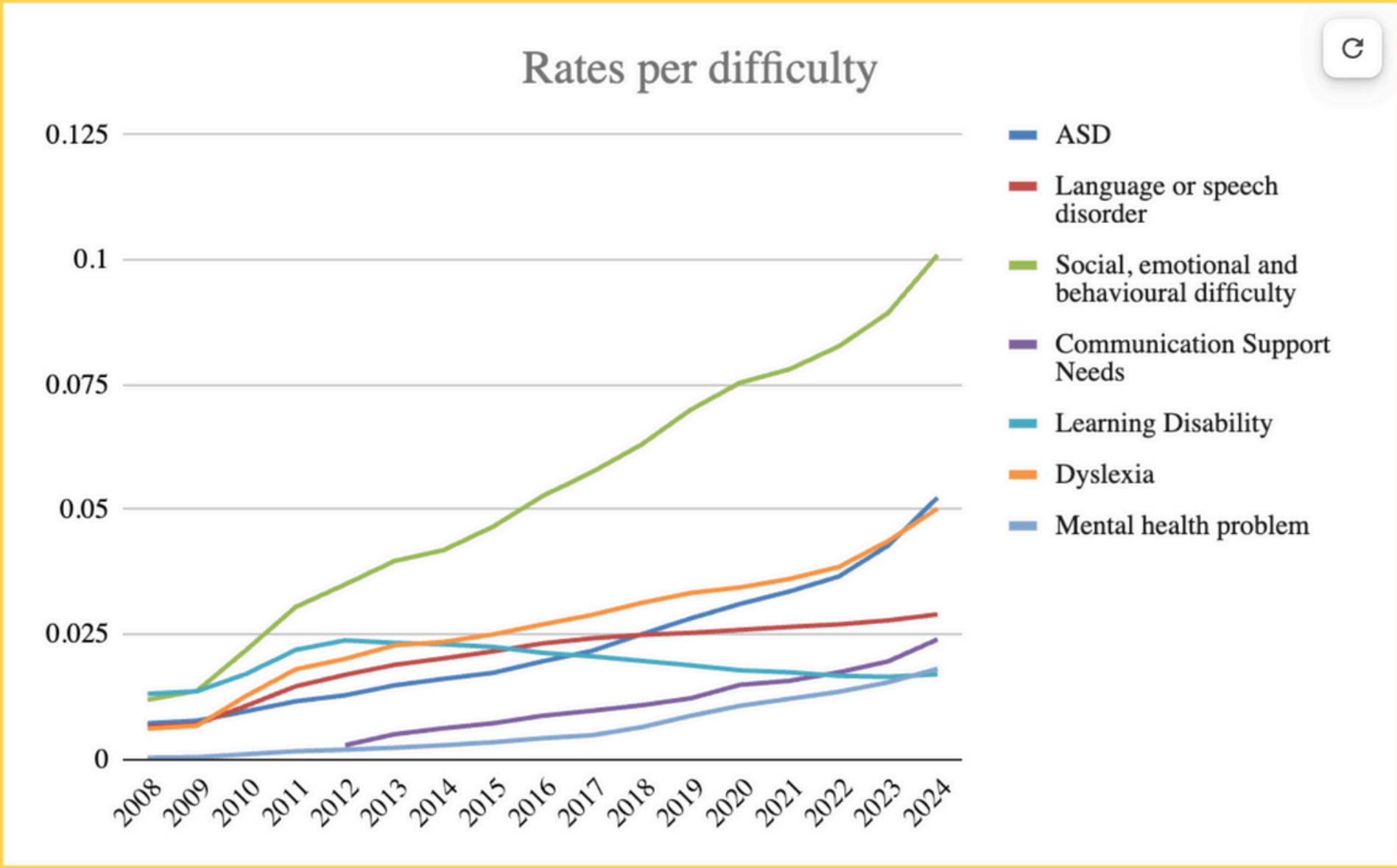
https://www.gov.scot/publications/pupil-census-supplementary-statistics/

Children with additional needs



https://www.gov.scot/publications/pupil-census-supplementary-statistics/

NEURODIVERSITY

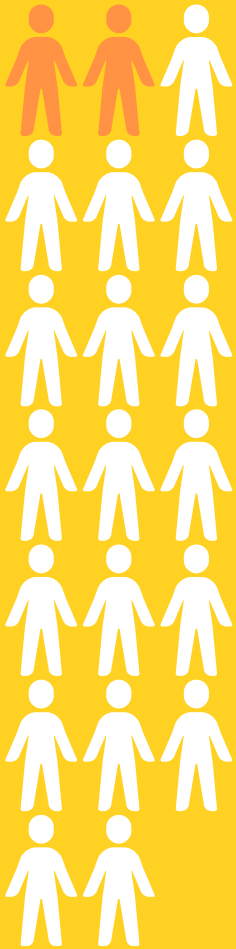


https://www.gov.scot/publications/pupil-census-supplementary-statistics/

NEURODIVERSITY

Social, Emotional & Behaviour

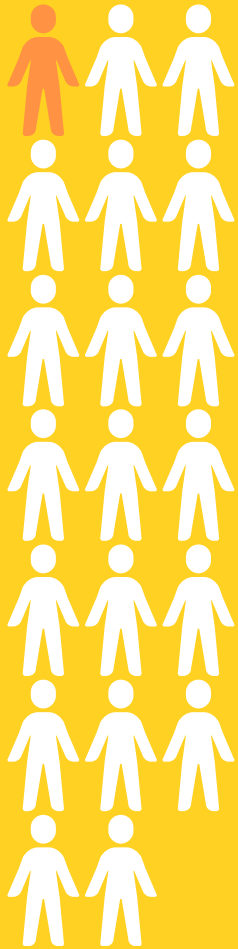
10%



2 OUT OF 20

ASD

5.2%



1 OUT OF 20

NEURODIVERSITY

Learning Disability
1.7%

Moderate Learning Disability
4.54%

Dyslexia
5.02%

Other specific learning difficulty (e.g. numeric)
4.14%

Language & Speech Disorder
2.90%

Communication Needs
2.4%

ASD
5.25%

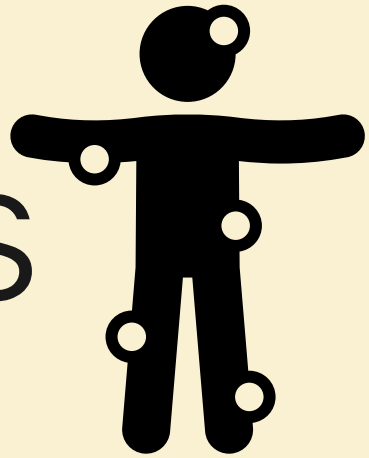
Mental Health
1.81%

Social, emotional & Behaviour
10.1%

AUTISM RATES SCHOOL CENSUS NORTHERN IRELAND

In 2022/23, **5% of school-aged children in Northern Ireland were diagnosed with autism**. This is based on data from the annual School Census.

