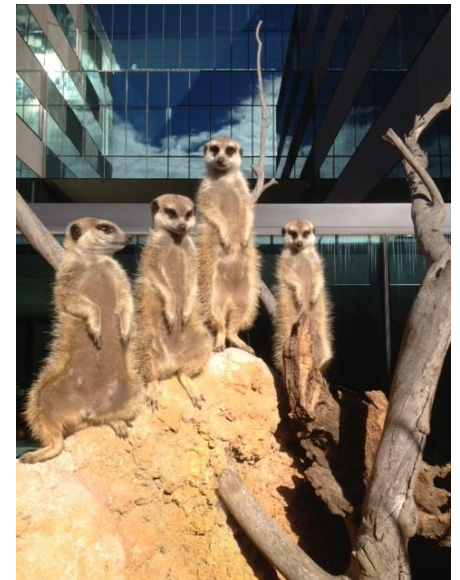# Quality of Life in Autism and other Neurodevelopmental Disorders

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Disclosures

- Professor Coghill served in an advisory or consultancy role for Lilly, Medice, Novartis, Shire/Takeda.

- He was paid for public speaking by Lilly, Janssen, Medice, Novartis, Shire/Takeda, Servier

- He has been involved in clinical trials conducted by Shire/Takeda.

- He received royalties from Oxford University Press.

- No funding was received in connection with the work presented in this presentation

Agenda

- What is Quality of Life and why does it matter
- Measuring Quality of Life
  - Age
  - The proxy question
  - Domains
- Quality of Life in Autism, ADHD and other disorders
- Relationship symptoms and QoL (and cognition)
- Ongoing issues and conclusions

What is Quality of Life and why does it matter?

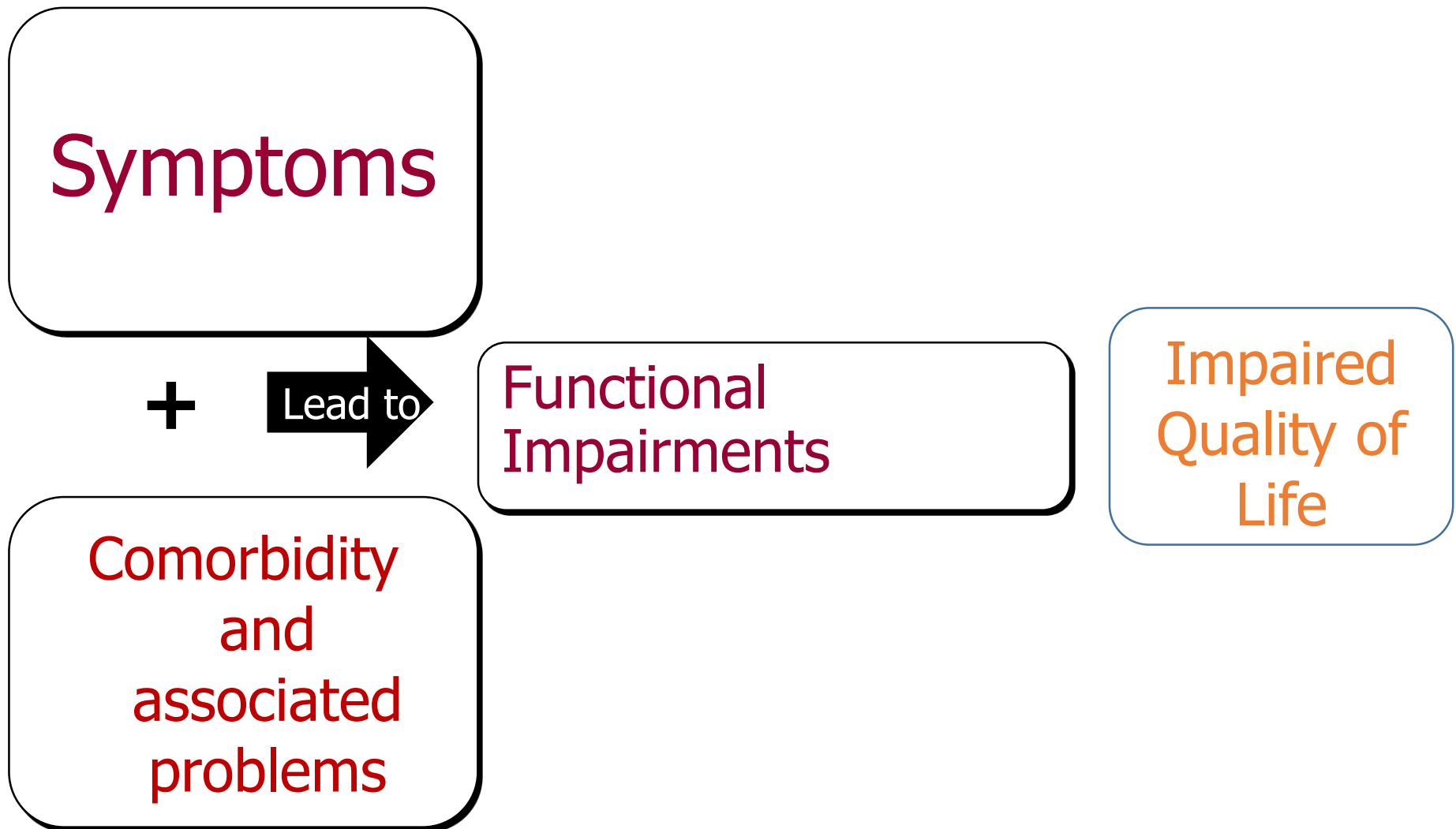# Functional impairment / QoL

Symptoms

+

Comorbidity and associated problems

Lead to →

Functional Impairments

Impaired Quality of Life

What is (HR)QoL?

WHO's definition:
Individual's <u>perception</u> of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.
Includes a person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment.

>>Life satisfaction, well-being, happiness

<u>**HR:**</u> Focus on the impact of a health condition on QoL

>> multidimensional construct
>> subjective reality (primary perspective > 7-8y)
>> large interindividual variability (incl ADHD)

What is functioning?

Abilities and disabilities as a complex interaction between the health condition of the individual and the contextual factors of the environment as well as personal factors.

The picture produced by this combination of factors and dimensions is of "*the person in his or her world*".

>> competence and performance!
>>multidimensional construct
>> objective reality
>> large interindividual variability (incl ADHD)

Functional Impairment

- Academic functioning
  - Achievement below intellectual capacities
  - Achievement x SD below age-mean
- Activities
  - Participates in less activities than other children his age
- Independence
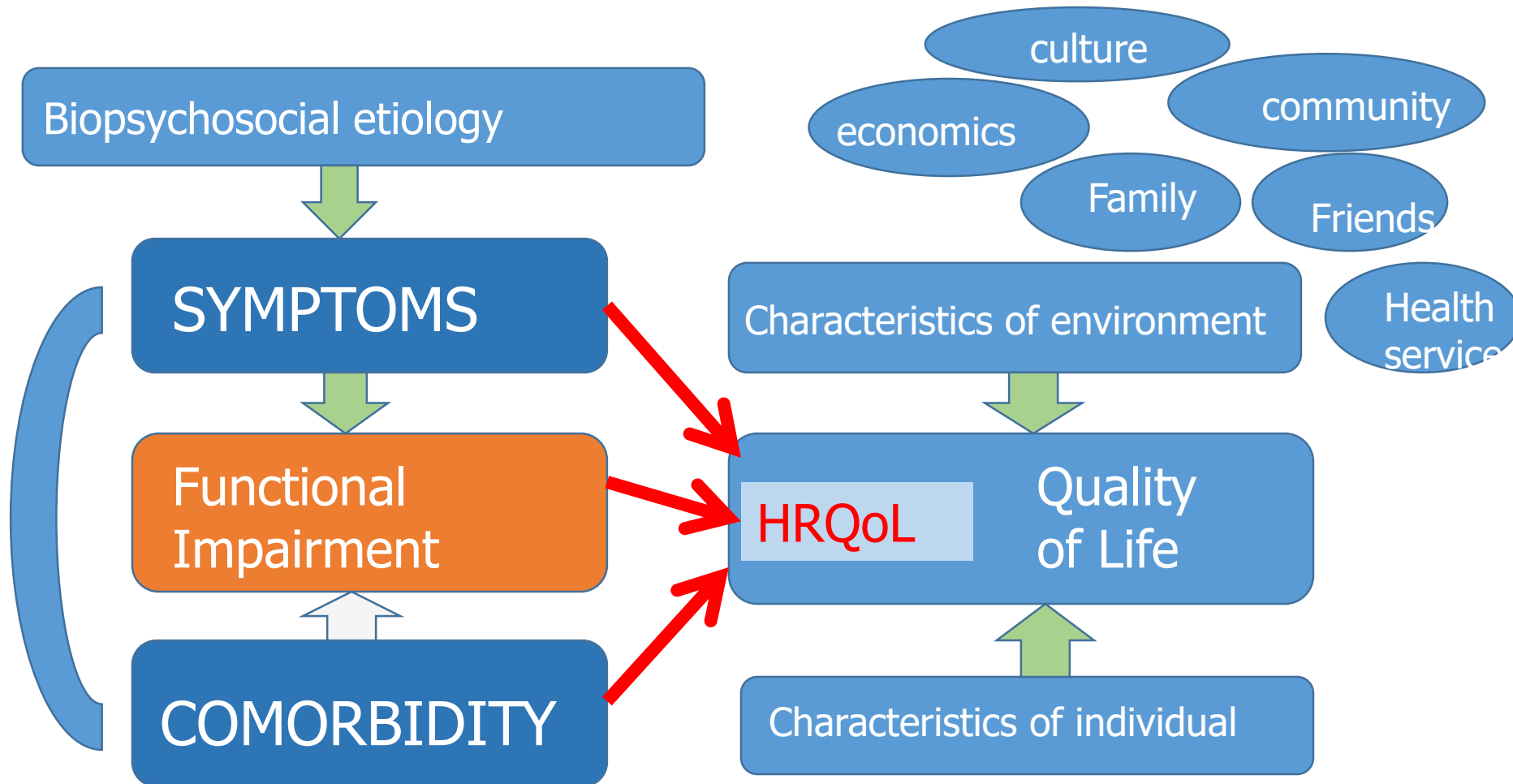 - Needs a lot of supervision in daily routines

