Take home message

• ADHD is a disorder of brain development with a strong genetic loading
• Environmental and GxE factors play additional roles
• ADHD is a very persistent disorder, 24 hours/day
• It is important to identify and treat ADHD as a disorder on its own and as a risk factor for other disorders
• A comprehensive treatment approach includes a combination of medical and psychological interventions
• Treatment should be
  – Systematic
  – 24 hours / day
  – Long-term

ADHD - Core Symptom Areas

Inattention

• Difficulty organizing
• Avoids tasks requiring sustained attention
• Loses things
• Easily distracted
• Forgetful

Impulsivity/Hyperactivity

• Blurs out answer before question is finished
• Difficulty awaiting turn
• Intermits or intrudes on others

ADHD: DSM-IV Criteria

• Inattention to details/makes careless mistakes
• Difficulty sustaining attention
• Seems not to listen
• Fails to finish tasks

• Difficulty organizing
• Avoids tasks requiring sustained attention
• Loses things
• Easily distracted
• Forgetful

• Blurs out answer before question is finished
• Difficulty awaiting turn
• Intermits or intrudes on others

• Fidgets
• Unable to stay seated
• Inappropriate running/climbing (restlessness)
• Difficulty in engaging in leisure activities quietly
• “On the go”
• Talks excessively
**Core Symptoms of ADHD**

- must be more severe than those seen in other children of the same age
- must be more severe than those seen in other children with the same developmental level
- must be present in several settings (eg family, school)
- must create serious problems in everyday life
- will change with age and can be life-long

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**Mortality in ADHD versus non-ADHD**

![Graph showing mortality rates in ADHD versus non-ADHD](image)

Dalsgaard et al. Lancet 2015. [Link](http://dx.doi.org/10.1016/S0140-6736(14)61683-6)

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**Mortality in ADHD versus non-ADHD**

![Graph showing adjusted mortality rates in ADHD](image)

Dalsgaard et al. Lancet 2015. [Link](http://dx.doi.org/10.1016/S0140-6736(14)61683-6)

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**Mortality in ADHD versus non-ADHD -mechanisms**

- Suicide
- Crime
- Substance misuse
- Accidents
- Fighting
- Emotional lability
- Poor health habits
- Hulk behavior

![Diagram showing pathways to premature death](image)

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**Core Symptoms of ADHD**

...but they can also have many strengths

- they can be open-minded
- they can be excitable
- they can be full of energy
- they can often joke around

They can be extremely intelligent

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CLINICAL PICTURE

INFANTS/ TODDLERS (1-3 years)
- Temperamental variation, regulatory disturbances and limited social adaptation in combination with parent/child interaction

Possible precursor to ADHD

PRESCHOOLERS (3-6 years)
- Reduced play intensity and duration
- Motor restlessness
- Associated problems and implications
  - Developmental deficits
  - Oppositional defiant behaviour
  - Problems of social adaptation

CLINICAL PICTURE

PRIMARY SCHOOL CHILDREN (6-12 years)
- Distractability
- Motor Restlessness
- Impulsive and disruptive behaviour
- Associated problems and implications
  - Specific learning disorders
  - Low self-esteem
  - Repetition of classes/grades
  - Rejection by peers
  - Impaired family relationships

Course of ADHD into Adolescence
- Symptoms of hyperactivity ↓
- Symptoms of inattention – or ↑
- School failure becomes an issue
  - Higher cognitive demands, multi-tasking
  - Adolescent is expected to be an independent student
  - Less structure in secondary school
  - More homework
- Social functioning is more complex
  - Complexity of friendships/relationships
  - Parents can no longer fully monitor their child
  - Time management issues

Impairment through the lifespan

<table>
<thead>
<tr>
<th>Childhood</th>
<th>Adolescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulties at school</td>
<td>Becomes Underachievement, no high school graduation</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>Becomes Carelessness, substance abuse, unwanted pregnancy</td>
</tr>
<tr>
<td>Repetitive failure</td>
<td>Becomes Hopelessness, frustration, depression, anxiety</td>
</tr>
<tr>
<td>ODD</td>
<td>Becomes Criminal involvement</td>
</tr>
<tr>
<td>Multiple injuries</td>
<td>Becomes Risk taking, accidental injuries</td>
</tr>
</tbody>
</table>

18 years and older
- Residual symptoms
- Associated problems
  - Other mental disorders
  - Antisocial behaviour/delinquency
  - Lack of achievement in academic and professional career
Is ADHD in Adults a Valid Diagnosis?

