

# Der Verlauf von ADHS



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**Verlauf**

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Adoleszenz

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# Verlauf in der Adoleszenz

- Hohe Raten an
  - Persistierender ADHS (10-85%)
    - höhere Raten bei Residualstörungen
  - Störungen des Sozialverhaltens (3-44%)
  - Schulleistungsstörungen
  - Straftaten
  - familiären Konflikten

Weiss et al., 1971; Feldman et al., 1979; Satterfield et al., 1982; August et al., 1983; Mannuzza & Gittelman 1984; Lambert et al., 1987; Barkley et al., 1990, 1991, 1993; Hart et al., 1995; Taylor et al., 1996; Biederman et al., 1996

# Verlauf

## Zürcher Verlaufsstudie

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- N= 35 Patienten mit ADHS und N=35 parallelisierte Kontrollen am Übergang vom Kindes- zum Jugendalter
- Mehrebenen-/ Multi-Informanten-Evaluation mit drei Messzeitpunkten
  - Verhalten und Psychopathologie
  - Neuropsychologie
  - Neurophysiologie (Brainmapping)

# Verlauf

## Clinical Course of Attention-Deficit/Hyperactivity Disorder From Childhood Toward Early Adolescence

HANS-CHRISTOPH STEINHAUSEN, M.D., Ph.D., RENATE DRECHSLER, Ph.D.,  
MONIKA FÖLDÉNYI, Ph.D., KATRIN IMHOF, Ph.D., AND DANIEL BRANDEIS, Ph.D.

# Verlauf

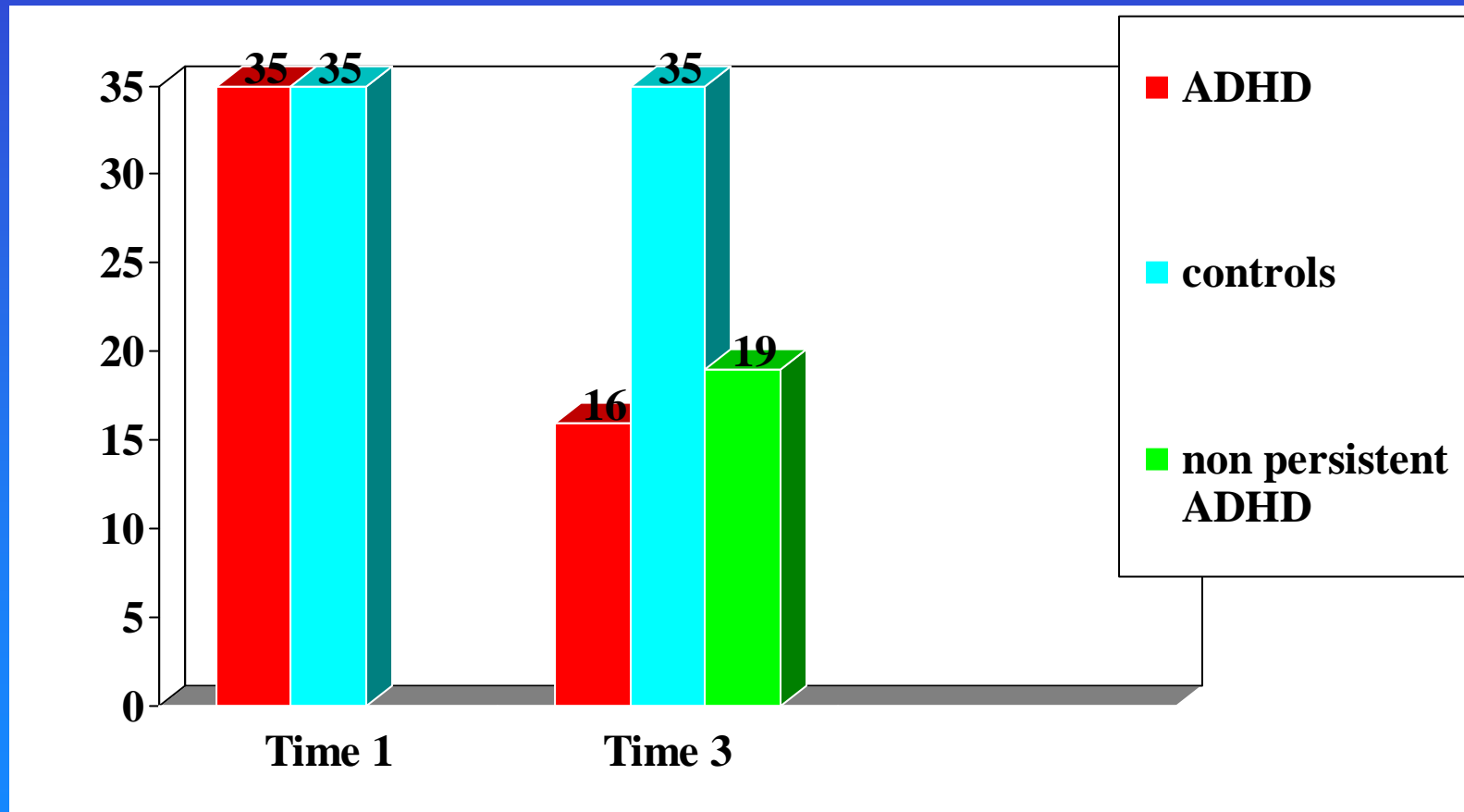
## ABSTRACT

**Objective:** To study the course of attention-deficit/hyperactivity disorder (ADHD) in late childhood to adolescence using a multi-informant and multi-assessment procedure. **Method:** Subjects were 35 children with ADHD and 35 matched controls with a mean age of 10 years at first assessment. *DSM-III-R*-based structured diagnostic interviews and behavioral questionnaires based on parents, teachers, and youth informants were used. Cross-informant behavioral syndromes were obtained by use of the Child Behavior Checklist, the Teacher's Report Form, and the Youth Self-Report. Subjects were reassessed after 1.5 and 2.6 years. **Results:** Behavioral differences between the two groups were significant for the majority of scales for all three informants at all three times. Diagnostic interviews revealed a persistence rate of 46% over 2.6 years. However, there were only few significant behavioral differences across informants between the nonpersistent and the persistent groups. The fit between interview-derived syndrome scores reflecting subtypes of ADHD and both parents and youth questionnaire data was good, whereas for the teacher ratings it was poor. A high rate of 89% correct classification of the outcome diagnoses was possible based on behavioral data at time 1. **Conclusions:** The study of the course of ADHD should be based both on interview and questionnaire data and should include several informants. Operationally defined diagnoses alone may lead to an underestimation of persistent behavioral problems. *J. Am. Acad. Child Adolesc. Psychiatry*, 2003, 42(9):1085–1092. **Key Words:** attention-deficit/hyperactivity disorder, course.