"Objective reality"

QoL

- Academic functioning
  - "I do OK at school but not well enough"
  - "I feel OK about how I am doing at school"
- Activities
  - "I can participate in social activities"
- Independence
  - "I don't need any supervision, the adults just treat me like a child"

"Subjective reality"

Impairment and Quality of Life

So why do impairment and QoL matter?

- They are inherent to the diagnostic criteria

- They may be less stigmatizing?

- Can be more important and meaningful than symptoms alone?

- Better describe individual's real world challenges, and difficulties

- Help to guide interventions

- In some circumstrances can be used to calculate health related service costs.

- Can provide a bridge for communication between experts, patient, family and society

- Can be less controversial than diagnosis/symptoms (sometime)

- Give and opportunity to stress strengths as well as difficulties

- Can reflect a more holistic view of impact of health difficulties

- Can help provide a comparison between the impact of physical and mental health problems.

Measuring Quality of Life

Measuring Quality of Life

- Two key conceptual issues
  - Self appraisal
  - Multidimensional
    - Core domains include
      - Social
      - Physical
      - Psychological
    - Also usually includes
      - Cognitive

Unfortunately these domains are often given obscure labels which can make it difficult to be sure about what is actually being measured

Methodological Issues in Paediatric HRQL Assessment

- What is the youngest age at which children can report their HRQL?

- The "proxy" question

- Age-appropriate tools
  - instrument formatting and design
  - creating multiple forms of a measure corresponding to different age groups

Age

- Children can begin reporting the more concrete domains of their own HRQL between 4 and 6 years old
  - E.g. physical domains

- However subjective or abstract domains of HRQL can only be reported accurately by older children
  - E.g. the emotional impact of illness

- The level of language and literacy will also clearly impact on the design of questionnaires

- The disease / disorder may also interact with age e.g. ADHD and asthma may differ in terms of what can be expected of a child at any particular age

Age appropriate instrument formatting and design

- What type of scale to use?

- Recall periods?

- Length of instrument?

- Children's degree of independence during administration?

In the past 4 weeks, how often did your parents eat meals with you?
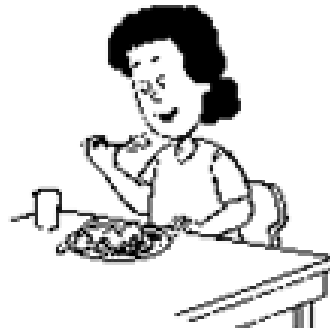
No Days	Very Few Days	Some Days	Almost Every Day	Every Day
○	○	○	○	○
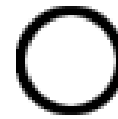
In the past 4 weeks, how often did you feel really worried?

Never	Almost Never	Sometimes	Almost Always	Always
○	○	○	○	○

Age appropriate instrument formatting and design

- Recall periods
  - Eight-year-old children have been shown to use a 4-week recall period with reasonable accuracy, but younger children may have difficulty with the concept of 1 week or 1 month. Use concrete events to anchor time

Creating multiple forms of a measure corresponding to different age groups

- Benefits
  - Ensures you have age appropriate tools

- Disadvantage
  - Can become hard to compare the scores across different ages
  - Makes it more difficult to conduct longitudinal studies

The Proxy Question

- Who is the most appropriate respondent
  - Child?
  - Parent/s? (one or both?)
  - Others? (teachers, sibs, peers?)
  - Multiple respondents?

- Empirical investigations of agreement between parent and child report of the child's health status and HRQL have yielded mixed results and suggest that agreement between parent and child report of HRQL varies considerably.
  - Correlations between parent and child report higher for observable physical domains than non-observable emotional domains
  - Studies that have considered the child's age have not reported consistent results.

The Proxy Question

- Research examining the impact of the child's health on parent–child agreement has yielded conflicting information.
  - Parents of children with a chronic disorder tend to rate child's QoL as lower than the child themselves
  - Parents of children from population samples tend to rate child's QoL as higher than the child themselves

- Ikeda (2013) recognized that for some disorders and domains, the level of disagreement between parent and childe might be particularly large,
  - For example in the social domain in ASD where parents often desire social integration of their children, while the children themselves might not be interested and may not want to be forced into it

The Proxy Question

- Whenever a child is able to provide reliable and valid data, the child's self report is the ideal strategy because it is consistent with the definition of HRQL, which emphasizes the patient's subjective perspective.

- Also the child is able to contribute information regarding the whole of their life experience e.g. home <u>and</u> school <u>and</u> when out with friends

The Proxy Question

- However in certain situations it may will be appropriate to ask an adult as a proxy respondant
  - When dealing with complex, abstract, psychologically oriented concepts
  - When a child is to sick to respond
  - For very young or severely disabled children

- The parent can also provide valuable information on the impact of the child's illness and treatment on family functioning, which is an integral part of children's HRQL.

- There are several disadvantages of using parents as proxy respondents.
  - Inconsistent with the QoL concept
  - Are mother's and father's reports equally valid?
  - Reports are likely to be biased by how they themselves are affected

The Proxy Question

- In view of these issues some suggest that getting information from both child and parents will give the best picture however this has its own problems
  - More costly
  - Do you pool data or keep it separate
  - If they don't agree how do you choose which to believe?

Domains of QoL

- Physical

- Psychological

- Social

- Cognitive

Clearly these can be described and sub-divided in many different ways

Different approaches in different measures

PedsQL

- Most frequently used measure in neurodevelopmental disorders
- Easiest to interpret
- Allows a Total Score
- Subscales
  - Physical
  - Emotional
  - Social
  - School

Child Health Questionnaire

- Physical functioning
- Role Limitations – Emotional/behavioural
- Role Limitations – Physical
- Bodily Pain
- Behaviour
- Mental Health

- Self Esteem
- General Health Perceptions
- Parental impact – Emotional
- Parental impact – Time
- Family Activities

CHIP - CE

Domains	Sub-domains
Satisfaction	Satisfaction with Health
	Satisfaction with Self
Comfort	Physical Comfort
	Emotional Comfort
	Restricted Activity
Risk Avoidance	Individual Risk Avoidance
	Threats to Achievement
Resilience	Family Involvement
	Physical Activity
	Social Problem Solving
Achievement	Academic Performance
	Peer Relations

An overview of QoL around the world (courtesy of Sven)

Happiness score of countries according to the World Happiness Report (2018)