HEALTH COMORBIDITIES

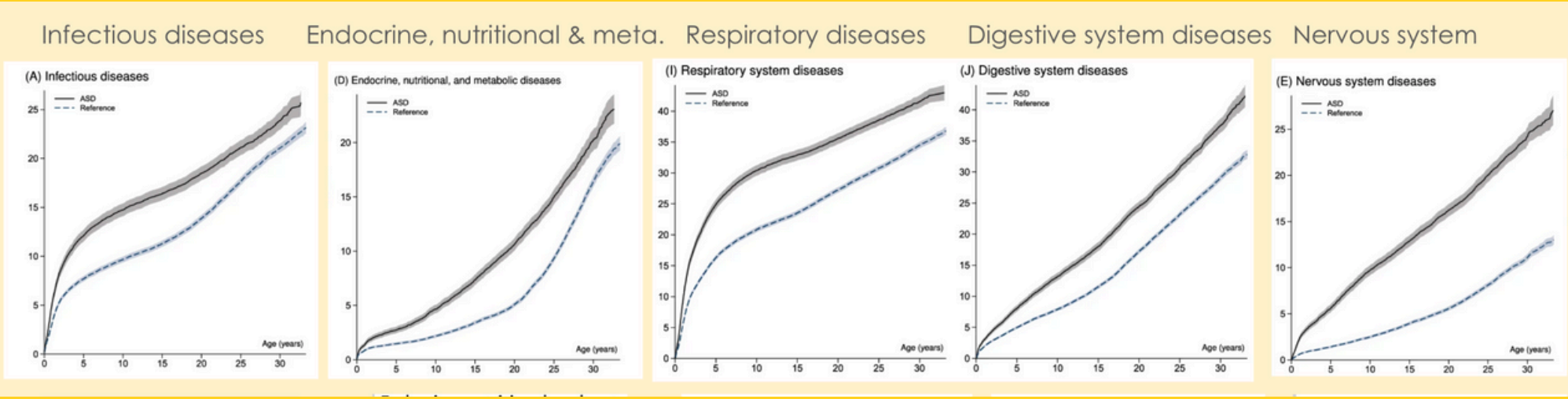


Health Presentation in a Large Population Study Birth Cohort (1984-1995)

- Danish Civil Registration System (CPR)
- A total of 826,416 registered individuals born between 1984 and 1995
- At the follow-up on April 30, 2018, 12,063 individuals (1.45%) had been diagnosed with Autism Spectrum Disorder (ASD)
- A 5% random sample of 41,251 individuals was selected from the total population
- Physical diagnoses were tracked from birth until the age of 33 years for the oldest cohort and 22 years for the youngest cohort, using ICD-10 codes

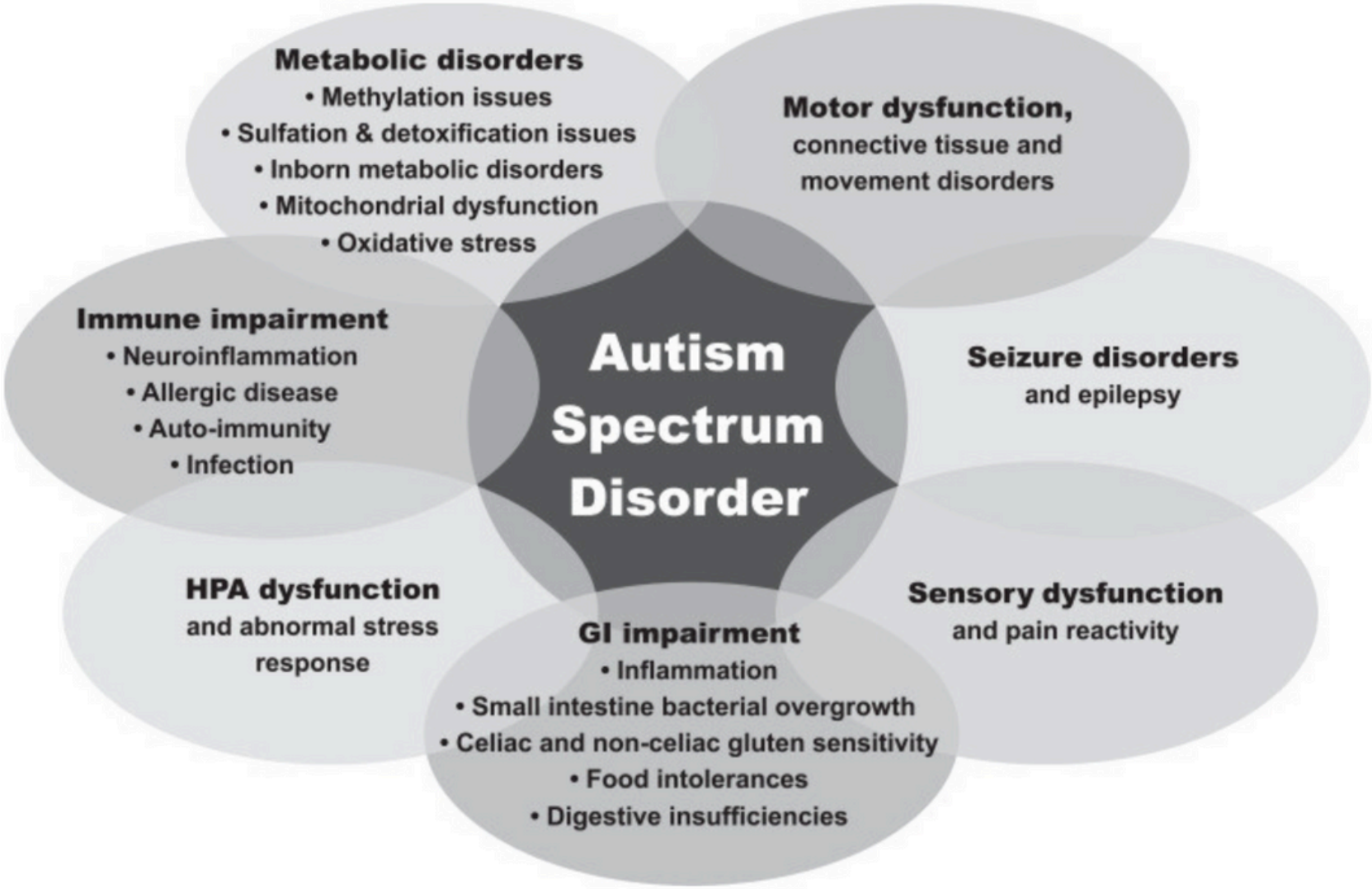
Reference: Steinhausen, H.C., Villumsen, M.D., Støving, R.K., et al. "Complete Spectrum of Physical Comorbidities with Autism Spectrum Disorder in a Nationwide Cohort." J Autism Dev Disord (2024). https://doi.org/10.1007/s10803-024-06476-2

Cumulative Incidence of Physical Diagnosis in ASD



Cumulative incidence curves with pointwise confidence intervals (CI; shaded) of the corresponding Physical Diagnosis category for the ASD and reference samples

Steinhausen, HC., Villumsen, M.D., Støving, R.K. et al. Complete Spectrum of Physical Comorbidities with Autism Spectrum Disorder in a Nationwide Cohort. J Autism Dev Disord (2024). https://doi.org/10.1007/s10803-024-06476-2



https://www.tandfonline.com/doi/full/10.2147/NDT.S251394#abstract
Sala, R., Amet, L., Blagojevic-Stokic, N., Shattock, P., & Whiteley, P. (2020). Bridging the gap between physical health and autism spectrum disorder. Neuropsychiatric Disease and Treatment, 1605-1618.