# Verlauf

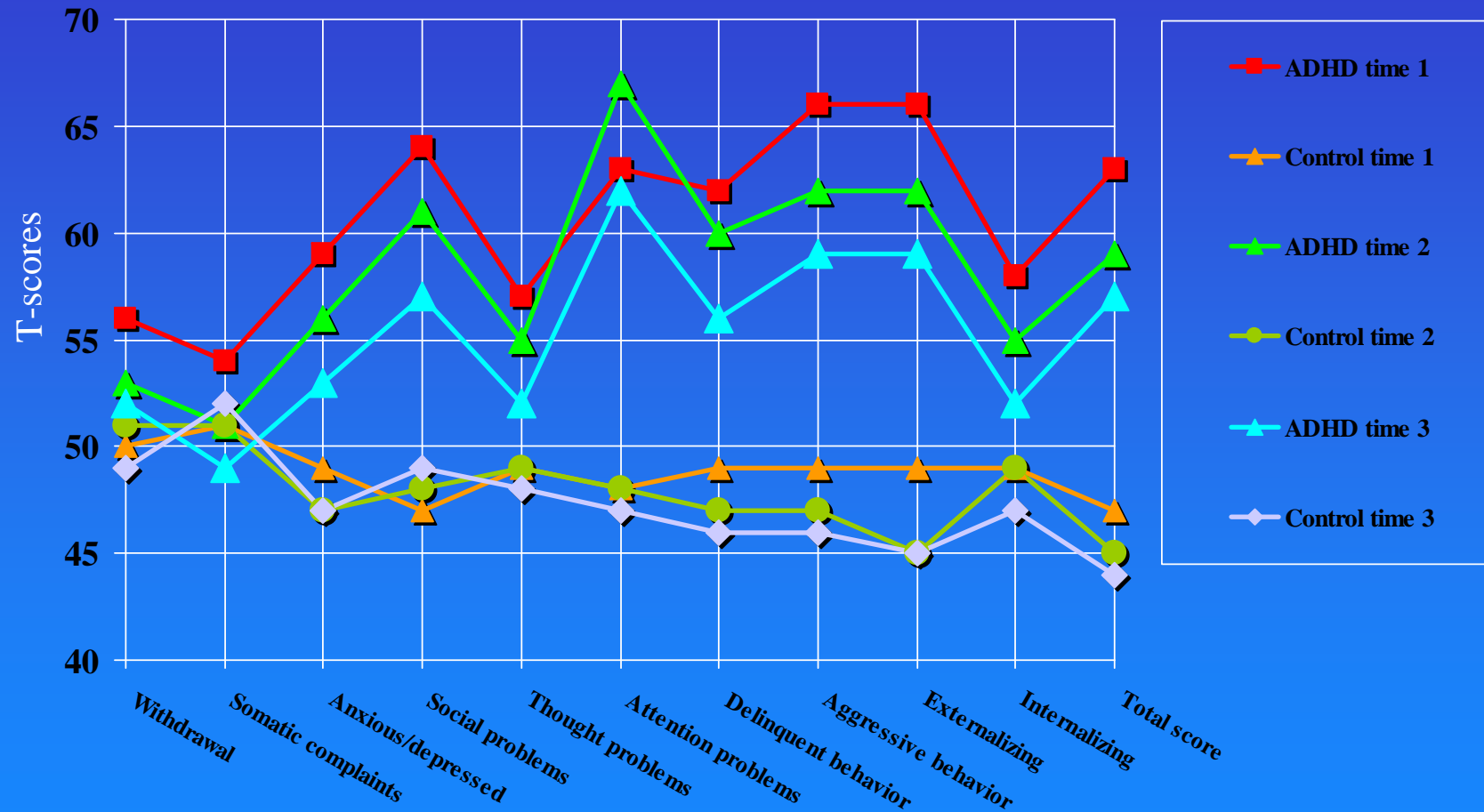
Zürcher Verlaufsstudie

Diagnosen nach 2,6 J



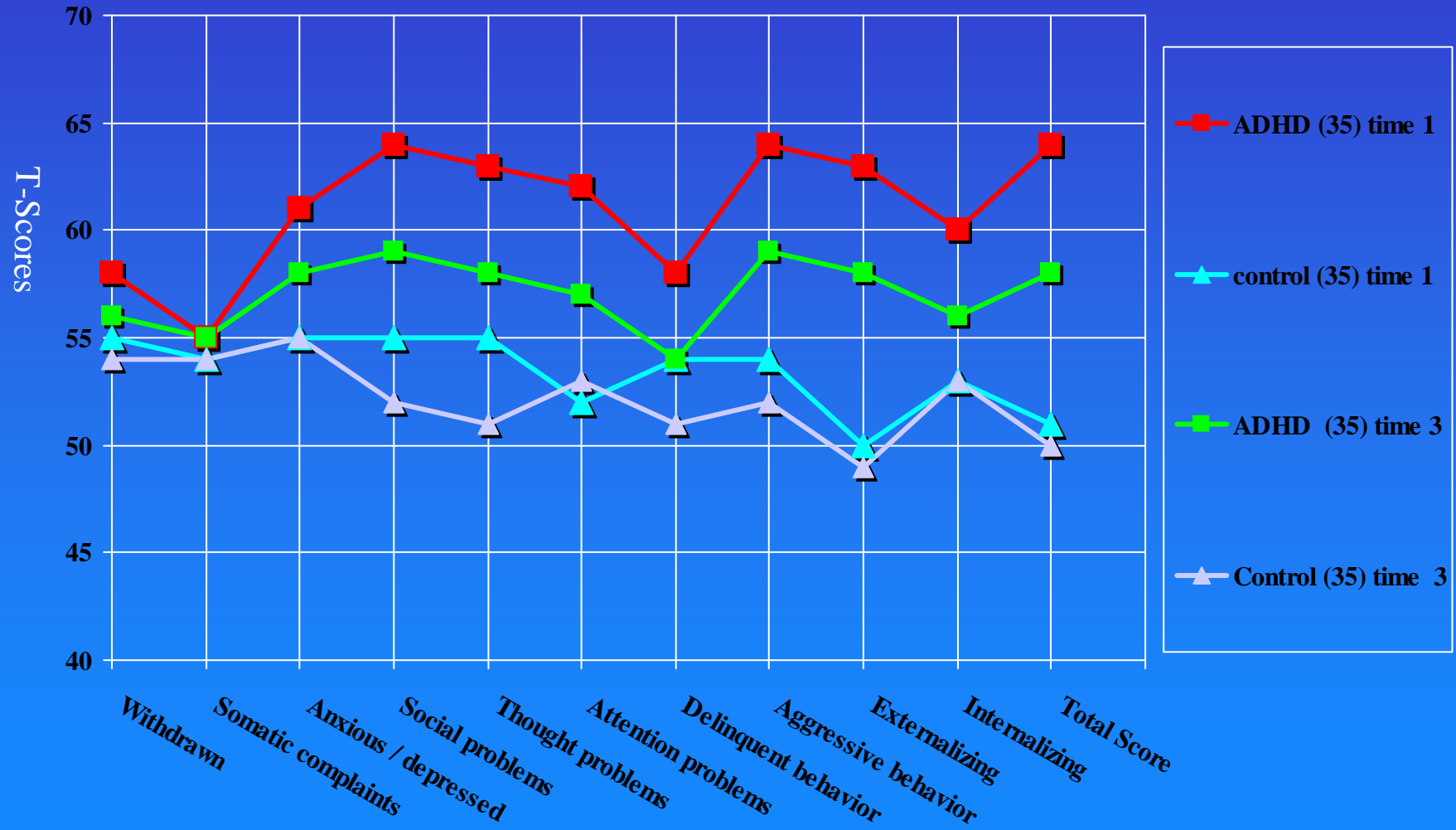


# CBCL Parent Ratings at Times 1, 2, and 3

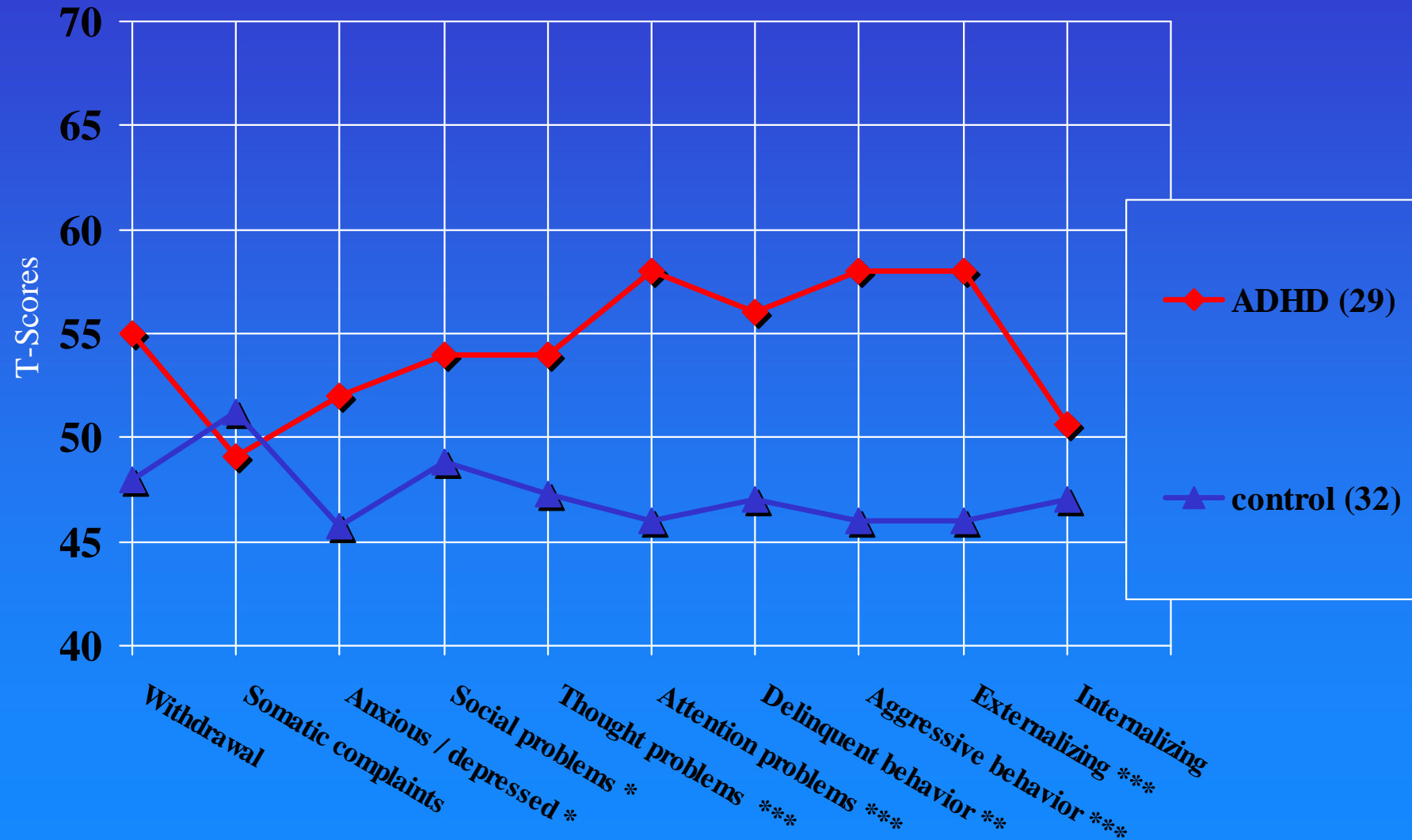




# TRF Teacher Ratings at Time 1 and 3



# YSR Adolescent Self – Ratings at Time 3

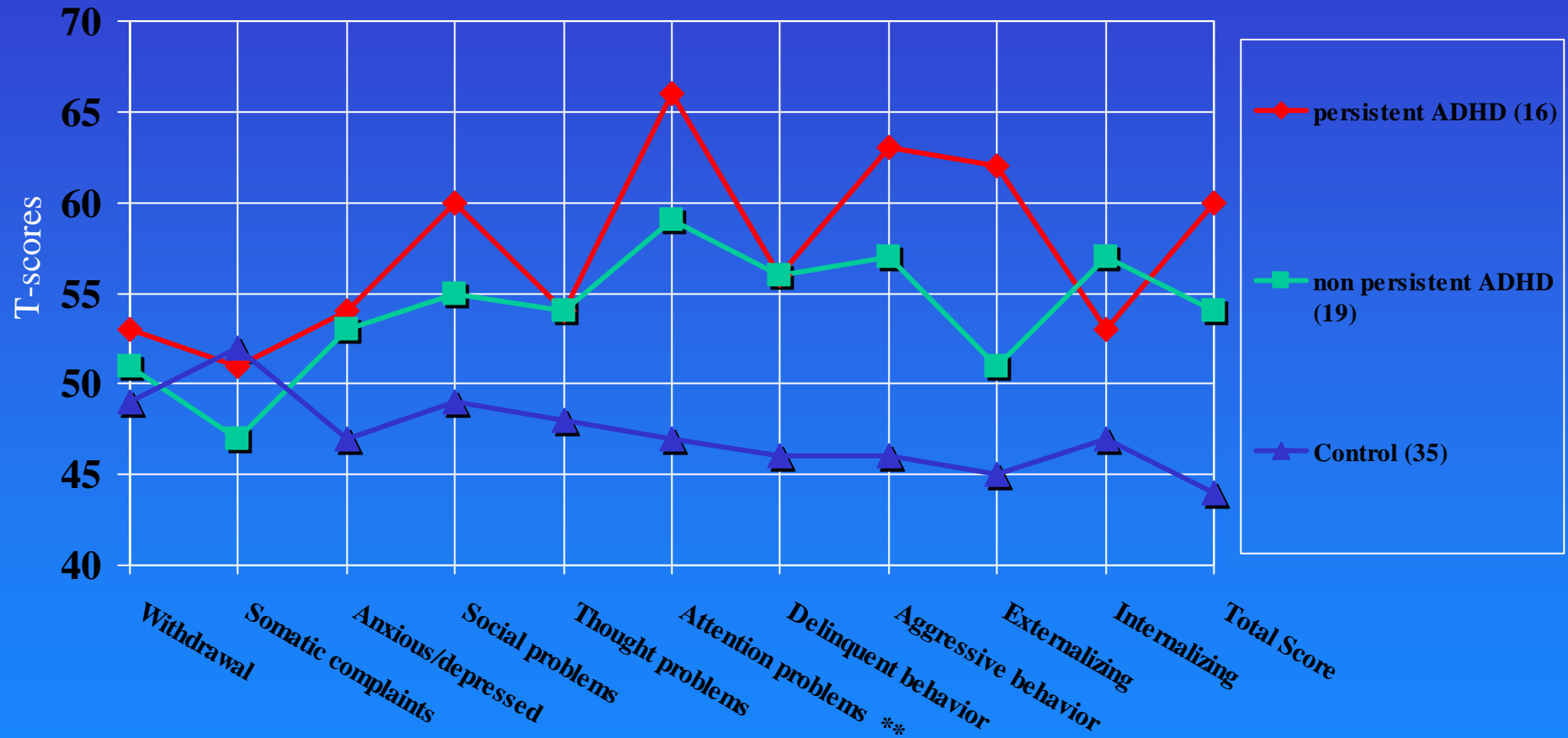


\* =  $p < 0.05$  ; \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$

Steinhausen et al., JAACAP (2003)

# CBCL Parent Ratings at Time 3

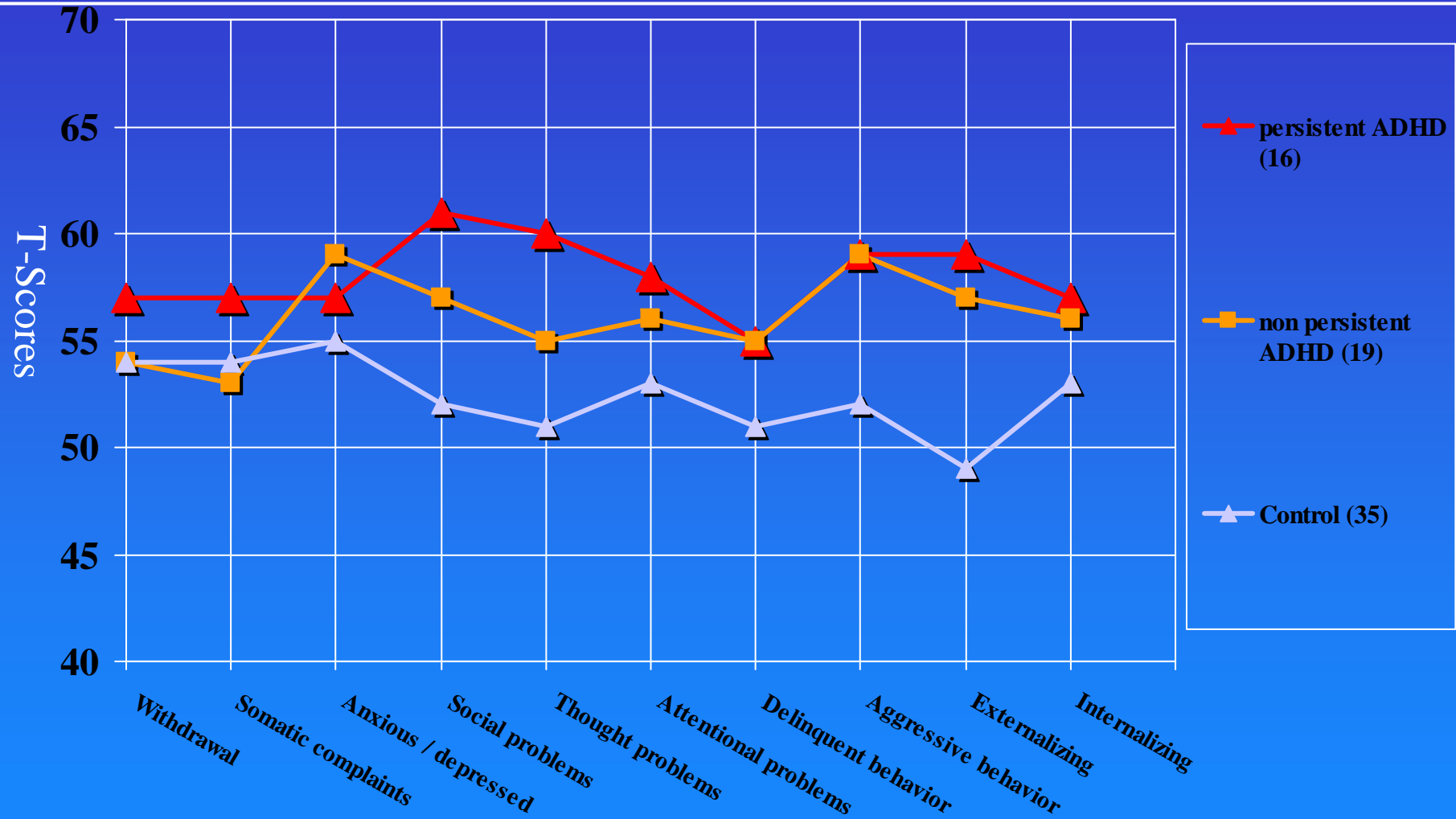
## Outcome-Groups



Differences between persistent / non persistent ADHD: \*\* =  $p < 0.01$

# TRF Teacher Rating at Time 3

## Outcome Groups



Group differences persistent / non-persistent ADHD: non significant

# Prediction of the Outcome Groups

Prediction of the Two Outcome Groups of Nonpersistent and Persistent ADHD by Syndromal and Behavioral Variables at Time 1