- >7
- 6.5–7
- 6–6.5
- 5.5–6
- 5–5.5
- 4.5–5
- 4–4.5
- 3.5–4
- 3–3.5
- <3
- No Data
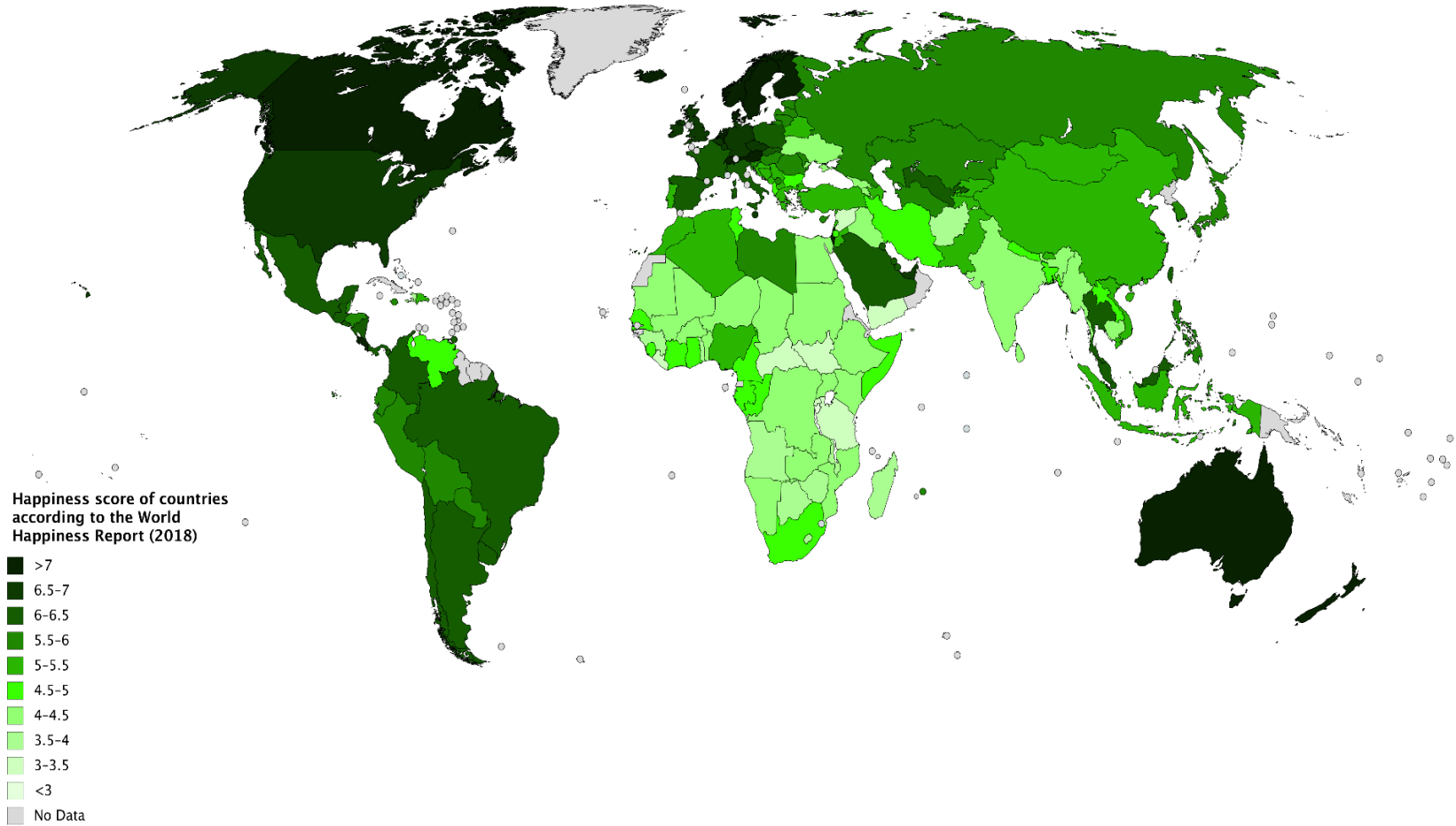
Annual Research Review: Quality of life and childhood mental and behavioural disorders – a critical review of the research

Ulf Jonsson,[1,2,3,*] Iman Alaie,[1,3,*] Anna Löfgren Wilteus,[1,2] Eric Zander,[1,2] Peter B. Marschik,[1,4] David Coghill,[5,6] and Sven Bölte[1,2]

[1]Neuropsychiatry Unit, Department of Women's and Children's Health, Center of Neurodevelopmental Disorders (KIND), Karolinska Institutet, Stockholm; [2]Child and Adolescent Psychiatry, Center of Psychiatry Research, Stockholm County Council, Stockholm; [3]Department of Neuroscience, Child and Adolescent Psychiatry, Uppsala University, Uppsala, Sweden; [4]iDN – Interdisciplinary Developmental Neuroscience, Institute of Physiology, Medical University of Graz, Graz, Austria; [5]Departments of Paediatrics and Psychiatry, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, Vic., Australia; [6]Division of Neuroscience, School of Medicine, University of Dundee, Dundee, UK

A total of 41 case–control studies were identified.

- Several studies examined QoL in ADHD, ASD, intellectual disability, Tourette's disorders and enuresis,

- **But**

- No eligible studies were detected for anxiety disorders, (early onset) schizophrenia and eating disorders

NB: A total of 14 different measures were used in these studies

Quality of Life in Autism

A rather complex question

The Autism Society

When we say "quality of life," we're talking about basic human rights that allow people to interact with one another and the world on their own terms.

- Recreation and Leisure – People with autism should be able to pursue their interests and spend their free time in a meaningful way
- Subjective Well-being – People with autism should feel happy and enjoy life
- Self-Identity and Acceptance – People with autism should understand and appreciate themselves, and feel understood and valued by others
- Autonomy and Self-Sufficiency – People with autism have the right to make their own decisions
- Pursuit of Dreams – People with autism should feel empowered to achieve their aspirations!

The Autism Society

When we say "quality of life," we're talking about basic human rights that allow people to interact with one another and the world on their own terms.

- **Respect and Dignity** – People with autism should feel respected by those around them
- **Inclusion** – People with autism should be welcomed to participate actively in their schools, workplaces and communities
- **Communication** – People with autism should be able to express themselves and interact with others in a meaningful way
- **Health and Well-being** – People with autism should feel and be well physically and have access to the services they need to stay healthy
- **Safety** – People with autism should feel secure and be able to get help from their communities, law enforcement and others as needed

The Autism Society

**When we say "quality of life," we're talking
about basic human rights that allow people to
interact with one another and the world on
their own terms.**

- Academic Success – People with autism should have the opportunity to participate in school to their fullest capability and learn in an environment and manner that enables them to succeed
- Social Connections – People with autism should have friends and supporters as well as ties to their communities
- Independent Living – People with autism have the right to lead their own lives, and they should also have support if they need help caring for themselves
- Meaningful Employment with Fair Wages – People with autism should have the opportunity to do work that contributes to their communities, and should receive compensation befitting their positions
- Financial Stability – People with autism should be able to afford the things and services they need

From a Blog by Bobb

Autism and quality of life

- A recent research publication from overseas says a "study concerning the elderly with autism showed that the difference in quality of life is similar in the elderly. Age, IQ and symptom severity did not predict quality of life in this sample. Across the lifespan, people with autism experience a much lower quality of life compared to people without autism." (see http://aut.sagepub.com/content/19/2/158....).

- Questions that spring to (my) mind are:

- Is it possible for most people with autism spectrum disorder to have a better or even good "quality of life"? [I believe the answer is "yes"]

- Is our community doing enough now to deliver best or better *quality of life* for people with autism spectrum disorder?

- Is sufficient effort going into research to improve *quality of life* for people with autism spectrum disorder?

This is what we mean when we talk about Quality of life

Meta-analysis of QoL in Autism - van Heijst and Geurts 2015
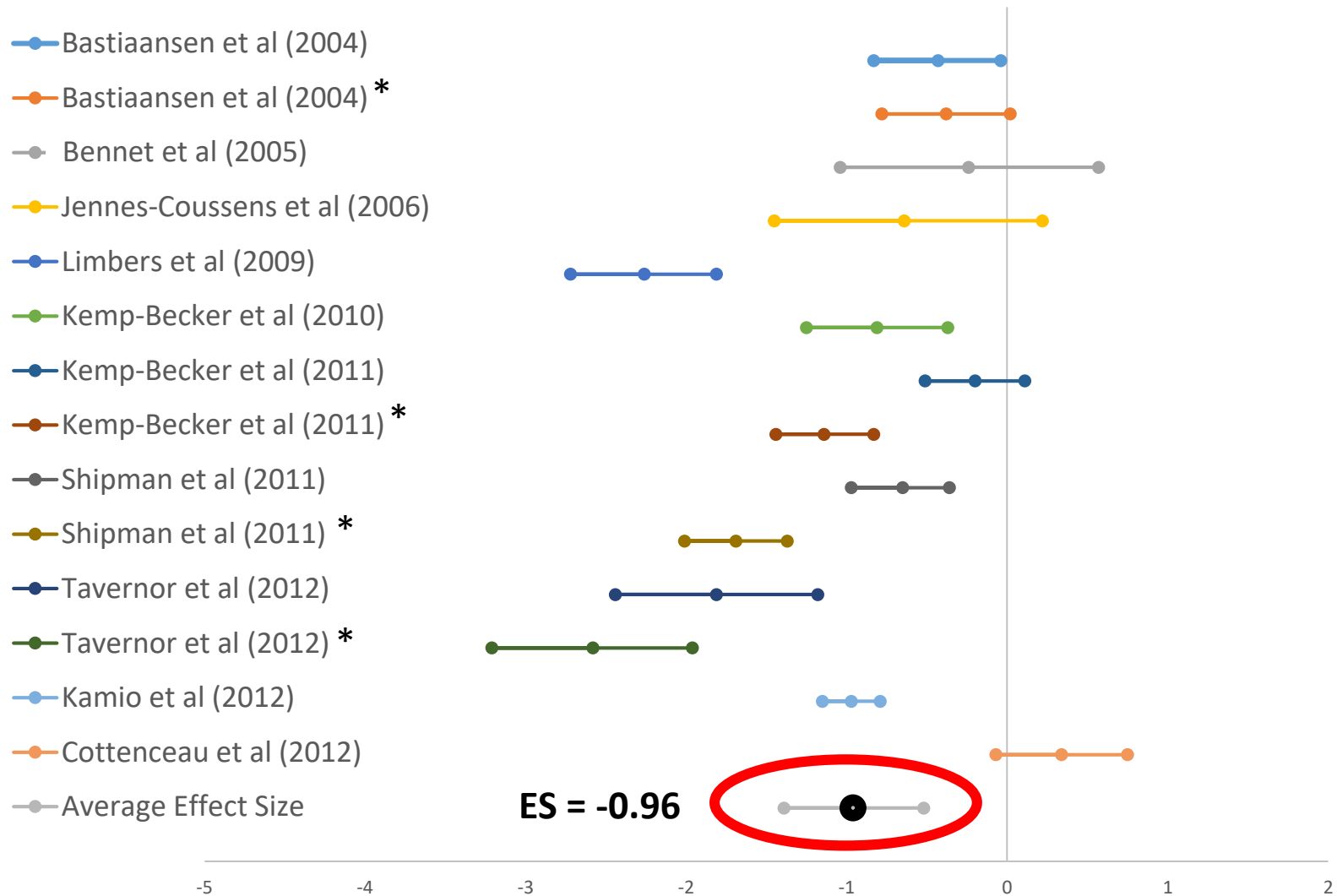
Van Heijst & Geurts (2015)

- Specifically investigated whether age had an effect on QoL – It did not

- They also conducted the first study of QoL in elderly adults with ASD and found the difference in QoL in this group to be similar to other age groups

Which factors are related to QoL in ASD?