Individuals with Autism Spectrum Disorder (ASD): Increased risk of early mortality.

- Hazard ratios are estimated to be between 2 and 9, with a higher prevalence observed in females.
- Risks include:
  - Self-harming
  - Suicide
  - Substance abuse
  - Drowning
  - Epilepsy
  - Respiratory issues
  - Gastrointestinal Issues
  - Infections
  - Neoplasm
  - Endocrine system
  - Circulatory system

Forsyth, L., McSorley, M., & Rydzewska, E. (2023). All-cause and cause-specific mortality in people with autism spectrum disorder: A systematic review. Research in autism spectrum disorders, 105, 102165.

Known contributing factors

Genetic Syndromes

Rett Syndrome
Fragile X
Tuberous Sclerosis
Timothy Syndrome
Cowden's Syndrome
Angelman Syndrome
Cohen Syndrome
Down Syndrome
De Lange Syndrome
Moebius Syndrome
Neurofibromatosis Type I
Phenylketonuria
Smith-Lemli-Opitz Syndrome
Purine Autism
>50 genetic disorders

Infectious agents

Rubella
Annual Birth pattern (March- August)
Herpes encephalitis
Congenital CMV infection
Haemophilus influenza encephalitis
Measles
Bacterial agents: Mycoplasma
Lyme disease and tick born
Streptococcus A
In utero, neonate, early postnatal
Immunocompromised

Toxic Syndromes

Foetal Alcohol Syndrome
Foetal Cocaine Exposure
Foetal Valproate Exposure
Thalidomide
Lead Toxicity
Mercury Toxicity
Others Xenobiotics

Multiple aetiologies

Cerebral Palsy
Premature birth
Twin pregnancies
Birth trauma
Brain hypoxia
Deaf and hearing impairment

Condition	Incidence / Prevalence
Fragile X Syndrome (FXS)	~1 in 4,000 males, ~1 in 8,000 females
Rett Syndrome	~1 in 10,000–15,000 females (rare in males)
Tuberous Sclerosis Complex (TSC)	~1 in 6,000–10,000
Phelan-McDermid Syndrome (22q13 Deletion Syndrome)	~1 in 8,000–15,000
16p11.2 Deletion/Duplication Syndrome	~1 in 1,000–5,000
PTEN-Associated Autism (Cowden Syndrome & Bannayan-Riley-Ruvalcaba Syndrome)	~1 in 200,000 (Cowden); rare for BRRS
CHD8-Related Autism	Rare, estimated <1 in 10,000
Angelman Syndrome	~1 in 12,000–20,000
Prader-Willi Syndrome	~1 in 10,000–30,000
Williams Syndrome	~1 in 7,500–10,000
Smith-Magenis Syndrome	~1 in 15,000–25,000
DYRK1A-Related Syndrome	Rare, estimated ~1 in 50,000
SYNGAP1-Related Intellectual Disability	~1 in 1,000–4,000 (among individuals with neurodevelopmental disorders)
CACNA1C-Related Disorders (e.g., Timothy Syndrome)	Extremely rare, ~1 in 1 million
SCN2A-Related Disorders	~1 in 2,000–5,000 (among individuals with epilepsy or neurodevelopmental conditions)

Largest Twin ASD study to date points to environmental factors as playing a greater role over genetic

Hallmayer, Joachim, et al. "Genetic heritability and shared environmental factors among twin pairs with autism." Archives of general psychiatry 68.11 (2011): 1095-1102.

ORIGINAL ARTICLE

ONLINE FIRST

Genetic Heritability and Shared Environmental Factors Among Twin Pairs With Autism

Joachim Hallmayer, MD; Sue Cleveland, BS; Andrea Torres, MA; Jennifer Phillips, PhD; Brianne Cohen, BA; Tiffany Torigoe, BA; Janet Miller, PhD; Angie Fedele, BA; Jack Collins, MBA; Karen Smith, BS; Linda Lotspeich, MD; Lisa A. Croen, PhD; Sally Ozonoff, PhD; Clara Lajonchere, PhD; Judith K. Grether, PhD; Neil Risch, PhD

A research study investigated autism spectrum disorder (ASD) in 1,156 pairs of twins, with assessments conducted for 202 pairs. Out of 404 individuals evaluated, 242 met the criteria for ASD, including 171 diagnosed with strict autism. The findings revealed high diagnostic sensitivity (94.6%) and specificity (84.6%) for ASD based on DDS data.

The genetic analysis focused on **192 twin pairs, consisting of 54 monozygotic and 138 dizygotic pairs**. Concordance rates for strict autism were found to be 58-60% in monozygotic twins and 21-27% in dizygotic twins, while for ASD, the rates were 77% and 31-36%, respectively. The unexpectedly high concordance rates in dizygotic twins influenced heritability estimates.

Modeling results indicated that shared environmental factors played a more significant role than genetic heritability in the risk for ASD. **The estimated heritability was 37-38%, whereas shared environmental influences accounted for 55-58%**, challenging the notion that autism is predominantly genetic.

Environmental contributions to neurodevelopmental disorders

1. Gene-Environment Interaction- Epigenetic
2. Detoxification and Metabolic Differences
3. The Gut-Brain Connection
4. Neuroinflammation
5. Endocrine disruption