Variable	Odds Ratio	Confidence Interval	<i>p</i>
Hyperactivity/Impulsivity score	0.19	0.05–0.70	.000
CBCL Delinquent Behavior	1.30	0.98–1.73	.009
CBCL Aggressive Behavior	0.71	0.51–0.99	.003

*Note:* Correct classification rate: nonpersistent ADHD ( $n = 19$ ), 89%; persistent ADHD ( $n = 16$ ), 88%; total group ( $n = 35$ ), 89%.

# Verlauf

*Journal of Child Psychology and Psychiatry* 46:8 (2005), pp 824–836

doi: 10.1111/j.1469-7610.2004.00384.x

## The course of neuropsychological functions in children with attention deficit hyperactivity disorder from late childhood to early adolescence

**Renate Drechsler, Daniel Brandeis, Monika Földényi, Katrin Imhof,  
and Hans-Christoph Steinhausen**

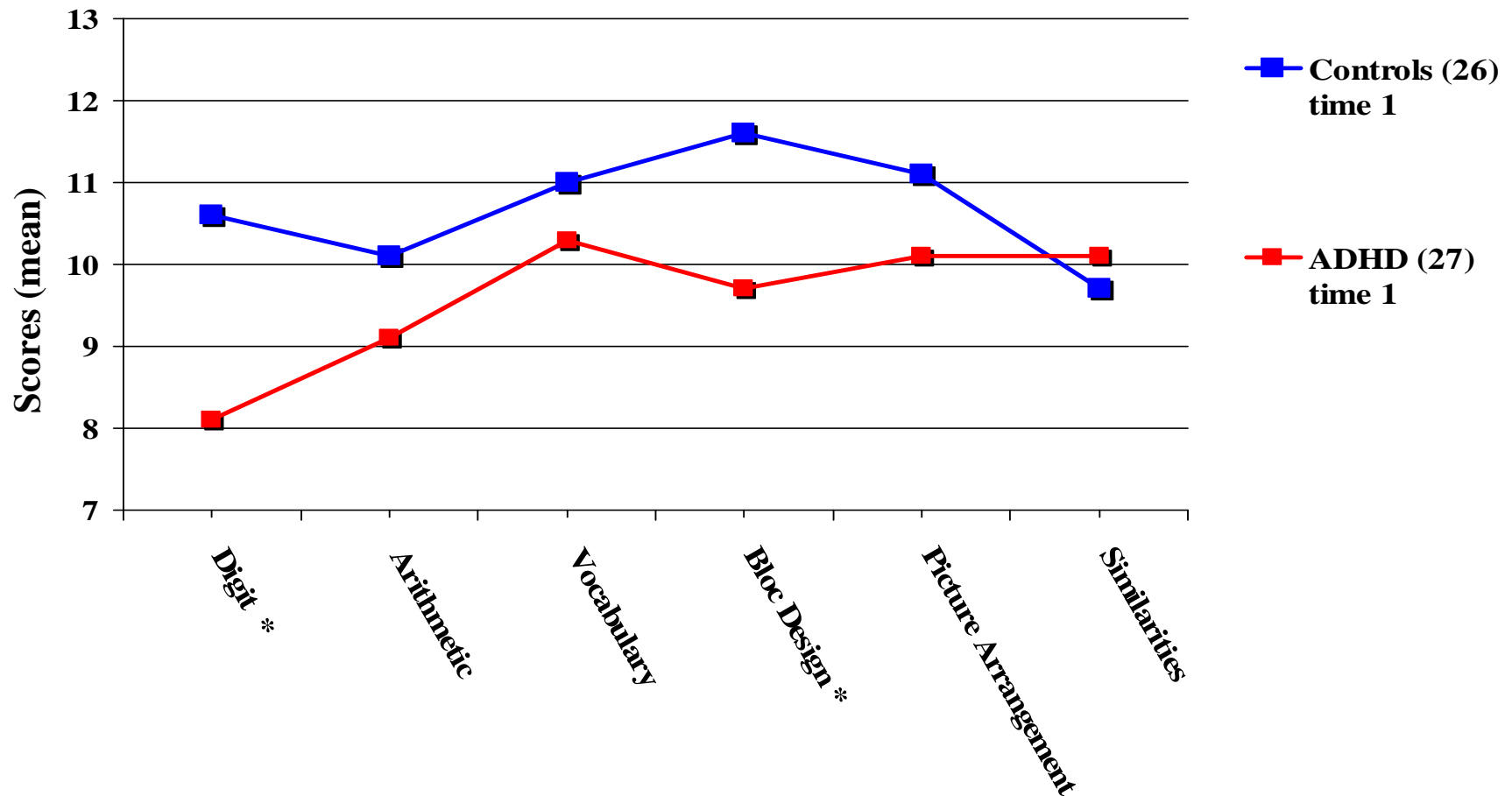
Department of Child and Adolescent Psychiatry, University of Zurich, Switzerland