Adults

- ↑ Behaviour Problems
- ↓ Leisure activities

Children

- Severity of autism
- ↑ Age
- ↑ Behaviour problems
- ↓ Social Skills
- ↓ Adaptive Behaviour
- ↓ Education
- ↑ Comorbid Psychiatric Conditions

Hsu-Min & Wineman (2014)

Predictors of QoL for Autistic Adults

- Younger adults reported better QoL than older
- Females reported better *social* QoL than males
- Males reported better *physical* QoL than females
- Positive Predictors of QoL were:
  - Being employes (physical)
  - Receiving support (social and environmental)
  - Being in a relationship (social)

But as with all of these studies cant tell the direction of impact

Mason et al (2018)

Predictors of QoL for Autistic Adults

Sample composition (N=
- 54% Male
- 95% had capacity to self report
- 41% in a relationship
- 50% received support
- 36% Currently employed
- 42% Had a degree
- 71% Current Mental health diagnosis
- 70% Current Physical health diagnosis

Mason et al (2018)

HR-QoL of parents of school age children with Asperger syndrome or high functioning autism

Alik, Larsson & Smedje 2006
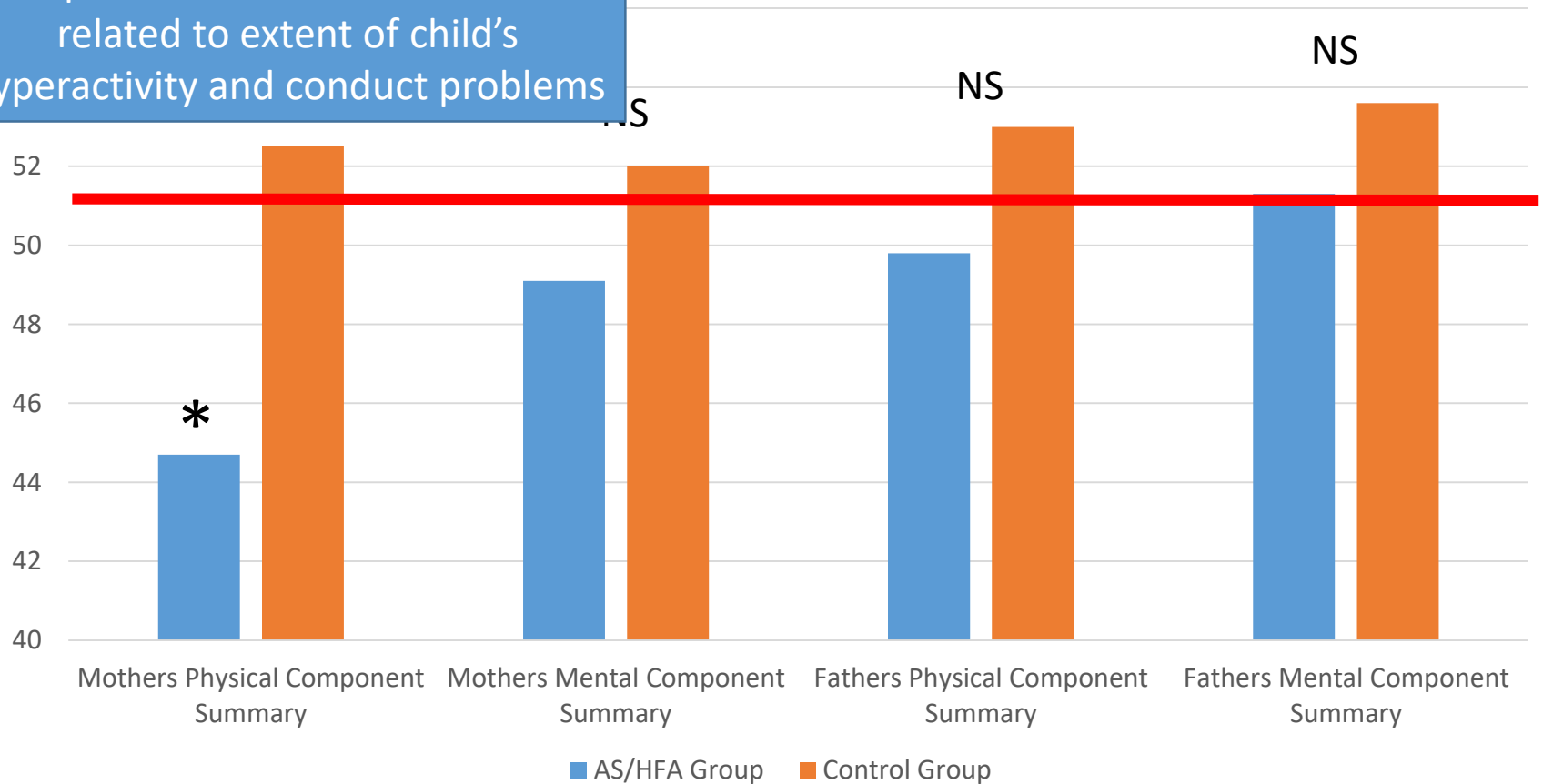
QoL in Autism
How should we look at it?

- The potential for complex interactions between core symptoms – particularly with regards:

  "**Persistent deficits in social communication and social interaction across multiple contexts**"

- Probably also a greater emphasis on 'normalizing' with the autistic community

  Bobb – "Is it possible for most people with autism spectrum disorder to have a better or even good "quality of life"? [I believe the answer is "yes"]"

QoL in ADHD

Self-reported quality of life in children with attention-deficit hyperactivity disorder, as compared to healthy controls

Study or subgroup	ADHD Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Std. mean difference IV, Random, 95% CI
Jafari 2011	62.39	17.2	72	78.5	12.8	140	12.1%	−1.11 [−1.42, −0.81]
Varni and Burwinkle 2006	70.17	18.28	72	84.29	12.56	3256	14.3%	−1.11 [−1.35, −0.88]
Coghill and Hodgkins 2015	71.5	17.5134	174	88	18.3883	106	13.7%	−0.92 [−1.18, −0.67]
Pongwilairat 2005	1,508.69	312.25	46	1,779.25	322.61	94	10.2%	−0.84 [−1.21, −0.48]
Kandemir 2014	72.13	15.02	76	83.35	13.1	59	10.6%	−0.78 [−1.14, −0.43]
Marques 2013	69.15	15.8984	45	79.28	9.3116	43	8.5%	−0.77 [−1.20, −0.33]
Thaulow and Jozefiak 2012	73.6	14.9	62	82	13.5	65	10.5%	−0.59 [−0.94, −0.23]
Patrick 2002	75.19	12.2044	68	82.2	12.2782	116	12.0%	−0.57 [−0.87, −0.26]
Göker 2011	75.1	15.8	50	79.6	10.5	30	8.1%	−0.32 [−0.77, 0.14]
Total (95% CI)			**665**			**3909**	**100.0%**	**−0.81 [−0.98, −0.64]**

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 18.76$, $df = 8$ ($p = .02$); $I^2 = 57\%$
Test for overall effect: $Z = 9.50$ ($p < .00001$)

Favours healthy controls   Favours ADHD

Figure 2 Self-reported quality of life in children with attention-deficit hyperactivity disorder, as compared to healthy controls [Colour figure can be viewed at wileyonlinelibrary.com]

Self Report SMD = -0.81

Parent-reported quality of life in children with attention-deficit hyperactivity disorder, as compared to healthy controls