ENVIRONMENTAL EXPOSURES

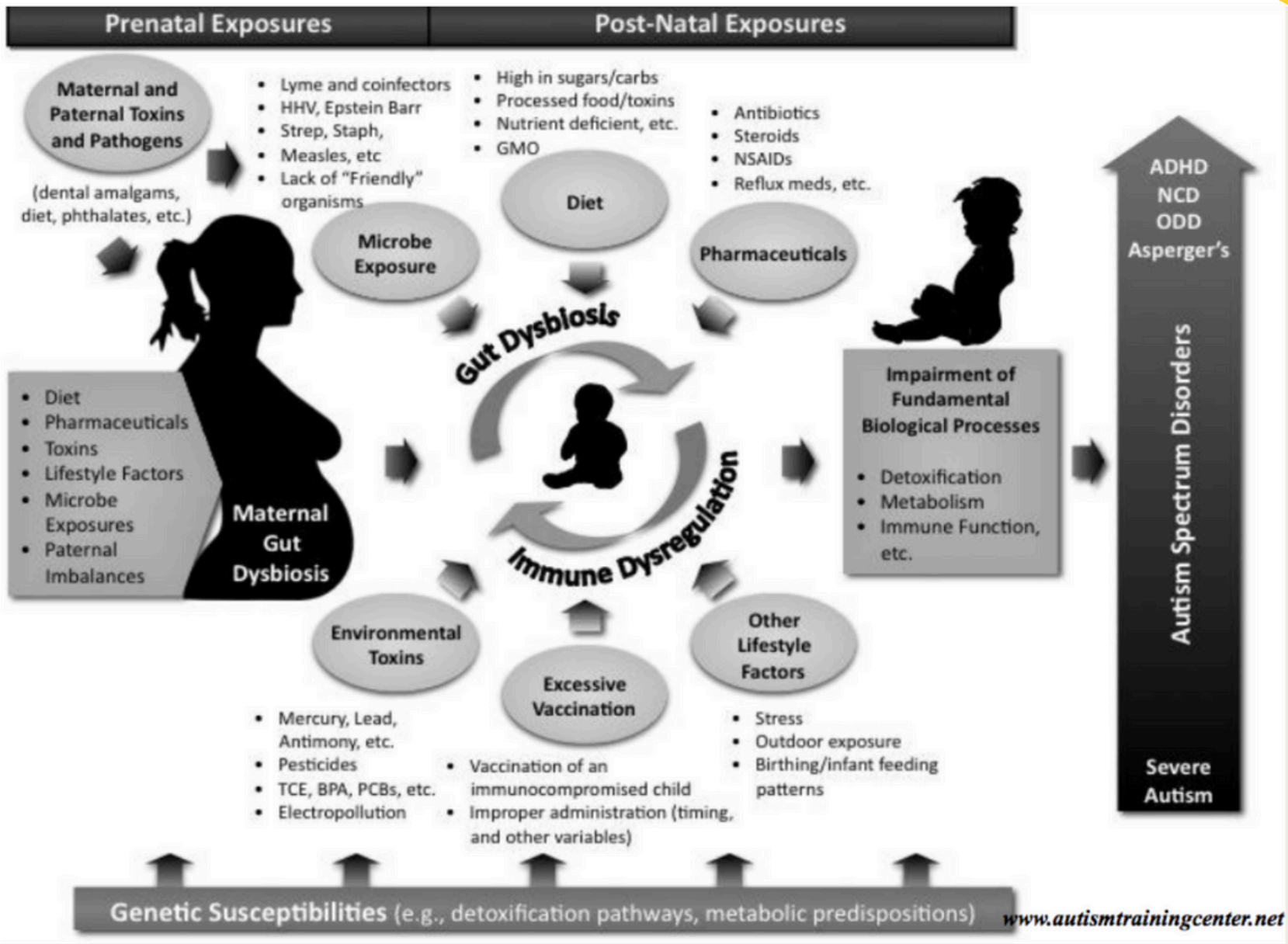
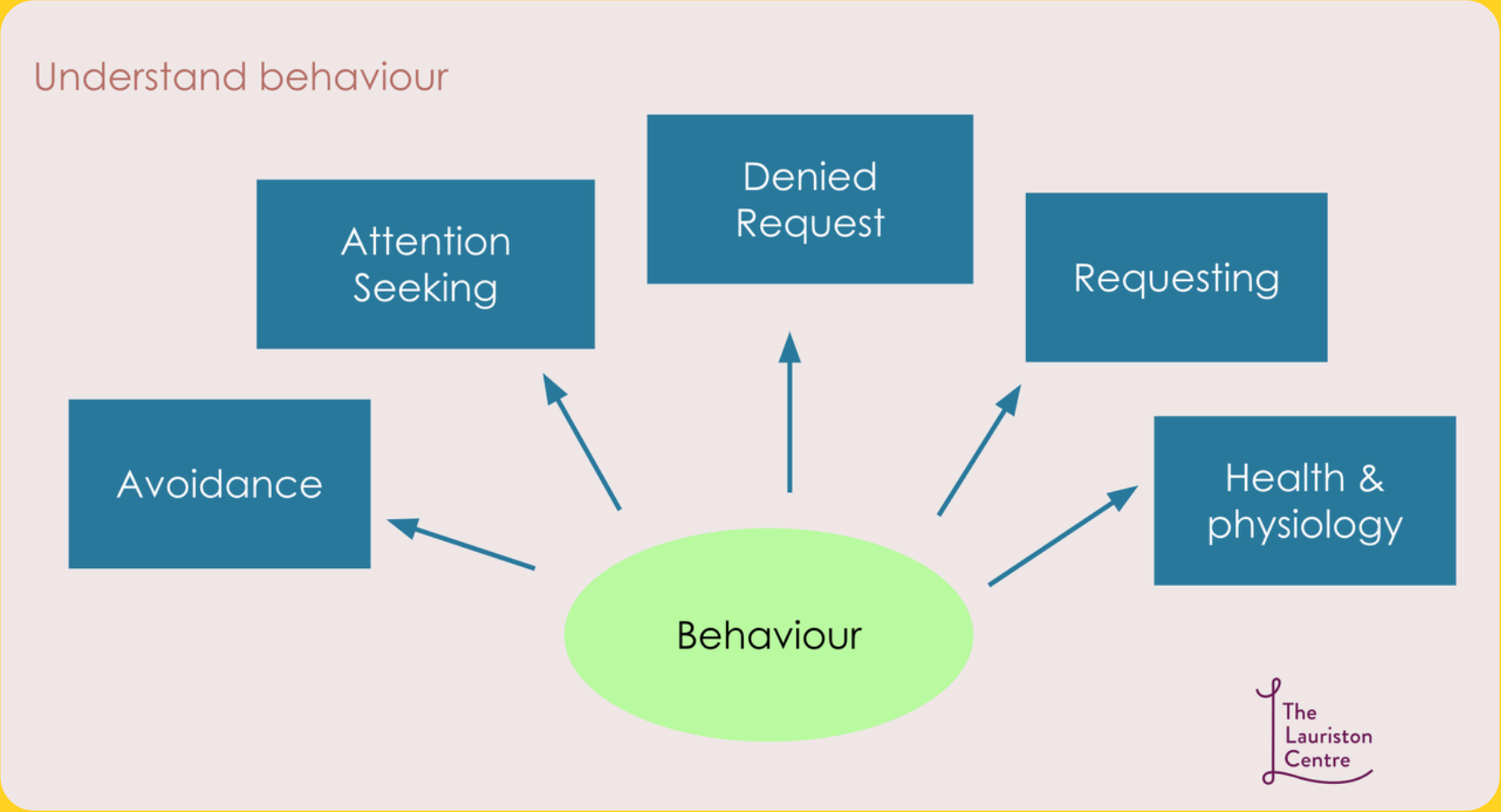


Table 1 Proposed mechanisms for how genetic and environmental factors interact to influence autism risk and severity.