# Verlauf

**Objective:** The aim of this follow-up study was to investigate the course of performance in attentional tasks in children with ADHD and normal controls in late childhood and preadolescence over short periods of time. The development of two dimensions of attention was compared: alertness/arousal and inhibitory control. **Method:** Children with ADHD ( $N = 28$ ) and normal controls ( $N = 25$ ) were examined at three times: at baseline (age mean = 10.8 years, SD = 1.5), after one year (age mean = 12.0 years, SD = 1.6), and after 2.6 years (age mean = 13.3 years, SD = 1.6). They performed two tasks of a computerized battery for attentional performance: Alertness – a test of simple reaction time to visual stimuli contrasting a condition with and without auditory warning signal, and Incompatibility – a test of spatial interference/inhibitory control. Clinical diagnosis according to DSM-III-R criteria was established at time 1 and time 3 by structured diagnostic interviews. **Results:** In the Alertness task significant group differences regarding increased reaction time variability in ADHD, but not for reaction time itself, were found at time 1 and more pronounced at time 2. At time 3 group differences had disappeared. In the Incompatibility task group differences in number of errors were not observed at time 1, whereas children with ADHD made significantly more errors at time 2 and less pronounced at time 3. The degree of clinical symptom remission after 2.6 years was not related to changes in neuropsychological performance. **Conclusion:** When measuring attentional functions, the selection of an appropriate time window seems to be essential for the detection of group differences between ADHD children and controls, because group differences are most pronounced before adolescence. The different developmental course of selective components of attention should be taken into account. **Keywords:** ADHD, alertness, attention, development, inhibitory control, longitudinal study.

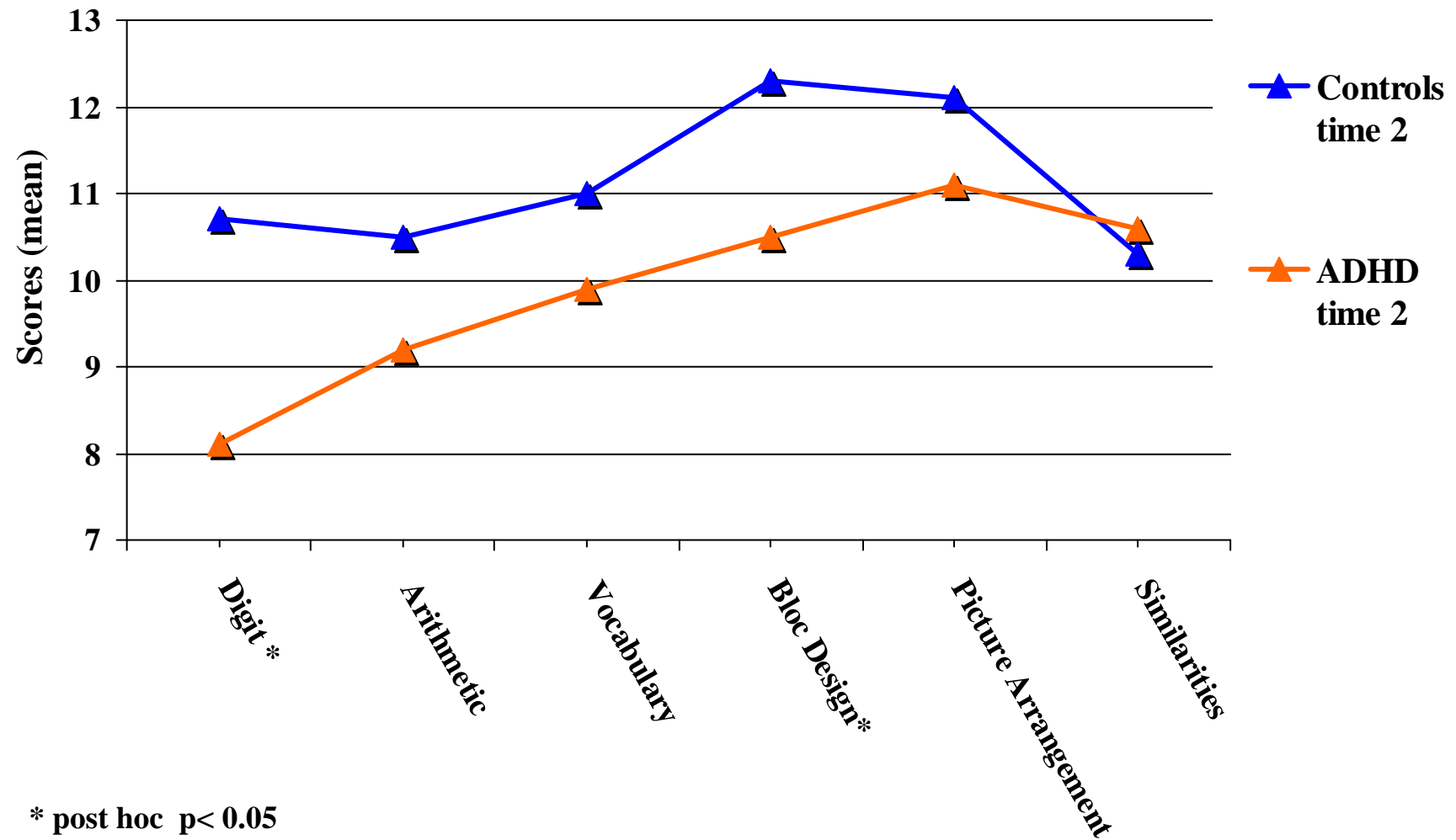


# WISC-R Time 1

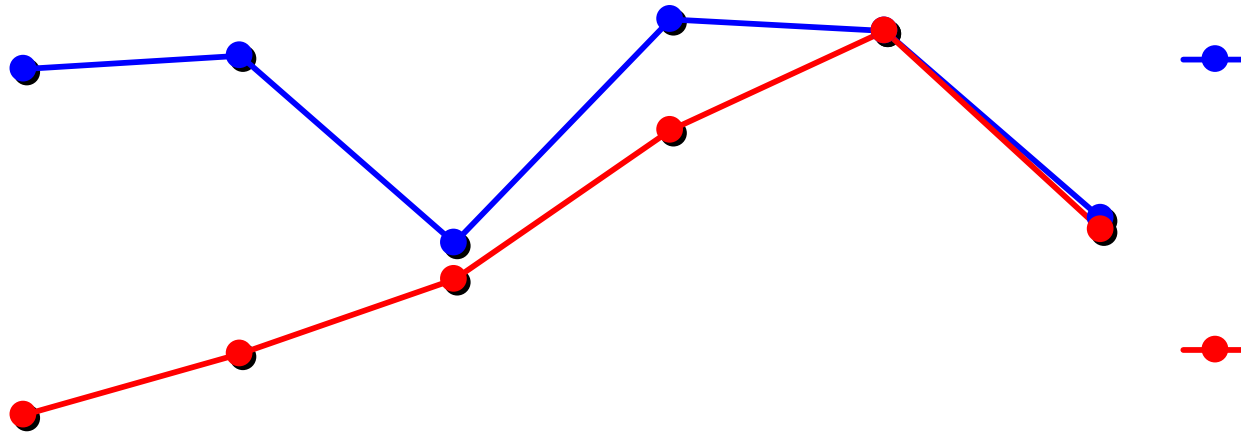


\* post hoc  $p < 0.05$

# WISC-R Time 2



# WISC-R Time 3



# WISC-R

## Summary

- Children with ADHD continuously show a reduced performance on the subtests Digit and Block Design over 2.4 years. At the third time of testing performance differences in Arithmetic become significant.
- There are no differences between the persistent and non-persistent ADHD groups (except for performances in picture arrangement at the third time of testing).

# Developmental Neuropsychology

## TAP: Alertness

Reaction time, attentional activation (intrinsic and phasic)

1. without auditory warning signal ( 2 blocks of 20 trials)



Please press the button as fast as possible  
when a cross appears

2. with auditory warning signal  
( 2 blocks of 20 trials)

Warning  
signal

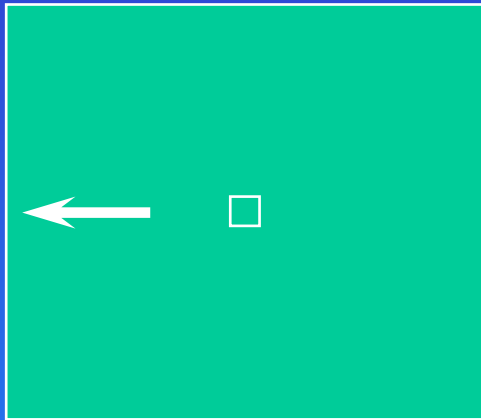


You will hear a warning  
signal before the cross  
appears. Please press the  
button as fast as possible  
when the cross appears.