Study or subgroup	ADHD Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Std. mean difference IV, Random, 95% CI
Thaulow and Jozefiak 2012	62.5	13.8	62	89.7	9.4	65	9.5%	−2.30 [−2.75, −1.85]
Escobar 2005	38.3	7.5	120	53.2	5.7	120	10.2%	−2.23 [−2.55, −1.91]
Marques 2013	67.1	14.8251	45	88.64	8.4591	43	9.2%	−1.76 [−2.25, −1.26]
Yang 2007	34.48	10.26	119	49.87	7.56	129	10.4%	−1.71 [−2.00, −1.42]
Coghill and Hodgkins 2015	61.8	17.2232	206	88.2	18.8786	110	10.5%	−1.48 [−1.74, −1.22]
Göker 2011	56.7	15.6	50	76.9	16.3	30	9.2%	−1.26 [−1.76, −0.77]
Jafari 2011	57.06	14.67	72	73.47	17.1	140	10.3%	−1.00 [−1.30, −0.70]
Kandemir 2014	69.06	14.32	76	81.92	13.15	59	10.0%	−0.93 [−1.28, −0.57]
Pongwilairat 2005	1,362.5	296.26	46	1,609.04	362.43	94	10.0%	−0.72 [−1.08, −0.35]
Varni and Burwinkle 2006	69.5	16.17	69	79.87	16.24	3251	10.6%	−0.64 [−0.88, −0.40]
Total (95% CI)			**865**			**4041**	**100.0%**	**−1.39 [−1.76, −1.02]**

Heterogeneity: $\tau^2 = 0.32$; $\chi^2 = 110.85$, $df = 9$ ($p < .00001$); $I^2 = 92\%$
Test for overall effect: $Z = 7.37$ ($p < .00001$)

Favours healthy controls Favours ADHD

Figure 3 Parent-reported quality of life in children with attention-deficit hyperactivity disorder, as compared to healthy controls [Colour figure can be viewed at wileyonlinelibrary.com]

Parent Report SMD = -1.39

Pearson R as a measure of the correlation between study outcomes

- Pearson correlation coefficient (R) is a measure of the strength of a linear relationship between paired data
  - Ranges from 0 (no correlation) to ±1 (perfect correlation)

| 0.8 | 0.4 | 0 | −0.4 | −0.8 |
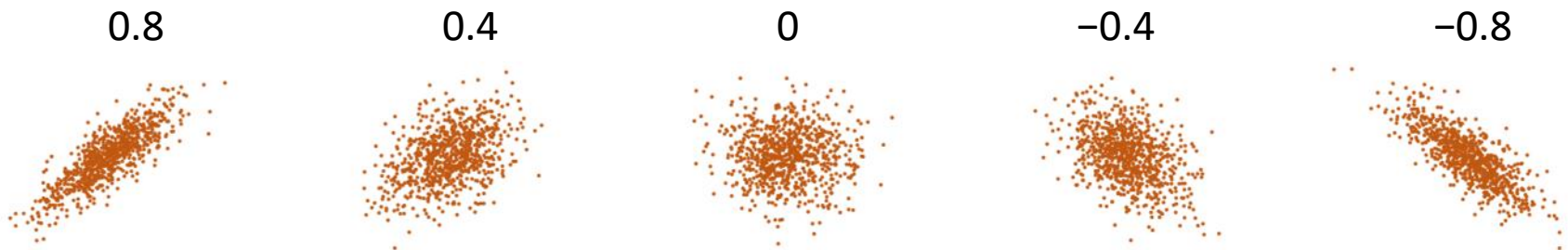
- The following tables use shading to show the strength of R

None	Weak	Moderate	Strong	Very strong	Perfect
0.0	0.2	0.4	0.6	0.8	1.0

Correlations between parent/carer and child ratings of HRQoL measurements - Coghill & Hodgkins 2015

PedsQL	Physical functioning	Emotional functioning	Social functioning	School functioning	Total score
All children (n = 335)	0.357***	0.439***	0.080	0.097	0.546***
ADHD (n = 199)	0.289***	0.365***	0.081	0.107	0.440***
T1DM (n = 51)	0.518***	0.395***	0.313*	0.500***	0.616***
Control (n = 117)	0.231*	0.280**	0.162	0.322**	0.290**
Age group:					
6 to <11 years (n = 138)	0.279***	0.390***	0.385***	0.497***	0.453***
≥11 years (n = 222)	0.405***	0.475***	0.102	0.113	0.593***

CHIP-CE	Satisfaction	Comfort	Resilience	Risk avoidance	Achievement
All children (n = 339)	0.274***	0.302***	0.310***	0.647***	0.517***
ADHD (n = 205)	0.380***	0.325***	0.283***	0.534***	0.442***
T1DM (n = 54)	0.466**	0.491**	0.320*	0.648***	0.540***
Control (n = 116)	0.146	0.188*	0.205*	0.333***	0.417***
Age group:					
6 to <11 years (n = 142)	0.122	0.220*	0.188*	0.483***	0.413***
≥11 years (n = 231)	0.348***	0.394***	0.356***	0.719***	0.558***

Self-reported results on the PedsQL across childhood mental disorders vs healthy controls

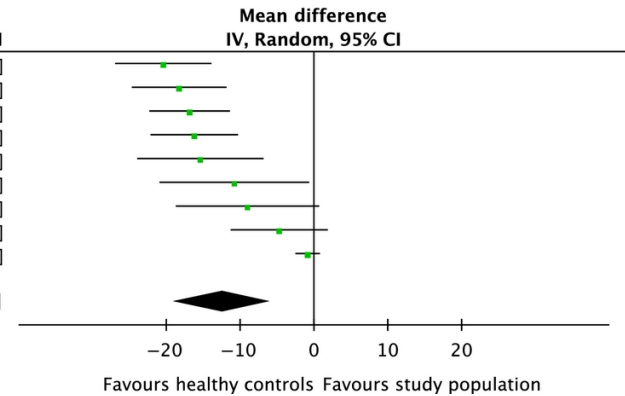| Study or subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
SLEEP–DISORDERED BREATHING (Crabtree 2004)	74.75	19.5	40	89.72	15.6	31	5.1%	−14.97 [−23.14, −6.80]
ASD (Potvin 2015)	71.12	17.31	30	85.22	10.65	31	5.9%	−14.10 [−21.34, −6.86]
ADHD (Jafari 2011)	66.41	20.23	72	79.9	15.55	140	8.2%	−13.49 [−18.83, −8.15]
ADHD (Coghill and Hodgkins 2015)	78.3	15.8291	174	89.3	18.5321	106	9.9%	−11.00 [−15.24, −6.76]
ENURESIS (Kilicoglu 2014)	72.79	18.17	82	81.11	12.77	93	9.2%	−8.32 [−13.03, −3.61]
TOURETTE (Hao 2010)	81.57	12.59	424	87.34	11.97	1583	14.6%	−5.77 [−7.11, −4.43]
ADHD (Varni and Burwinkle 2006)	82.63	17.47	72	88.02	13.26	3256	10.2%	−5.39 [−9.45, −1.33]
ID (Golubovic 2013)	80.6	18.52	67	84.17	11.74	122	8.9%	−3.57 [−8.47, 1.33]
ADHD (Göker 2011)	75.2	18.6	50	78.7	16	30	5.5%	−3.50 [−11.20, 4.20]
ADHD (Kandemir 2014)	77.53	16.85	76	80.33	18.13	59	7.3%	−2.80 [−8.78, 3.18]
ADHD (Marques 2013)	78.56	16.1668	45	80.88	10.4263	43	7.8%	−2.32 [−7.98, 3.34]
ENURESIS (Al–Zaben and Sehlo 2015)	80.45	14.7542	43	81.3	12.2696	40	7.5%	−0.85 [−6.67, 4.97]
Total (95% CI)			**1175**			**5534**	**100.0%**	**−6.90 [−9.14, −4.65]**

Heterogeneity: $\tau^2 = 8.54$; $\chi^2 = 30.27$, $df = 11$ ($p = .001$); $I^2 = 64\%$
Test for overall effect: $Z = 6.03$ ($p < .00001$)

Physical Functioning

Mean difference IV, Random, 95% CI. Favours healthy controls — Favours study popualtion

Study or subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
SLEEP–DISORDERED BREATHING (Crabtree 2004)	57	23.1	40	75.97	24.2	31	5.5%	−18.97 [−30.10, −7.84]
ADHD (Coghill and Hodgkins 2015)	68.9	22.4245	174	85.2	24.7095	106	12.2%	−16.30 [−22.06, −10.54]
ADHD (Varni and Burwinkle 2006)	65.27	25.74	72	79.54	18	3256	11.8%	−14.27 [−20.25, −8.29]
ADHD (Jafari 2011)	54.79	25.02	72	68.85	20.37	140	10.6%	−14.06 [−20.75, −7.37]
TOURETTE (Hao 2010)	74.17	16.21	424	83	14.97	1583	20.9%	−8.83 [−10.54, −7.12]
ENURESIS (Al–Zaben and Sehlo 2015)	73.7	22.0986	43	81.5	10.9415	40	9.4%	−7.80 [−15.22, −0.38]
ADHD (Marques 2013)	63.33	20.3929	45	70.66	16.787	43	8.9%	−7.33 [−15.12, 0.46]
ID (Golubovic 2013)	71.87	20.45	67	76.97	14.38	122	12.7%	−5.10 [−10.62, 0.42]
ADHD (Göker 2011)	71	22.9	50	72.8	16	30	7.9%	−1.80 [−10.35, 6.75]
Total (95% CI)			**987**			**5351**	**100.0%**	**−10.23 [−13.23, −7.24]**