Comorbidity and Neuropsych Deficits

Family- Genetic Studies

SYNDROMATIC CONTINUITY

Imaging Studies

Treatment Effectiveness

Impairments

Revisiting the Role of the Prefrontal Cortex in ADHD (Halperin et al. 2006, 2008)

Cortical dysfunction (PFC)
- Secondary
- Compensatory

Clinical severity

Course

Subcortical dysfunction (dopamine, noradrenaline)
- Automatic processing
- Less effortful processing

Early onset

Enduring

Onset versus Persistence vs Remission

Genes, E GxE

Remission

Genes, E GxE

Persistence

Onset

Dynamics of Genetic and Environmental Risk Factors

Chang et al. JAMA Psychiatry 2013

Executive function and developmental disorders: the flip side of the coin

Mark H. Johnson

Centre for Brain and Cognitive Development, Department of Psychology, Birkbeck College, Henry Wellcome Building, Malet Street, London WC1E 7HX, UK

With improvements in executive function (EF), contrary to the prevailing view, I suggest that, within populations at-risk, the association with EF is found because individuals with strong EF skills are better able to compensate for atypicalities in other brain systems early in life, and are therefore less likely to receive a diagnosis later in life.

Trends In Cognitive Sciences, 2012
Onset versus Persistence vs Remission

Different factors that influence onset and that influence remission

Genes, E GxE

Persisten

Onset

Genes, E GxE

Remission

Representative birth cohort of 1,037 individuals born in Dunedin, New Zealand, in 1972 and 1973 and followed to age 38, with 95% retention.

Symptoms of ADHD, associated clinical features, comorbid disorders, neuropsychological deficits, ADHD polygenic risk, and life impairment indicators were assessed. Data sources were participants, parents, teachers, informants, neuropsychological test results, and administrative records. Adult ADHD diagnoses used DSM-5 criteria, apart from onset age and cross-setting corroboration.

Two samples defined: childhood ADHD and adult ADHD

Follow-forward and follow-backward analyses of ADHD

The childhood ADHD and adult ADHD groups comprised virtually nonoverlapping sets; 90% of adult ADHD cases lacked a history of childhood ADHD.

The adult ADHD group did not show tested neurocognitive deficits in childhood or adulthood, nor did they show polygenic risk for childhood ADHD.

At least 2 studies reported similar findings (Agnew-Blais JAMA Psychiatry 2016 1:73(7):713-20; Caye et al. JAMA Psychiatry 2016 73(7):705-12).

Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence From a Four-Decade Longitudinal Cohort Study

Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence From a Four-Decade Longitudinal Cohort Study

Am J Psychiatry 2015

Terrie E. Moffitt, Ph.D., Renate-Houts, Ph.D., Philip Asherson, M.D., Daniel W. Belsky, Ph.D., David L. Corcoran, Ph.D., Maggie Hammett, B.A., Honalaye Harrington, B.A., Sean Hogan, M.B., Madeline H. Reiss, Ph.D., Guhaeramy Palancar, M.D., Richelle Poulton, Ph.D., Sandhya Ramnath, Ph.D., Janet Sugden, Ph.D., Benjamin Williams, B.A., Luis Augusto Rohde, M.D., Abstract: Cep, Ph.D.

Follow-forward analyses

A. Follow-Forward: Did Those With Childhood ADHD (N=60) Continue to Have Adult ADHD?

Follow-back analyses

B. Follow-Back: Did Those With Adult ADHD (N=32) Have Childhood ADHD?

Late-onset ADHD – what does it mean?

• At least 2 studies reported similar findings (Agnew-Blais JAMA Psychiatry 2016 1:73(7):713-20; Caye et al. JAMA Psychiatry 2016 73(7):705-12).

• Is this a developmental phenotype of ADHD, or quasi-ADHD (but in terms of neurobiology and etiology, a different disorder) ?

• Treatment implications unknown.
Treatment – General approach

Aims and objectives of treatment

– Reduce symptoms of ADHD
– Reduce comorbid symptoms
– Reduce risk of further complications
– Educate the patient and the environment about the disorder
– Adapt the environment to the patient’s needs
– Enhance patient, parent, teacher et al’s coping skills
– Change maladaptive views

– Go beyond symptoms
– Address functional impairments

More than cure

Efficacy of interventions

Psychopharmacotherapy

– Proven short-term effects
– Long-term effects well documented for up to 2 years

Parent management training

– Proven short-term effects
– Proven short- and long-term effects in children with oppositional disorder

Neurotransmitter systems and substances

DOPAMINERGIC
Methylphenidate
D-amphetamine sulphate
Pemoline

NORADRENERGIC
Atomoxetine
Desipramine
Clonidine, Guanfacine

Non-pharmacological treatments; the importance of a good design

• Psychopharmacotherapy
  – Proven short-term effects
  – Long-term effects well documented for up to 2 years
• Parent management training
  – Proven short-term effects
  – Proven short- and long-term effects in children with oppositional disorder
32 papers were analyzed (versus 15 in Sonuga-Barke et al. 2013)

Significant effects on other domains – parents and children

- SMD = 0.63, p < .001
- SMD = 0.43, p < .001
- SMD = 0.31, p < .001

Thus

- Parent training is more effective for comorbid or associated problems than for the core ADHD symptoms