# Developmental Neuropsychology

## TAP: Incompatibility

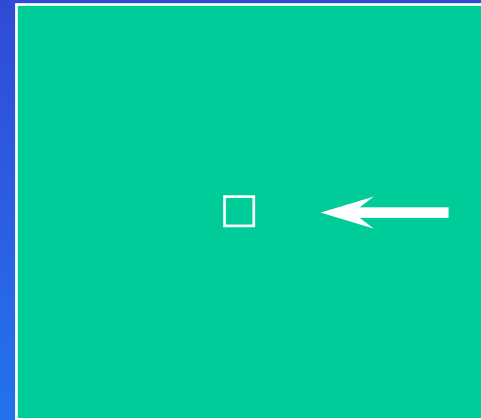
Inhibition of a preponderant response, response selectivity



left button



right button



left button



right button

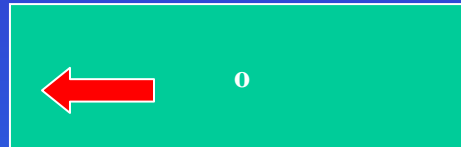


Please press the left button when the arrow points to the left side.  
Press the right button when the arrow points to the right side.

# Developmental Neuropsychology

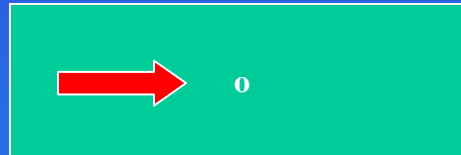
## TAP: Interference

**Condition 1:**  
left field, left button



No interference

**Condition 2:**  
left field, right button



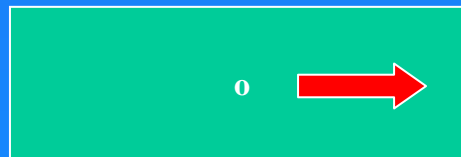
Interference

**Condition 3:**  
right field, left button



Interference

**Condition 4:**  
right field, right button



No interference



# Developmental Neuropsychology

## Results

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- Task dependent group differences and developmental trajectories
  - WISC-R: at time 1, 2, and 3 (Digit, Bloc, Design)
  - Alertness: at time 1 and 2 (SD)
  - Incompatibility: at time 2 and 3 (number of errors)
- Group differences depend on time window and choice of test

# Developmental Neurophysiology

## **Mapping Attention-Deficit/Hyperactivity Disorder from Childhood to Adolescence—No Neurophysiologic Evidence for a Developmental Lag of Attention but Some for Inhibition**

Mirko Doehnert, Daniel Brandeis, Katrin Imhof, Renate Drechsler, and Hans-Christoph Steinhausen

BIOL PSYCHIATRY 2010;67:608–616

# Developmental Neurophysiology

**Background:** The role of a developmental lag for deficits of higher brain functions in attention-deficit/hyperactivity disorder (ADHD) has not yet been tested in longitudinal studies. We examined the development of neurophysiological markers of attention (Cue P300; contingent negative variation [CNV]) and inhibition (NoGo P300) in ADHD and control groups from childhood to adolescence for support of the developmental lag hypothesis of ADHD.

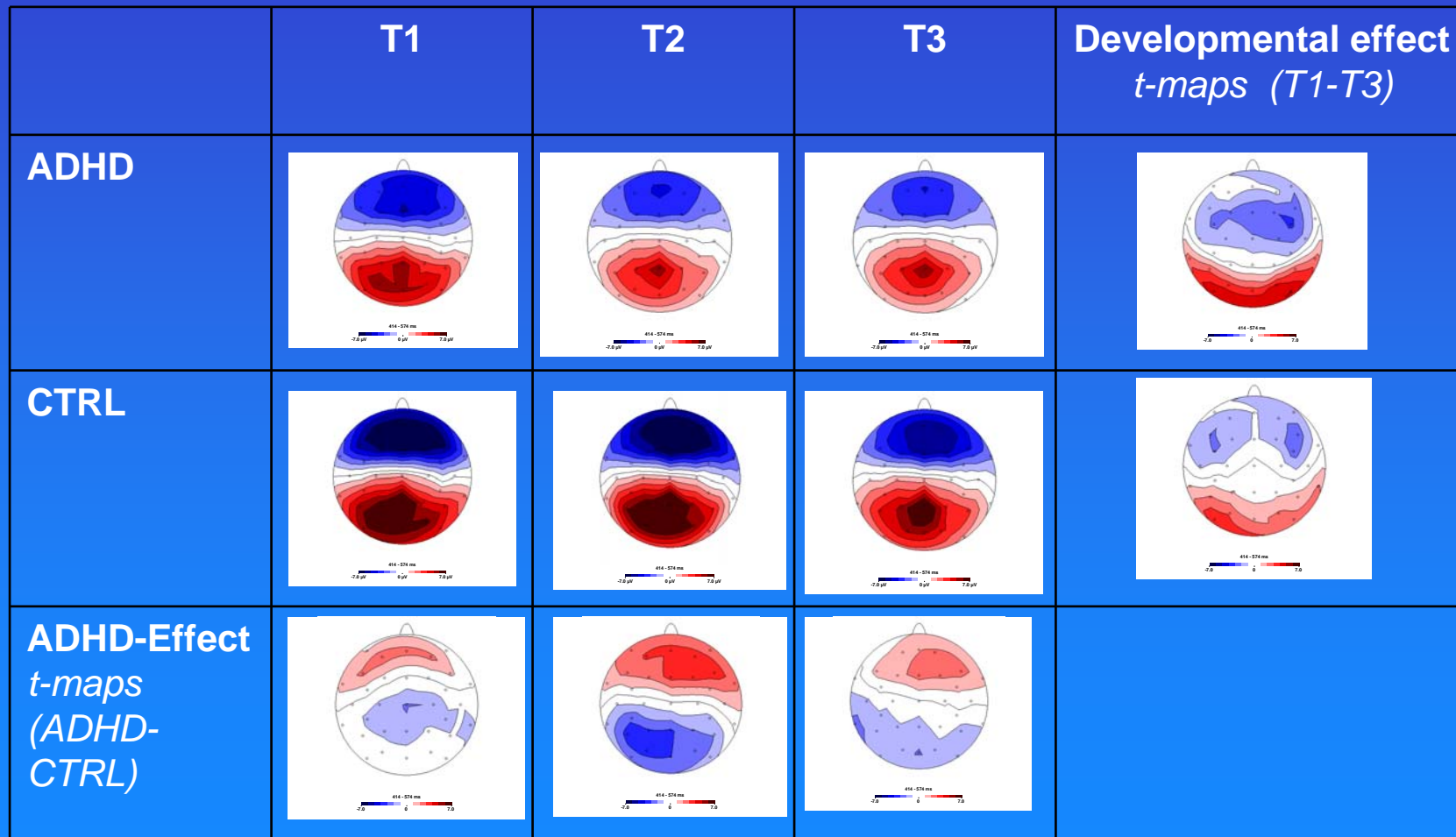
**Methods:** ADHD ( $n = 28/3$  girls) and control ( $n = 22/5$  girls) subjects were assessed at baseline (Time 1; ADHD age  $10.8 \pm 1.8$  years, controls  $10.4 \pm 1.1$  years) and at two follow-up examinations (Time 2 after 1.2 years, Time 3 after 2.5 years). Event-related potential maps were recorded during a cued Continuous Performance Test (CPT) at all assessments and analyzed using scalp and source (sLORETA) measures.

**Results:** CPT performance showed common effects of ADHD and younger age, consistent with (but not specific to) developmental lag. The NoGo P300 developed earlier and became stronger in control subjects than in the ADHD group, again consistent with an initial developmental lag. In contrast, the attenuation of the Cue P300 and the CNV with ADHD at all assessments was opposite to the enhancement with younger age and thus inconsistent with developmental lag. The sLORETA source localization also differed between ADHD and developmental effects.

**Conclusions:** These results provide strong evidence for multiple and persistent neural processing deficits in ADHD. They do not support the developmental lag hypothesis for attentional dysfunction in ADHD despite partial evidence that developmental lag contributes to inhibitory brain dysfunction during early adolescence.