Heterogeneity: $\tau^2 = 10.41$; $\chi^2 = 19.00$, $df = 8$ ($p = .01$); $I^2 = 58\%$
Test for overall effect: $Z = 6.70$ ($p < .00001$)

Emotional Functioning

Mean difference IV, Random, 95% CI. Favours healthy controls — Favours study population

Self-reported results on the PedsQL across childhood mental disorders vs healthy controls

Social Functioning

Study or subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
ADHD (Varni and Burwinkle 2006)	65.55	28.12	72	85.95	16.49	3256	11.3%	−20.40 [−26.92, −13.88]
ADHD (Jafari 2011)	66.11	24.88	72	84.37	17.19	140	11.4%	−18.26 [−24.67, −11.85]
ID (Golubovic 2013)	76.94	21.9	67	93.77	8.61	122	11.7%	−16.83 [−22.29, −11.37]
ADHD (Coghill and Hodgkins 2015)	75	22.4245	174	91.2	25.7391	106	11.5%	−16.20 [−22.13, −10.27]
ADHD (Marques 2013)	65.77	26.6316	45	81.16	11.9345	43	10.5%	−15.39 [−23.95, −6.83]
SLEEP−DISORDERED BREATHING (Crabtree 2004)	73.25	23.2	40	84.03	20.3	31	9.8%	−10.78 [−20.92, −0.64]
ENURESIS (Al−Zaben and Sehlo 2015)	73.7	26.6888	43	82.7	17.8985	40	10.0%	−9.00 [−18.72, 0.72]
ADHD (Göker 2011)	83.3	18.2	50	88	11.8	30	11.3%	−4.70 [−11.28, 1.88]
TOURETTE (Hao 2010)	89.19	16.03	424	90.04	12.85	1583	12.6%	−0.85 [−2.50, 0.80]
Total (95% CI)			**987**			**5351**	**100.0%**	**−12.42 [−19.00, −5.83]**

Heterogeneity: $\tau^2 = 88.63$; $\chi^2 = 101.32$, $df = 8$ ($p < .00001$); $I^2 = 92\%$
Test for overall effect: $Z = 3.70$ ($p = .0002$)

Favours healthy controls Favours study population

School Functioning

Study or subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
ADHD (Coghill and Hodgkins 2015)	61	22.4245	174	86	25.7391	106	11.3%	−25.00 [−30.93, −19.07]
SLEEP−DISORDERED BREATHING (Crabtree 2004)	61	20.7	40	85	14.5	31	9.4%	−24.00 [−32.20, −15.80]
ADHD (Varni and Burwinkle 2006)	59.76	21.23	72	81.5	16.1	3256	12.1%	−21.74 [−26.67, −16.81]
ADHD (Marques 2013)	63.22	18.5146	45	83.95	12.328	43	10.7%	−20.73 [−27.28, −14.18]
ADHD (Jafari 2011)	59.86	25.23	72	80.03	19.04	140	10.7%	−20.17 [−26.80, −13.54]
TOURETTE (Hao 2010)	70.35	16.96	424	85.21	13.25	1583	14.1%	−14.86 [−16.60, −13.12]
ADHD (Göker 2011)	71.1	19.3	50	78.9	13.8	30	10.1%	−7.80 [−15.08, −0.52]
ENURESIS (Al−Zaben and Sehlo 2015)	75.43	23.7379	43	82.44	12.7124	40	9.4%	−7.01 [−15.13, 1.11]
ID (Golubovic 2013)	75.45	17.23	67	81.64	13.61	122	12.2%	−6.19 [−10.97, −1.41]
Total (95% CI)			**987**			**5351**	**100.0%**	**−16.37 [−20.60, −12.15]**

Heterogeneity: $\tau^2 = 32.18$; $\chi^2 = 48.10$, $df = 8$ ($p < .00001$); $I^2 = 83\%$
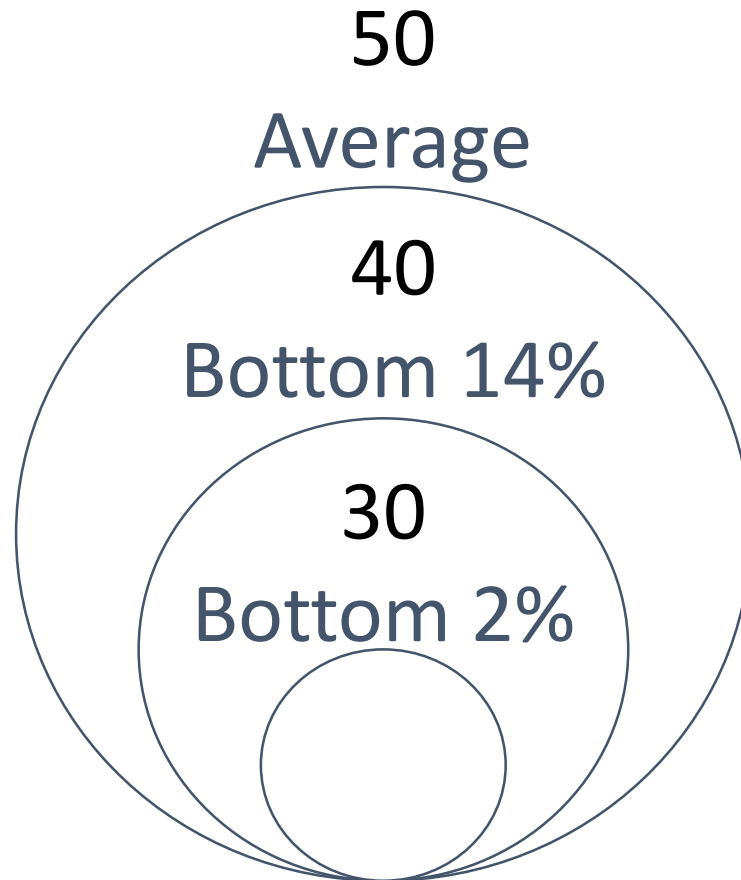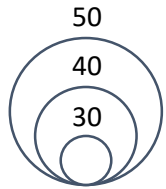Test for overall effect: $Z = 7.59$ ($p < .00001$)
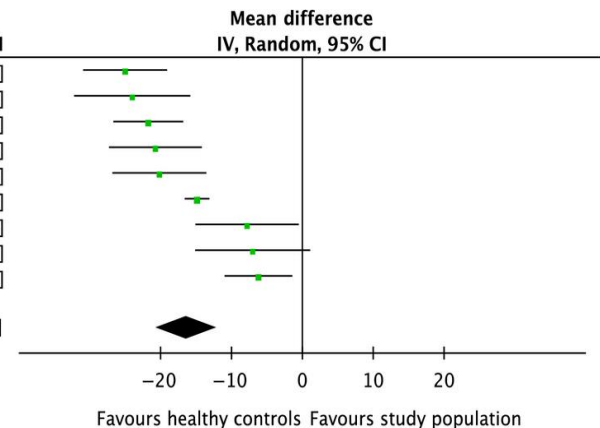
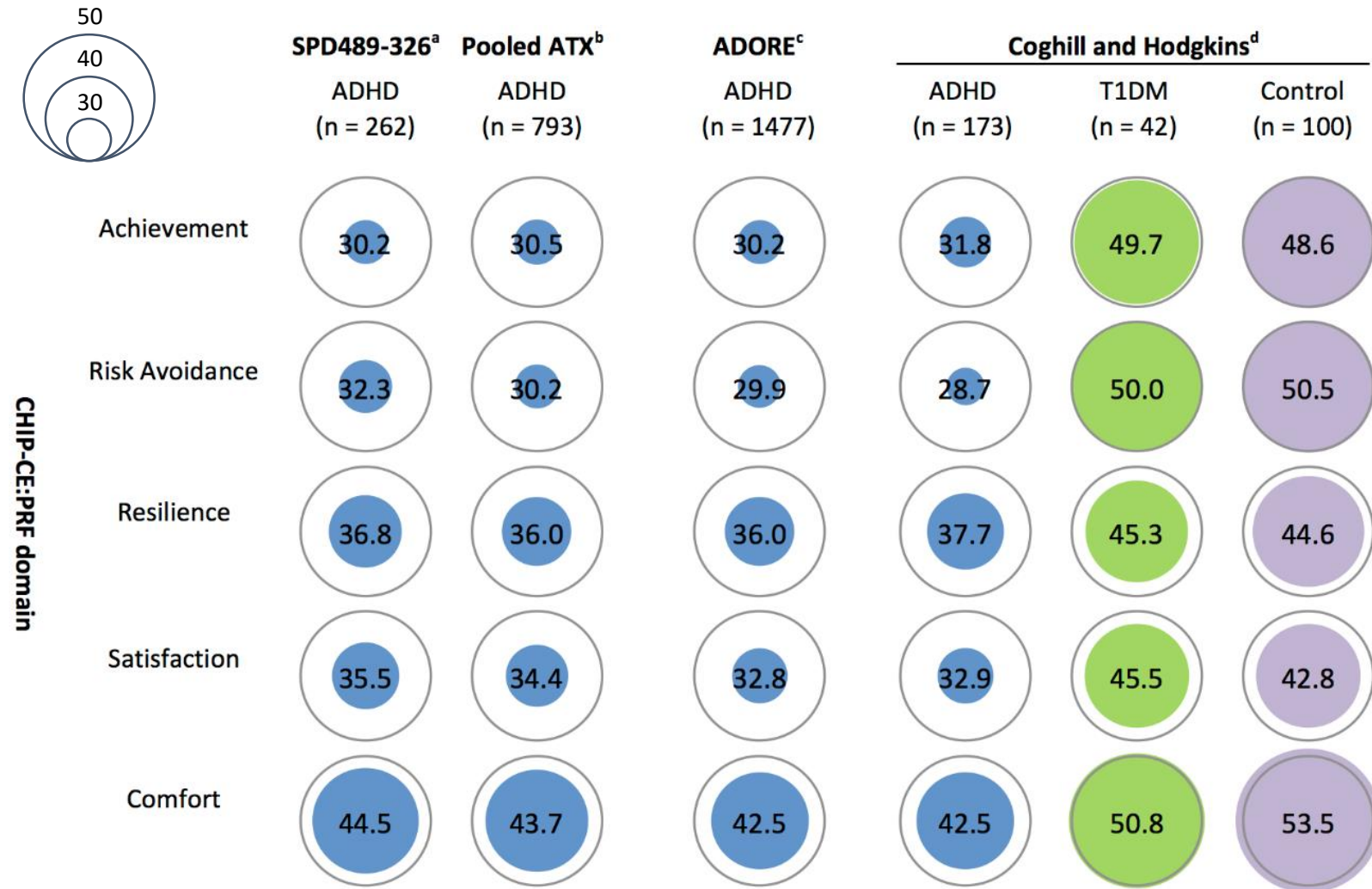Favours healthy controls Favours study population