Mechanism	Rationale	References
Heritable deficits in xenobiotic metabolism	Genetic mutations in enzymes that metabolize environmental chemicals have been linked to increased autism risk. A decreased ability to detoxify environmental chemicals or an increased effectiveness in converting benign parent compounds to neurotoxic metabolites might increase the neurotoxicity of an environmental chemical contaminant.	Bjorklund et al. (2021) Herbert (2010) Rock and Patisaul (2018)
Disruption of the gut microbiome	Clinical and experimental data indicate that the gut microbiome regulates neurodevelopment; the gut microbiota in children with autism differs from that of neurotypical children. Toxicological studies show that the gut microbiome influences xenobiotic metabolism and disposition, and, conversely, environmental chemicals can alter the gut microbiome.	Balaguer-Trias, Deepika, Schuhmacher, and Kumar (2022) Bertotto, Catron, and Tal (2020) Needham et al. (2022) Rosenfeld (2017) Vuong et al. (2020) Yousefi et al. (2022)
Endocrine disruption	Endocrine signaling, including signaling by thyroid hormones, sex steroids and glucocorticoids, critically modulates neurodevelopment. The incidence of autism exhibits a pronounced sex bias, with a male:female ratio of 4:1. Diverse environmental chemicals have been shown to alter endocrine signaling via various mechanisms.	Demeneix (2019) Moosa, Shu, Sarachana, and Hu (2018) Mari-Bauset et al. (2022) Ramirez et al. (2022) Weiss (2012)
Epigenetic mechanisms	Epigenetic mechanisms are critically important in regulating brain development. Environmental chemicals can alter DNA methylation, histone acetylation and miRNA expression profiles, and these parameters are altered in at least some children with autism.	Keil and Lein (2016) Kong, Zhou, and Sun (2020) Park, Lee, Kim, and Yi (2022) Parra and Johnston (2022)
Inflammation and/or immune dysregulation	Crosstalk between nervous and immune systems is essential for normal neurodevelopment, and environmental chemicals can trigger systemic and neuroinflammation as well as alter immune function. Clinical and experimental data confirm neuroinflammation and immune dysregulation in autism.	Arambula and McCarthy (2020) McLellan, Kim, Bruce, Ramirez-Celis, and Van de Water (2022) Meltzer and Van de Water (2017) Sotgiu et al. (2020)
Convergence of G × E on signaling pathways that regulate brain development	Many genetic risk factors for autism converge on several major signaling pathways that critically regulate synaptic connectivity in the developing brain. Environmental chemicals have been identified that target these same signaling pathways.	Ansel et al. (2016) Ebert and Greenberg (2013) Pourtavakoli and Ghafouri-Fard (2022) Purushotham et al. (2022) Stamou et al. (2013)

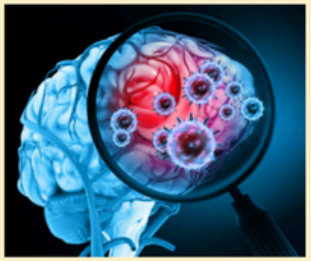
What does the behaviour tell us about the child?



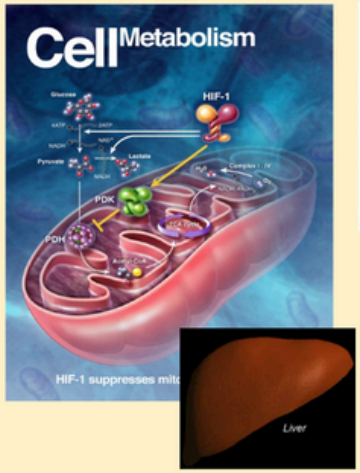
HEALTH- RELATED BEHAVIOURS

Testing guided by symptoms

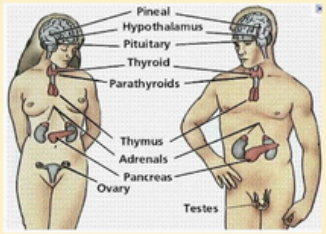
Digestive Function



Immune Function
PANS/PANDAS
Inflammation
Lyme Disease
In utero
Perinatal
Pot-natal