# Developmental Neurophysiology

Cue Condition P3b microstate (414-574ms): activity remains reduced in ADHD; stronger activity in younger age (increased attentional demand)



Main effects: Time  $p < .001$ ; Group  $p = .000$ ; Interaction: Time  $\times$  Group:  $p = .04$  (Döhnert et al., 2010)

# Verlauf

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Erwachsenenalter

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# Verlauf im jungen Erwachsenenalter

- Hohe Raten:
  - persistierende ADHS (8 - 80%)
    - höhere Raten bei Residualstörungen
  - dissoziale Persönlichkeitsstörungen (18 - 45%)
  - Substanzmissbrauch (16 – 43 %)
  - Persönlichkeitsstörungen
  - Schullaufbahnstörungen
  - niedriger beruflicher Status
  - Straftaten

Borland & Heckman, 1976; Loney et al., 1983; Weiss et al., 1985; Weiss & Hechtman, 1986; Gittelman et al., 1985; Mannuzza et al., 1989, 1990; 1991, 1993, 1998; Klein & Mannuzza 1991; Claude & Firestone, 1995; Yan 1996; Rasmussen & Gillberg, 2000; Barkley et al., 2002, 2004, 2006; Fischer et al., 2002

# Verlauf

*Psychological Medicine*, 2006, **36**, 159–165. © 2005 Cambridge University Press  
doi:10.1017/S003329170500471X First published online 3 May 2005. Printed in the United Kingdom

## REVIEW ARTICLE

### The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies

STEPHEN V. FARAONE<sup>1\*</sup>, JOSEPH BIEDERMAN<sup>2,3</sup> AND ERIC MICK<sup>2,3</sup>

<sup>1</sup> *Medical Genetics Research Program and Department of Psychiatry, SUNY Upstate Medical University, Syracuse, NY, USA;* <sup>2</sup> *Pediatric Psychopharmacology Unit of the Child Psychiatry Service, Massachusetts General Hospital, Boston, MA, USA;* <sup>3</sup> *Harvard Medical School, Boston, MA, USA*

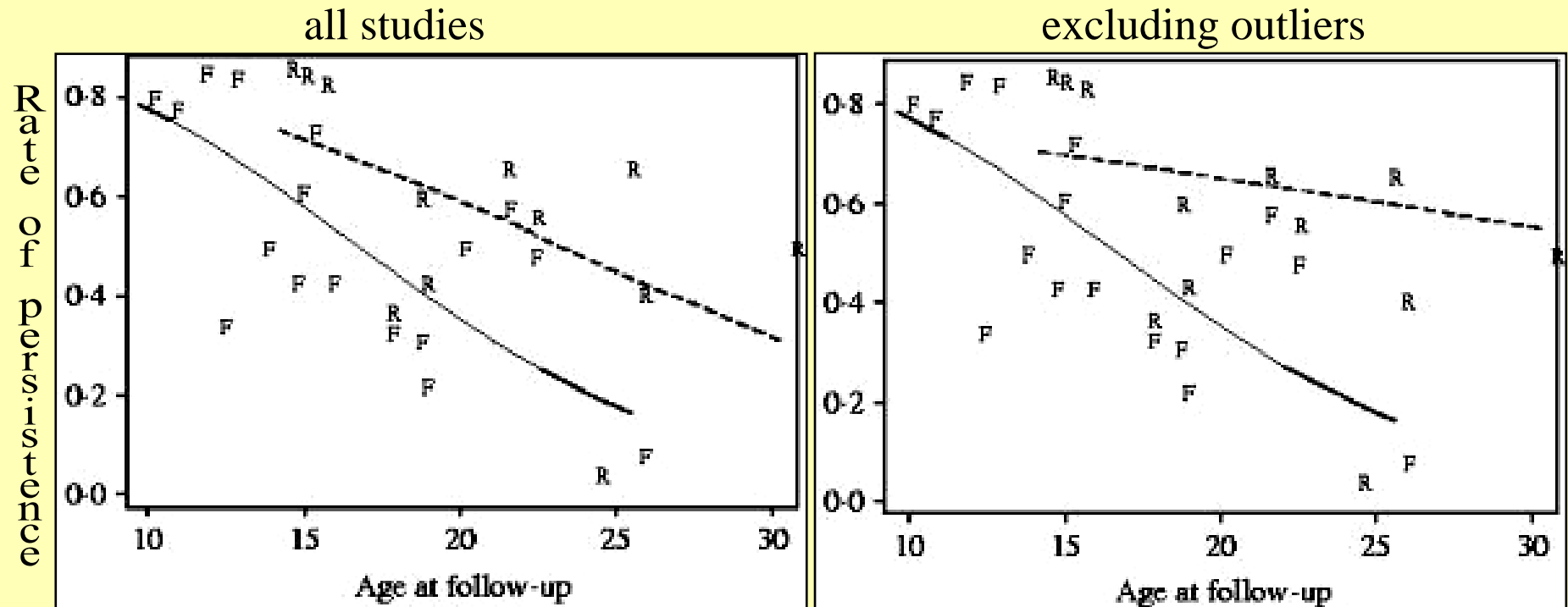


# Verlauf

## Altersabhängige Remission

- **Meta-Analyse von kontrollierten Verlaufsstudien**
  - Klinische Kohorten mit z.T. multiplen Verlaufsmessungen bzw. Subgruppen vornehmlich aus Nord-Amerika
  - Persistierende ADHS (Kriterien voll erfüllt) im Alter von 25 J:
    - **15%**
  - Persistenz unter Einschluss von Teilremission:
    - **40-60%**
  - Tatsächliche Rückbildung vs. mangelnde Entwicklungssensibilität der diagnostischen Kriterien des DSM-IV?

# Verlauf



Predicted rate of persistence for full (F) diagnoses (—) and residual (R) diagnoses (----)

# Verlauf

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**Age-dependent decline of symptoms of attention-deficit hyperactivity disorder: impact of remission definition and symptom type**

Biederman J, Mick, E., Faraone, SV (2000), Am J Psychiatry, 157: 816-8

# Verlauf

## **OBJECTIVE**

Symptom decline in attention deficit hyperactivity disorder (ADHD) was examined with different definitions of remission.

## **METHOD**

Symptoms in 128 boys were measured five times over 4 years. The prevalences of syndromatic (less than full syndrome), symptomatic (less than subthreshold diagnosis), and functional (full recovery) remission were estimated as a function of age with multivariate logistic regression.

# Verlauf

## RESULTS

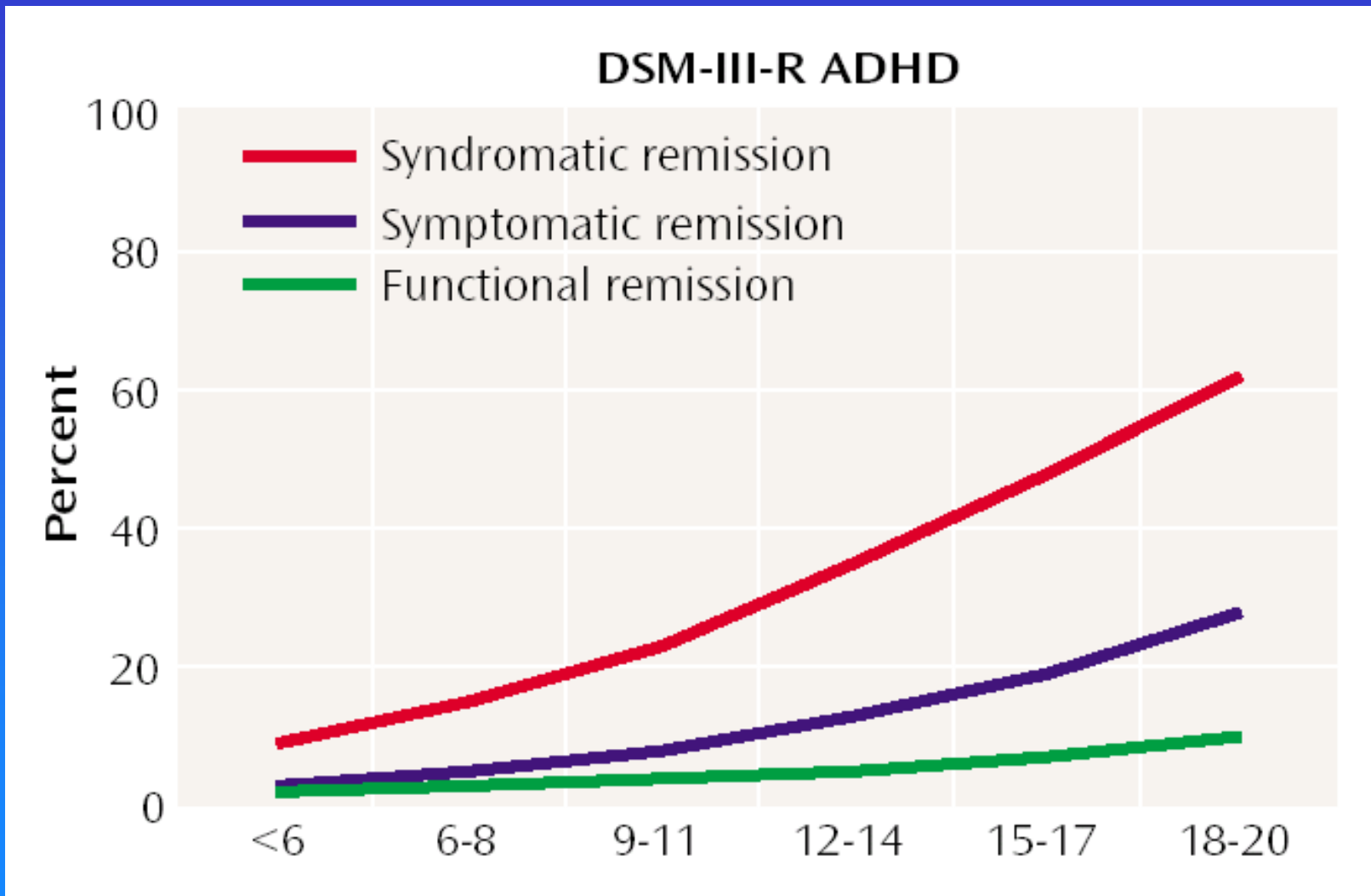
Age was significantly associated with decline in total ADHD symptoms and symptoms of hyperactivity, impulsivity, and inattention. Symptoms of inattention remitted for fewer subjects than did symptoms of hyperactivity or impulsivity. The proportion of subjects experiencing remission varied considerably with the definition used (highest for syndromatic remission, lowest for functional remission).