ADHD IS IMPAIRING

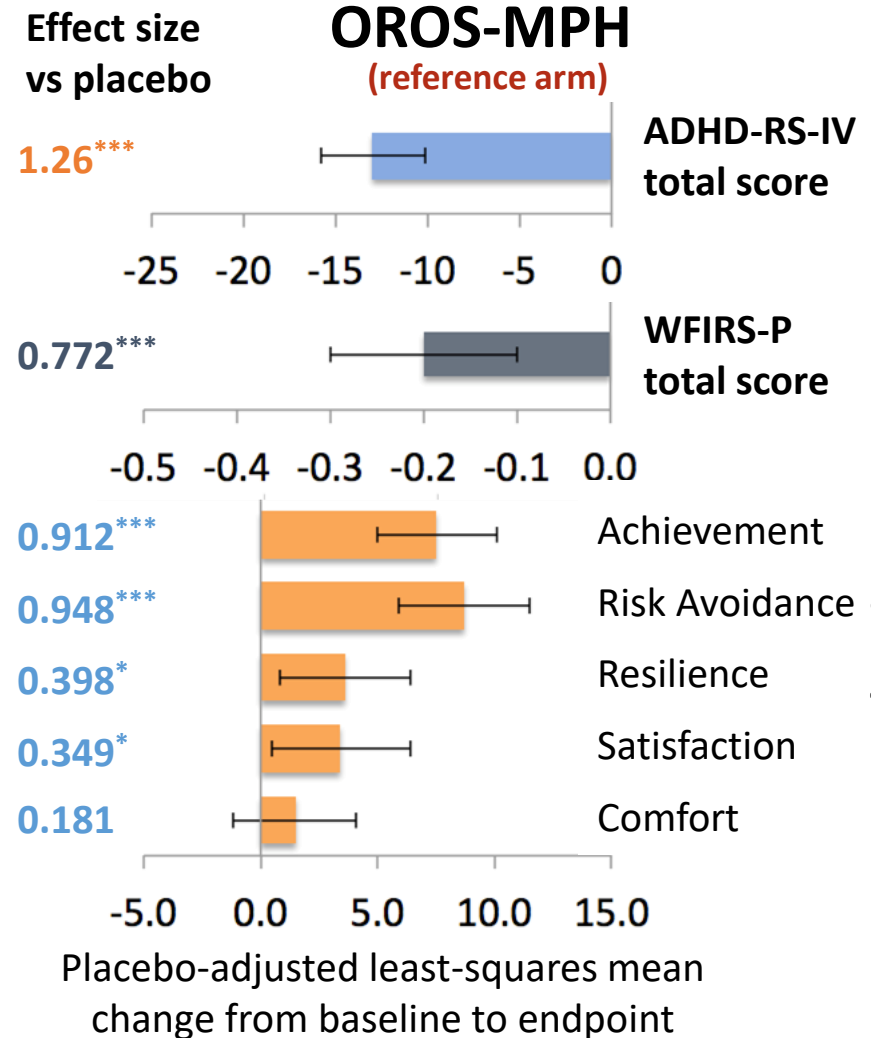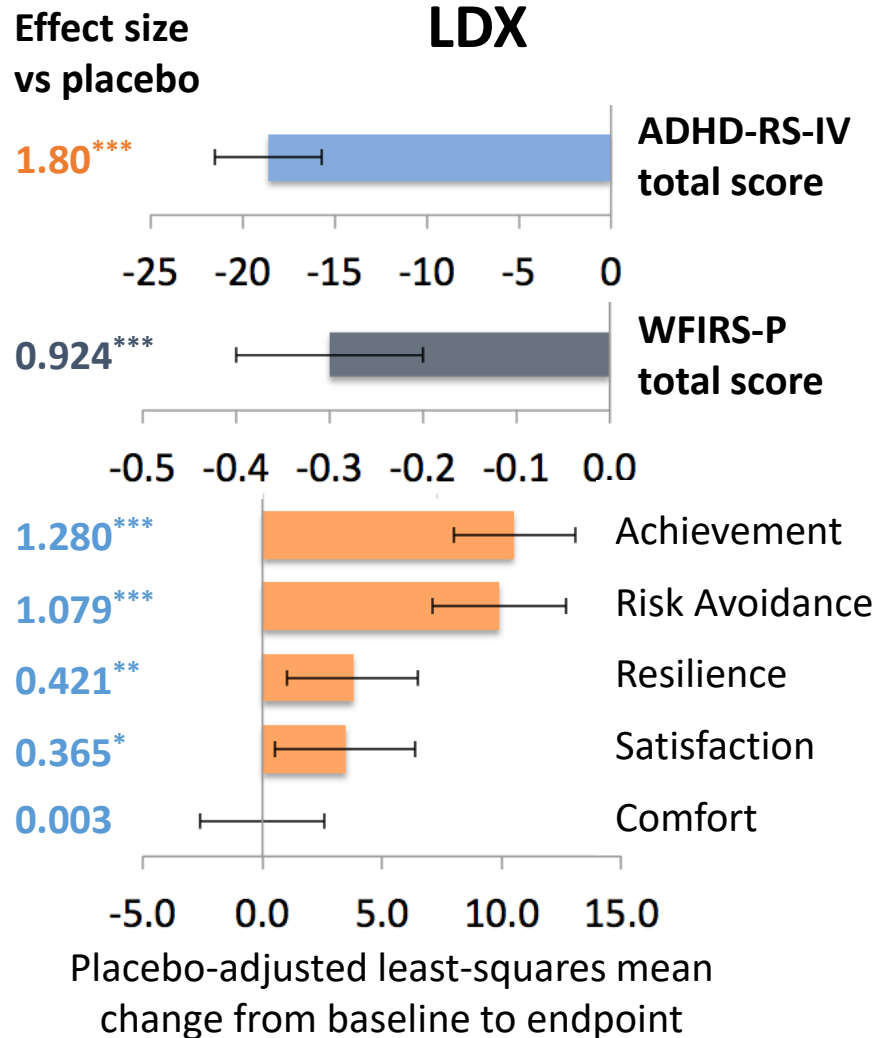Pre-treatment T-scores for Quality of Life in four ADHD study populations and controls

ADHD IS IMPAIRING

Pre-treatment T-scores for Quality of Life in four ADHD study populations and controls

| | SPD489-326[a] ADHD (n = 262) | Pooled ATX[b] ADHD (n = 793) | ADORE[c] ADHD (n = 1477) | Coghill and Hodgkins[d] | | |
				ADHD (n = 173)	T1DM (n = 42)	Control (n = 100)
Achievement	30.2	30.5	30.2	31.8	49.7	48.6
Risk Avoidance	32.3	30.2	29.9	28.7	50.0	50.5
Resilience	36.8	36.0	36.0	37.7	45.3	44.6
Satisfaction	35.5	34.4	32.8	32.9	45.5	42.8
Comfort	44.5	43.7	42.5	42.5	50.8	53.5

CHIP-CE:PRF domain

CHIP CE Domains

SPD489-325 published outcomes: symptoms, functioning and HRQoL

LDX

Effect size vs placebo

- 1.80*** ADHD-RS-IV total score
- 0.924*** WFIRS-P total score

(axis: -25 -20 -15 -10 -5 0)
(axis: -0.5 -0.4 -0.3 -0.2 -0.1 0.0)