Metabolism &
mitochondrial function
Oxidative stress

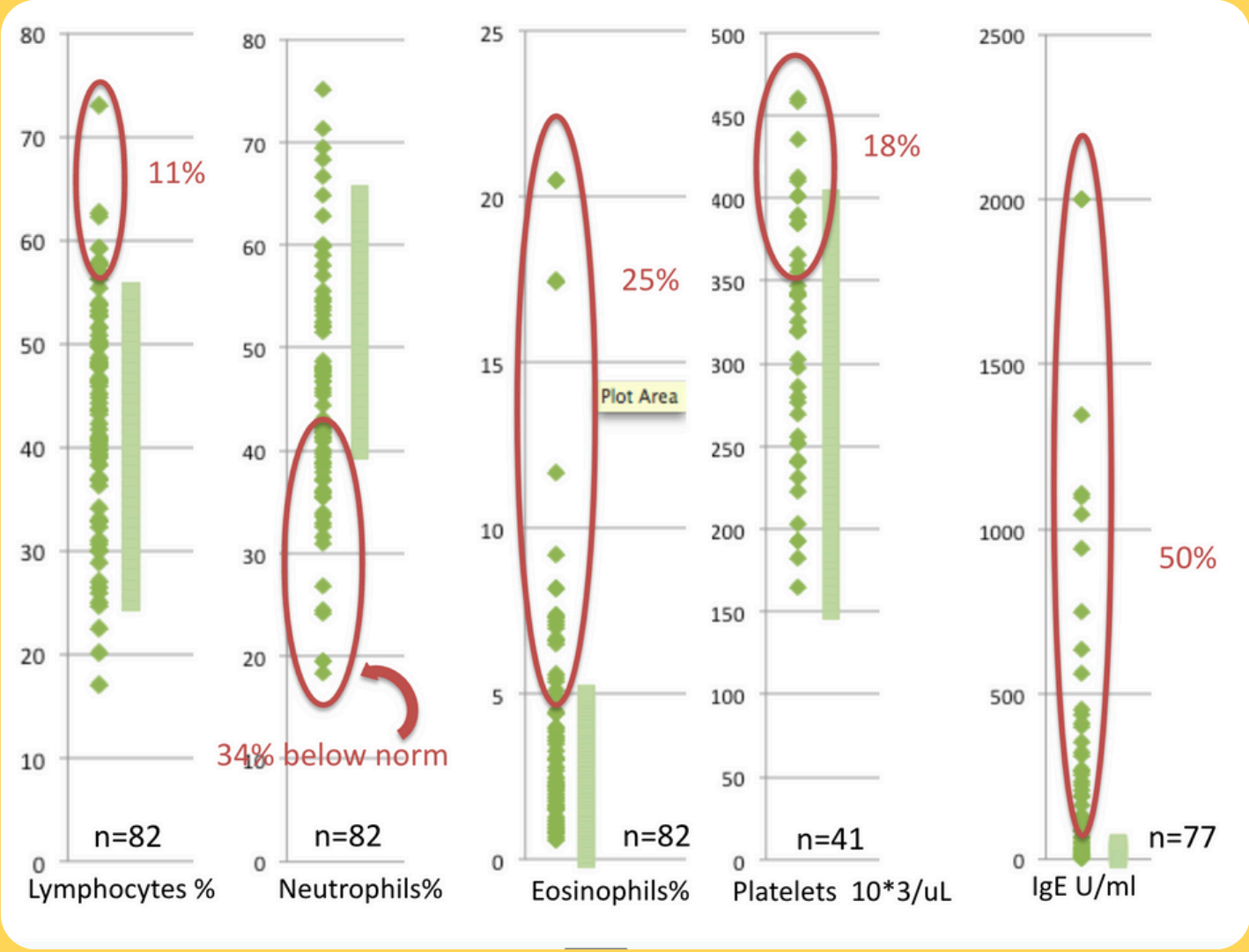


Endocrine System

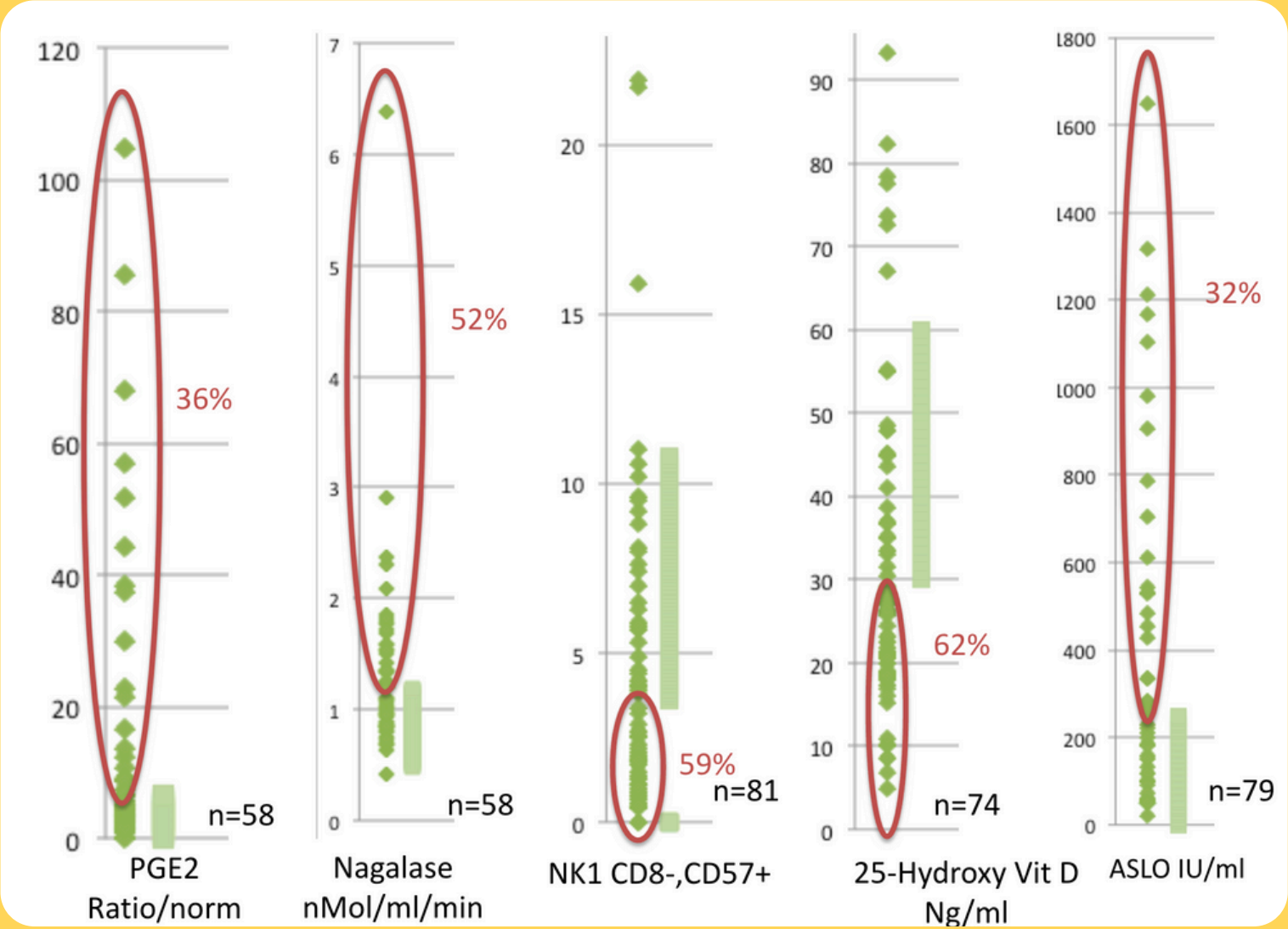
Xenobiotics
Prenatal and
postnatal

Genetics
Genetic conditions
Snp
E.g. Vit D
Methylation

Complete blood count- illustrative results



Specialised immune markers



Treatment ratings >27,000 families- Pharmaceuticals

DRUGS	Parent Ratings: Got Worse[A]	No Effect	Got Better	Better: Worse	No. of Cases[B]
Actos	19%	60%	21%	1.1:1	140
Aderall	43%	26%	31%	0.7:1	894
Amphetamine	47%	28%	25%	0.5:1	1355
Anafranil	32%	39%	29%	1.1:1	440
Antibiotics	33%	50%	18%	0.5:1	2507
Antifungals[C]					
Diflucan ★	5%	34%	62%	13:1	1214
Nystatin ★	5%	43%	52%	11:1	1969
Atarax	26%	53%	21%	0.8:1	543
Benadryl	24%	50%	26%	1.1:1	3230
Beta Blocker	18%	51%	31%	1.7:1	306
Buspar	29%	42%	28%	1.0:1	431
Chloral Hydrate	42%	39%	19%	0.5:1	498
Clonidine	22%	32%	46%	2.1:1	1658
Clozapine	38%	43%	19%	0.5:1	170
Cogentin	20%	53%	27%	1.4:1	198
Cylert	45%	35%	19%	0.4:1	634
Depakene[D]					
Behavior	25%	44%	31%	1.2:1	1146
Seizures ★	12%	33%	55%	4.6:1	761
Desipramine	34%	35%	32%	0.9:1	95

DRUGS	Parent Ratings: Got Worse[A]	No Effect	Got Better	Better: Worse	No. of Cases[B]
Dilantin[D]					
Behavior	28%	49%	23%	0.8:1	1127
Seizures	16%	37%	47%	3.0:1	454
Fenfluramine	21%	52%	27%	1.3:1	483
Haldol	38%	28%	34%	0.9:1	1222
IVIG ★	7%	39%	54%	7.6:1	142
Klonapin[D]					
Behavior	31%	40%	29%	0.9:1	270
Seizures	29%	55%	16%	0.6:1	86
Lithium	22%	48%	31%	1.4:1	515
Luvox	31%	37%	32%	1.0:1	251
Mellaril	29%	38%	33%	1.2:1	2108
Mysoline[D]					
Behavior	41%	46%	13%	0.3:1	156
Seizures	21%	55%	24%	1.1:1	85
Naltrexone	18%	49%	33%	1.8:1	350
Low Dose ★ Naltrexone	11%	52%	38%	4.0:1	190
Paxil	34%	32%	35%	1.0:1	471
Phenobarb.[D]					
Behavior	48%	37%	16%	0.3:1	1125
Seizures	18%	44%	38%	2.2:1	543