## CONCLUSIONS

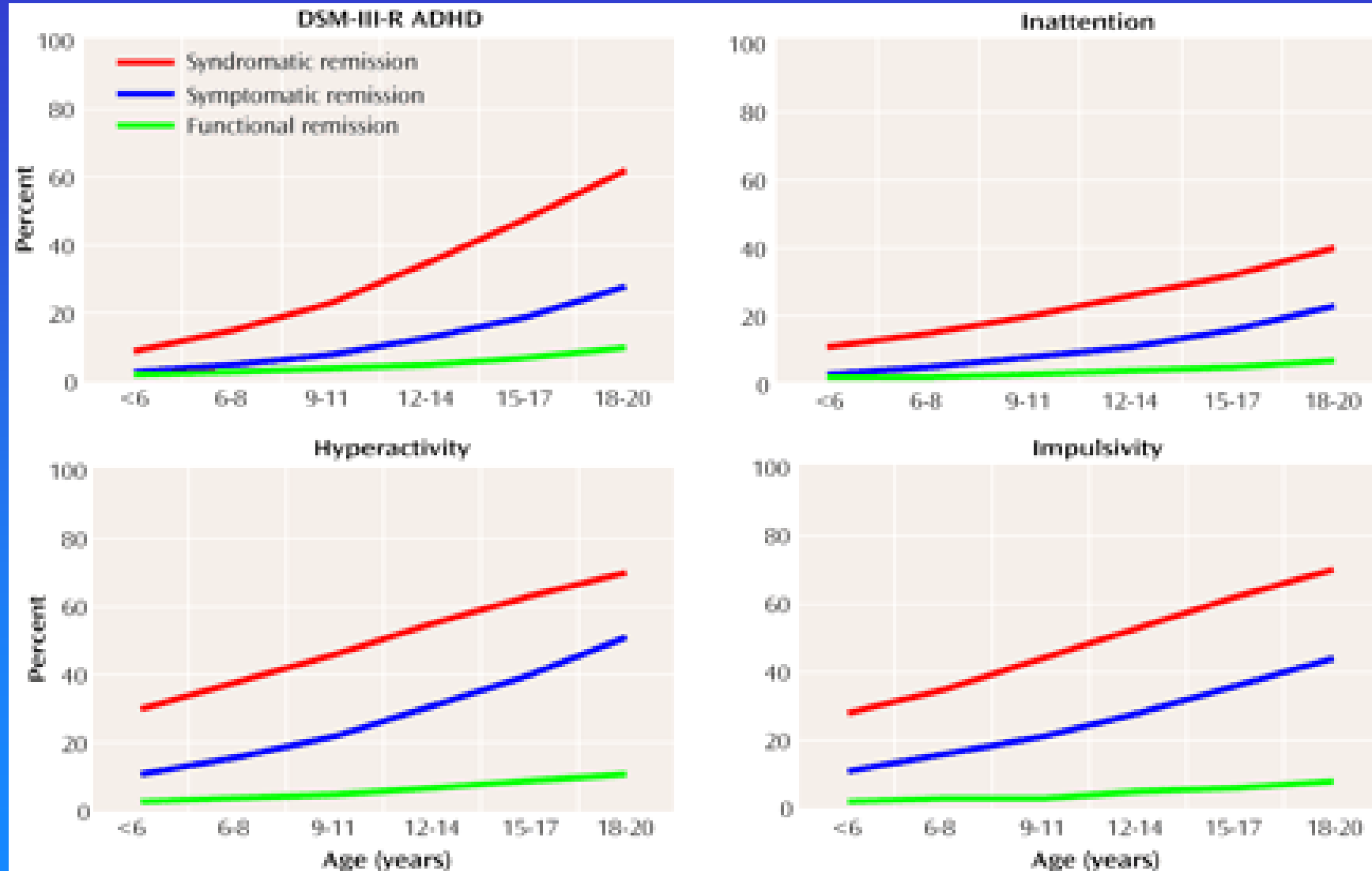
These results indicate that differences in reported remission rates reflect the definition used rather than the disorder's course. They provide systematic support for the clinical observation that hyperactivity and impulsivity symptoms tend to decline at a higher rate than inattention symptoms