CHIP-CE:PRF domain T-score

- 1.280*** Achievement
- 1.079*** Risk Avoidance
- 0.421** Resilience
- 0.365* Satisfaction
- 0.003 Comfort

(axis: -5.0 0.0 5.0 10.0 15.0)

Placebo-adjusted least-squares mean change from baseline to endpoint

OROS-MPH
(reference arm)

Effect size vs placebo

- 1.26*** ADHD-RS-IV total score
- 0.772*** WFIRS-P total score

(axis: -25 -20 -15 -10 -5 0)
(axis: -0.5 -0.4 -0.3 -0.2 -0.1 0.0)

CHIP-CE:PRF domain T-score

- 0.912*** Achievement
- 0.948*** Risk Avoidance
- 0.398* Resilience
- 0.349* Satisfaction
- 0.181 Comfort

(axis: -5.0 0.0 5.0 10.0 15.0)

Placebo-adjusted least-squares mean change from baseline to endpoint

*p < 0.05, **p < 0.01, ***p < 0.001 versus placebo (nominal except for LDX ADHD-RS-IV and Achievement)
Banaschewski T et al. CNS Drugs 2013;27:829–40; Coghill D et al. Eur Neuropsychopharmacol 2013;23:1208–18

Post hoc Pearson correlation coefficients for changes in symptoms, functioning and HRQoL

Symptoms

Functional impairment

ADHD-RS-IV total score

WFIRS-P total score

SPD489-325 **ADHD-RS-IV vs WFIRS-P**	
LDX	OROS-MPH
0.51	0.49

- All correlations were weak to moderate
- CHIP-CE:PRF correlations were strongest in Achievement and Risk Avoidance

SPD489-325 **ADHD-RS-IV vs CHIP-CE:PRF**		
LDX	OROS-MPH	
−0.36	−0.48	Achievement
−0.44	−0.42	Risk Avoidance
−0.29	−0.01	Resilience
−0.25	−0.31	Satisfaction
−0.39	−0.31	Comfort

SPD489-325 **WFIRS-P vs CHIP-CE:PRF**		
	LDX	OROS-MPH
Achievement	−0.65	−0.59
Risk Avoidance	−0.62	−0.62
Resilience	−0.37	−0.24
Satisfaction	−0.50	−0.44
Comfort	−0.42	−0.33

HRQoL

CHIP-CE:PRF domain T-scores

Shading key					
0.0	0.2	0.4	0.6	0.8	1.0

Shading indicates value of Pearson R; grey text indicates descriptive $p > 0.05$

52

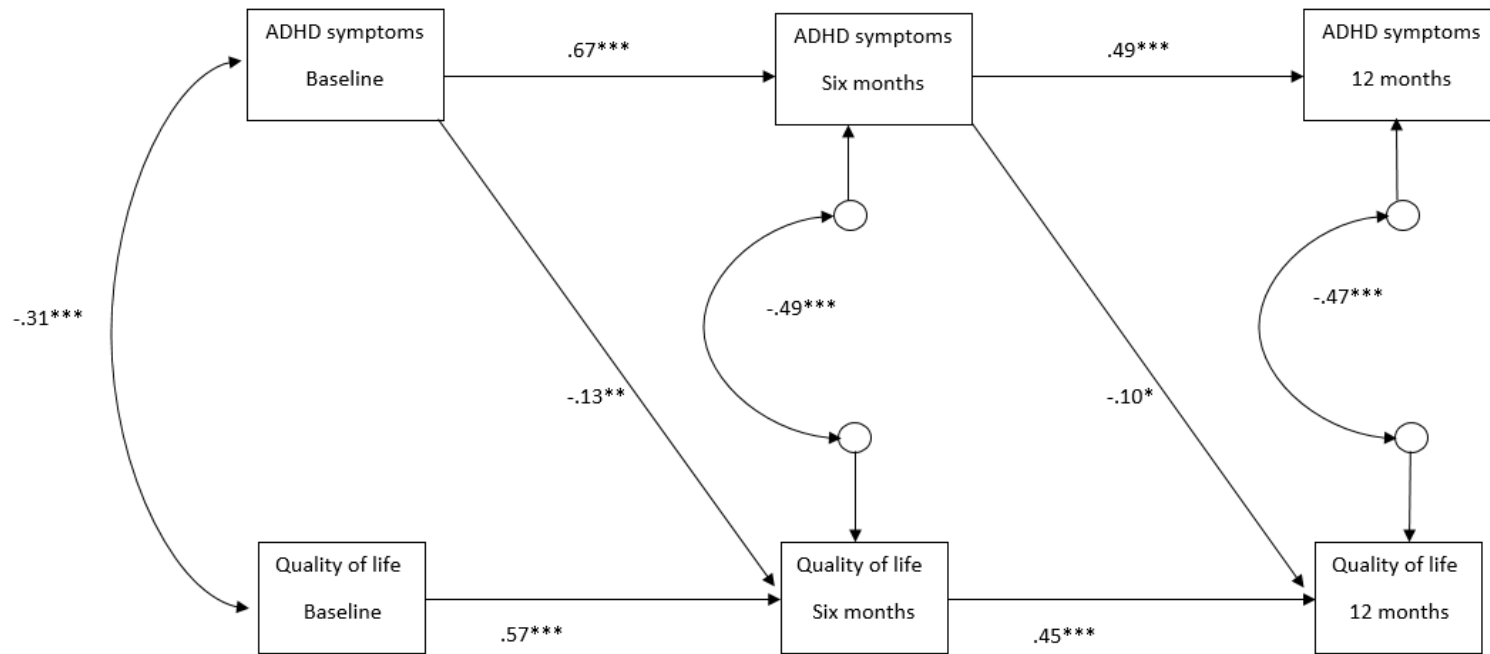# Relationship between ADHD symptoms and QoL

Figure 1. Standardized parameter estimates from the final model for the relations between parent-reported ADHD symptoms and psychosocial quality of life across a 12 month period.

The presence of sleep problems moderated the relationship between parent-reported ADHD symptoms and QoL so that ADHD symptoms predicted later QoL for children with no/mild sleep problems but not for children with moderate/severe sleep problems.

Cognition, symptoms and QoL
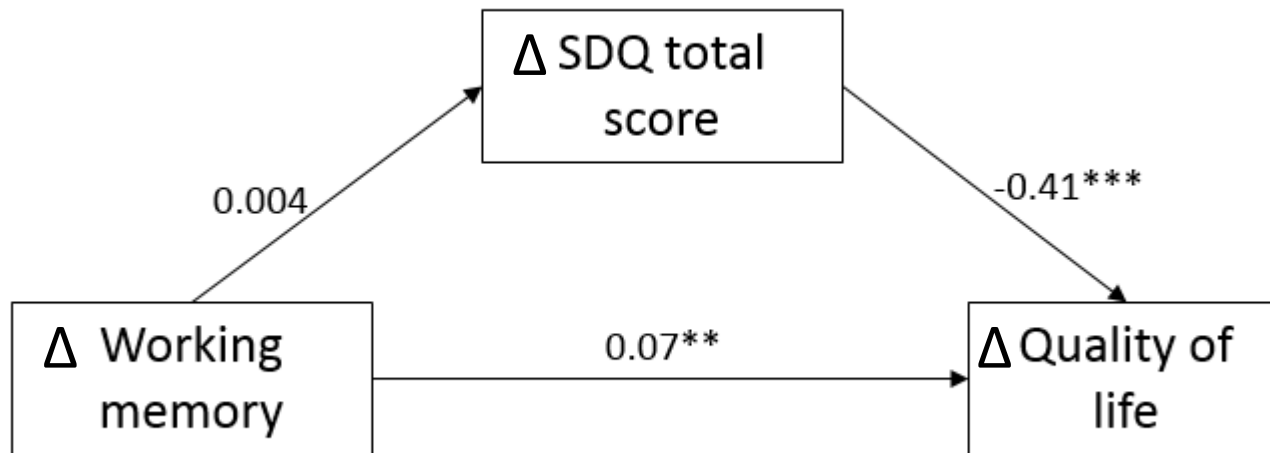
Data from a longitudinal study with time interval of 2 years

Ongoing Challenges (Jonsson et al 2017

1. There are still major gaps in the literature in terms of non- and under investigated childhood disorders and their QoL profiles
   - Non NDD
   - Head to Head studies

2. There is a nontrivial risk of bias in available studies
   - Under representation of females
   - Family composition
   - Other social/sociodemographic variables
   - Comorbidities

3. The generalizability of the results across contexts and heterogeneous diagnostic groups is unclear
   - E.g. clinical vs population samples

4. There are several threats to the validity of the measurements of QoL.
   - What do QoL measures actually measure?
   - Perhaps link with EMA

Clinical Relevance

- Impact of ADHD on Quality of Life is very significant and consistent

- It does however vary across domains

- ADHD symptoms are one, but not the only factor impacting on QoL

- Treatment can improve QoL along with symptoms and functioning <u>but</u> these are not strongly correlated which suggests that treatments should aim not only to relieve symptoms, but also to reduce functional impairment and improve HRQoL

Quality of Life should be considered as a core outcome for clinical work

- As an adjunct to assessment

- When setting treatment baseline

- Monitoring progress