DRUGS	Parent Ratings: Got Worse[A]	No Effect	Got Better	Better: Worse	No. of Cases[B]
Prolixin	30%	41%	28%	0.9:1	109
Prozac	33%	32%	35%	1.1:1	1391
Risperidal ★	21%	26%	54%	2.6:1	1216
Ritalin	45%	26%	29%	0.6:1	4256
Secretin					
Intravenous	7%	50%	43%	6.4:1	597
Transderm.	9%	56%	35%	3.9:1	257
Stelazine	29%	45%	26%	0.9:1	437
Steroids	34%	30%	36%	1.1:1	204
Tegretol[D]					
Behavior	25%	45%	30%	1.2:1	1556
Seizures	14%	33%	53%	3.8:1	872
Thorazine	36%	40%	24%	0.7:1	945
Tofranil	30%	38%	32%	1.1:1	785
Valium	35%	42%	24%	0.7:1	895
Valtrex ★	8%	42%	50%	6.7:1	238
Zarontin[D]					
Behavior					
Seizures					
Zoloft					

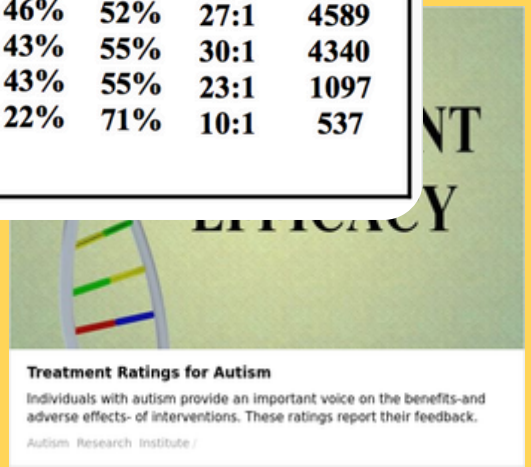
Good outcomes with anti-fungal, Low Dose Naltrexone, Valtrex, i.v.Ig, Anti-epileptic medications

Treatment ratings >27,000 families- Diet and nutrition

BIOMEDICAL/ NON-DRUG/ SUPPLEMENTS	Parent Ratings: Got Worse[A]	No Effect	Got Better	Better: Worse	No. of Cases[B]
Calcium[E]	3%	60%	36%	11:1	2832
Cod Liver Oil ★	4%	41%	55%	14:1	2550
Cod Liver Oil with Bethanecol	11%	53%	36%	3.4:1	203
Colostrum ★	6%	56%	38%	6.8:1	851
Detox. (Chelation)[C] ★	3%	23%	74%	24:1	1382
Digestive Enzymes ★	3%	35%	62%	19:1	2350
DMG ★	8%	50%	42%	5.3:1	6363
Fatty Acids ★ ★	2%	39%	59%	31:1	1680
5 HTP	11%	42%	47%	4.2:1	644
Folic Acid ★	5%	50%	45%	10:1	2505
Food Allergy Trtmnt ★	2%	31%	67%	27:1	1294
Hyperbaric Oxygen Therapy ★	5%	30%	65%	12:1	219
Magnesium ★	6%	65%	29%	4.6:1	301
Melatonin ★ ★	8%	26%	66%	8.3:1	1687
Methyl B12 (nasal) ★	10%	45%	44%	4.2:1	240
Methyl B12 (subcut.) ★	6%	22%	72%	12:1	899
MT Promoter	8%	47%	44%	5.5:1	99
P5P (Vit. B6) ★	11%	40%	48%	4.3:1	920
Pepcid	11%	57%	32%	2.9:1	220
SAMe	16%	62%	23%	1.4:1	244
St. Johns Wort	19%	64%	18%	0.9:1	217
TMG	16%	43%	41%	2.6:1	1132

BIOMEDICAL/ NON-DRUG/ SUPPLEMENTS	Parent Ratings: Got Worse[A]	No Effect	Got Better	Better: Worse	No. of Cases[B]
Transfer Factor ★	8%	47%	45%	5.9:1	274
Vitamin A ★	3%	54%	44%	16:1	1535
Vitamin B3 ★	4%	51%	45%	10:1	1192
Vit. B6/Mag. ★	4%	46%	49%	11:1	7256
Vitamin C ★	2%	52%	46%	20:1	3077
Zinc ★	2%	44%	54%	24:1	2738
SPECIAL DIETS					
Candida Diet ★	3%	39%	58%	21:1	1141
Feingold Diet ★	2%	40%	58%	26:1	1041
Gluten- /Casein-Free Diet ★	3%	28%	69%	24:1	3593
Low Oxalate Diet ★	7%	43%	50%	6.8:1	164
Removed Chocolate ★	2%	46%	52%	28:1	2264
Removed Eggs	2%	53%	45%	20:1	1658
Removed Milk Products/Dairy ★	2%	44%	55%	32:1	6950
Removed Sugar ★	2%	46%	52%	27:1	4589
Removed Wheat ★	2%	43%	55%	30:1	4340
Rotation Diet ★	2%	43%	55%	23:1	1097
Specific Carbo-hydrate Diet ★	7%	22%	71%	10:1	537

Many interventions with excellent outcomes!!!!



Open Access Comment

The Implementation of Randomization Requires Corrected Analyses. Comment on "Comprehensive Nutritional and Dietary Intervention for Autism Spectrum Disorder—A Randomized, Controlled 12-Month Trial, *Nutrients* 2018, *10*, 369"

by **Colby J. Vorland** [1,*], **Andrew W. Brown** [1], **Stephanie L. Dickinson** [2], **Andrew Gelman** [3] and **David B. Allison** [2,*]

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Study Design: An open-label survey involving 161 participants, compared to a three-month randomised controlled trial (RCT)

Initial evaluation of autism severity and overall functioning level.

Physical examination by the study physician to verify that the participant is in sufficient good health to participate in the study. Initial blood draw and first-morning urine collection.

Day 0: Vitamin/Mineral supplementation begins.

Day 30: Essential Fatty Acid supplementation begins.

Day 60: Epsom salt baths begin.

Day 90: Carnitine Supplementation begins.

Day 180: Digestive Enzyme supplementation begins.

Day 210: Healthy, casein-free, gluten-free diet begins.

Day 365: Final assessment of autism severity and overall functioning status. Final blood draw and urine collection.

Adams, J. B., Audhya, T., Geis, E., Gehn, E., Fimbres, V., Pollard, E. L., ... & Quig, D. W. (2018). Comprehensive nutritional and dietary intervention for autism spectrum disorder—a randomized, controlled 12-month trial. Nutrients, 10(3), 369.

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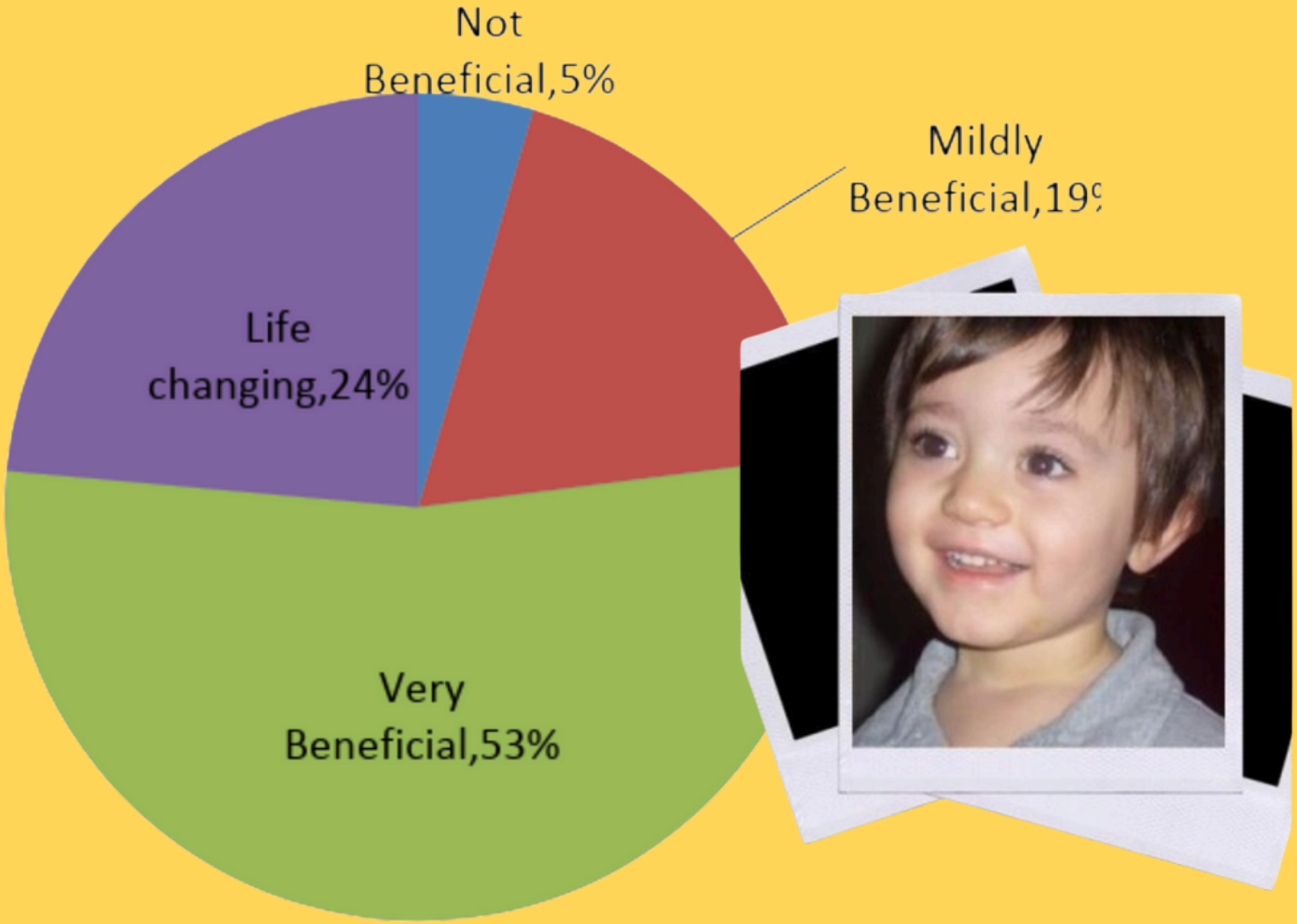
Key Findings:

- High Benefit: 73% of participants reported Moderate to Great improvement, outperforming other supplements and medications.
- Minimal Side Effects: Low adverse effect rating (0.25/3.0), significantly lower than psychiatric/seizure medications.
- Wide Applicability: Benefits observed across all demographics and ASD severity levels.

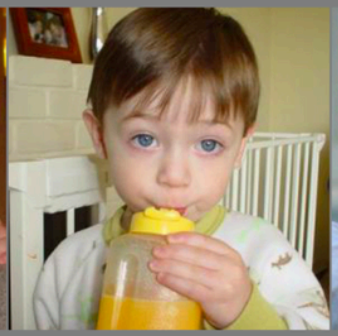
Outcomes



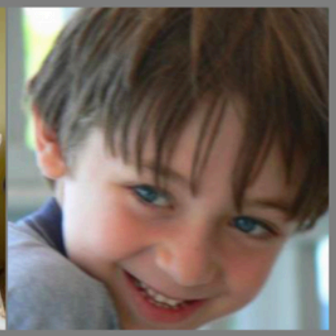
Survey 220 families

Photogallery

Ryder Before Autism



Ryder With Autism



Ryder Recovered

Makena

Makena Recovered

Sidney before

Sidney Dec 14

Scott

Scott Recovered

Food first approach*

- Eliminate pro-inflammatory foods, such as gluten and milk, but do so cautiously.
  - Fermented dairy and whole wheat options (like sourdough) may be acceptable.
- Cut out sugary items, carbonated beverages, sweets, biscuits, cakes, and fruit juices; avoid artificial sweeteners.
- Prefer fruits that are low in sugar, and consider further limiting their intake.
- Reduce processed foods to less than 5% of your diet.
- Monitor carbohydrate intake; choose whole grains over refined options, such as brown rice instead of white rice.
- Emphasise a high-plant diet that includes fresh herbs, spices, legumes, beans, and bitter foods like salads, along with prebiotic-rich options.
- Use Extra-Virgin Olive Oil.
- Incorporate oily fish (excluding larger fish like tuna) three times a week.
- Include eggs, preferably organic.
- Include beef for its Carnitine content and ensure it's of good quality.
- Choose berries carefully based on their country of origin.
- Whenever possible, opt for seasonal, home-cooked meals made from whole foods.
- Include some fermented foods.

*taking into account allergies and intolerances

How can we change the diet of a child who has a highly restricted diet and food phobias?

Evaluate Food Preferences: Consider taste, colours, and texture.

Evaluate Need for Control: For instance, some children may prefer sandwiches to be cut in specific ways or may not want different foods to touch each other.

Implement the Crowding Out Concept: Gradually blend more healthy foods with those the child already accepts.

Repeated Exposures: Be aware of neophobia (the fear of new foods).
Utilise Instructional Control:

Create Individualised Plans: Employ a variety of strategies:

- Modelling and play
- Involving the child in cooking when possible
- Allowing the child to make choices while controlling the options
- Using some reinforcers, but avoid bribery or forcing foods.

Remember, progress may be gradual for some children and may require initial focus on specific nutrients, such as B12, to spark interest in a wider variety of foods.

The approach needs to be tailored to each child.

Key nutrients to consider

- Folinic acid
- Methylation donors, B12, Methyl-B complex
- Omega-3
- Vitamin D
- Zinc
- Magnesium
- Probiotics
- Digestive enzymes
- N-Acetyl Cysteine
- Sulforaphane
- Acetyl-Carnitine
- Epsom salt baths

Thank you!

The Lauriston Centre

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