# Verlauf

## Differenzielle Remission

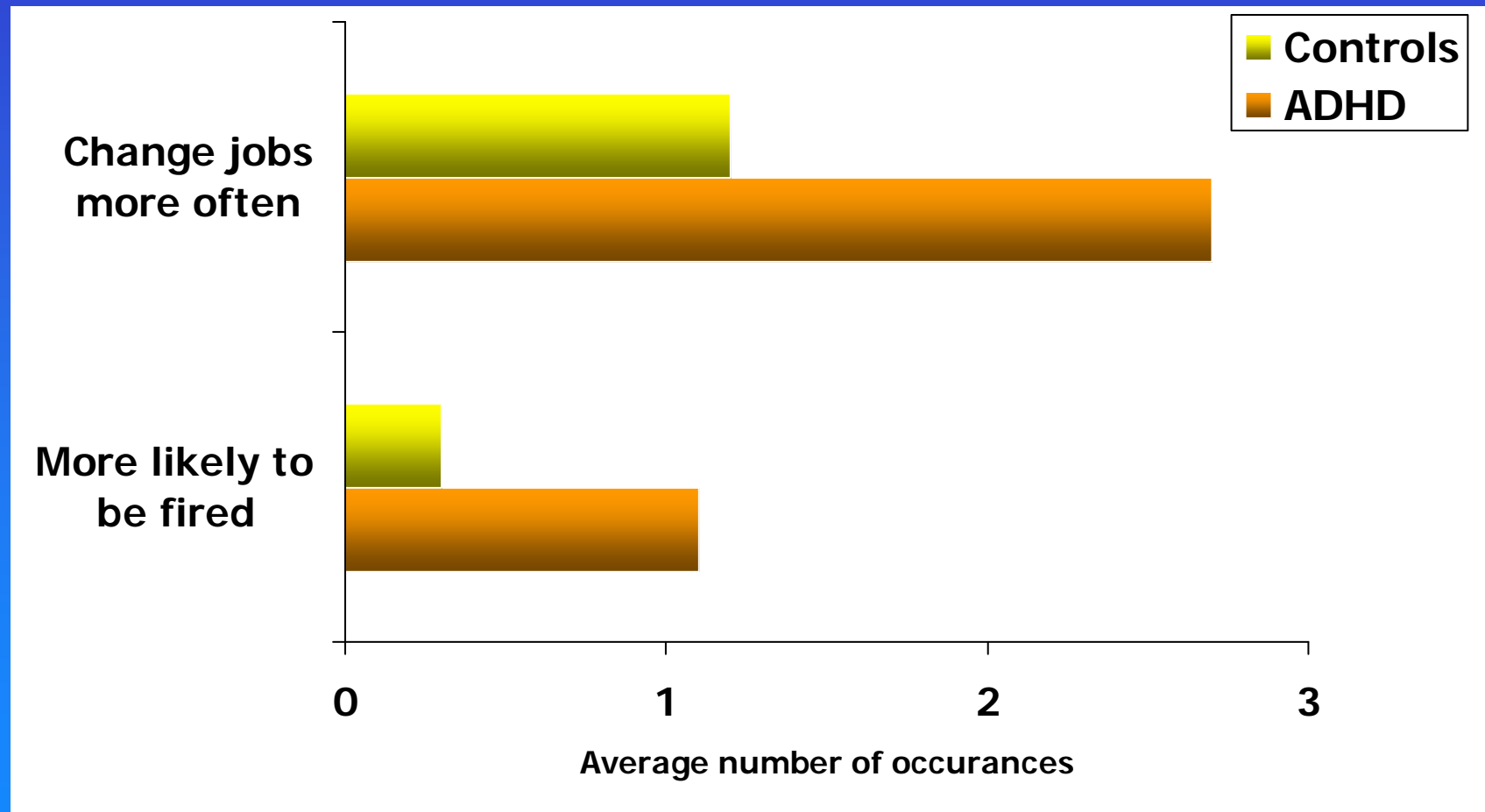


# Verlauf Remission

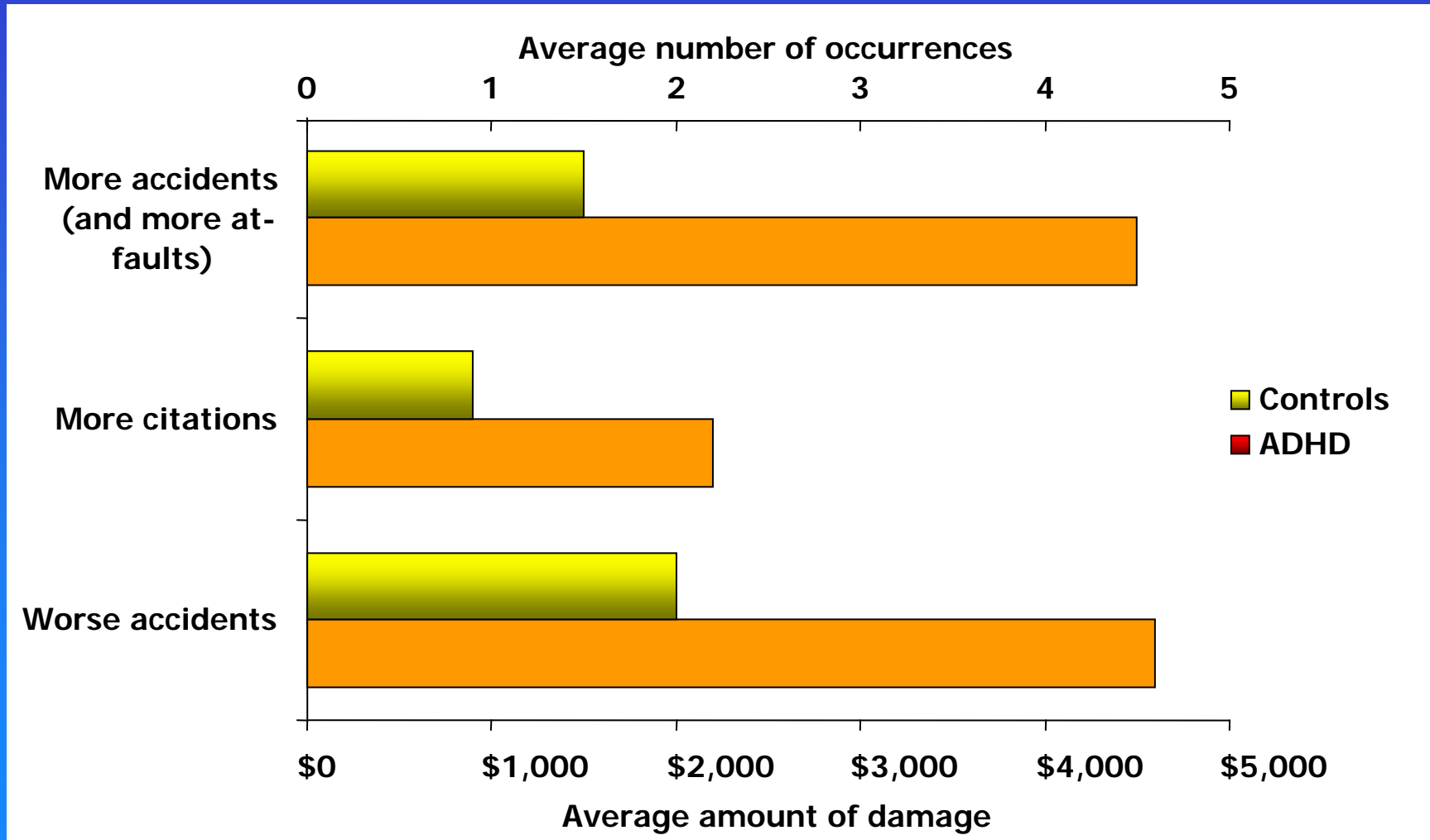




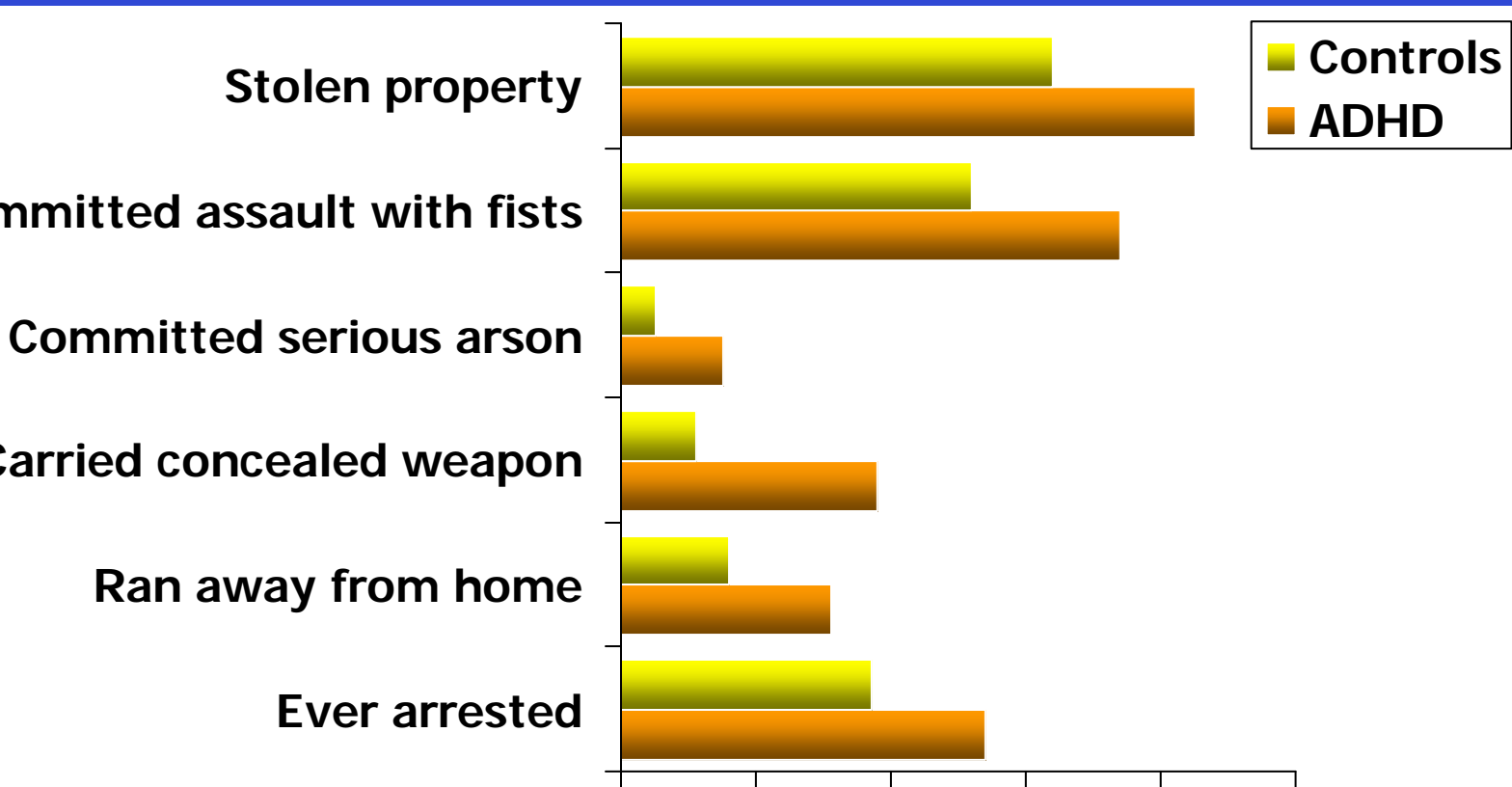
# Verlauf



# Verlauf

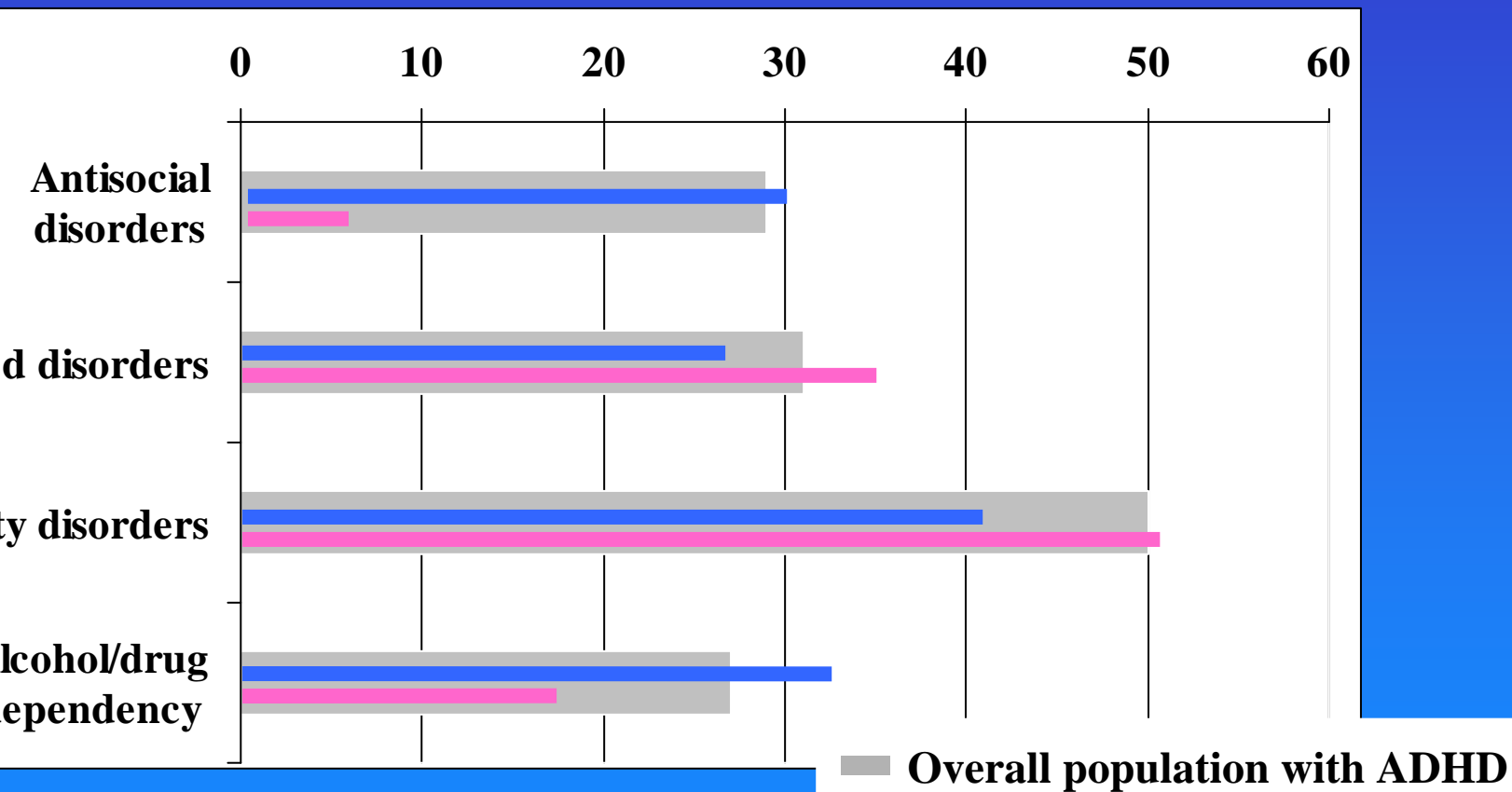


# Verlauf



# Verlauf

Lifetime Prevalence of Comorbid Diagnoses in Adults with ADHD (%)



# Verlauf

Journal of Psychiatric Research 45 (2011) 150–155

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: [www.elsevier.com/locate/psychires](http://www.elsevier.com/locate/psychires)



ers of persistent ADHD: An 11-year follow-up study

derman <sup>a,\*</sup>, Carter R. Petty <sup>a</sup>, Allison Clarke <sup>a</sup>, Alexandra Lomedico <sup>a</sup>, Stephen V. Faraone <sup>b</sup>

<sup>a</sup>Psychiatry, Massachusetts General Hospital and Harvard Medical School, 55 Fruit Street, YAW 6A-6900, Boston, MA 02114, USA

<sup>b</sup>Psychiatry and Neuroscience & Physiology, SUNY Upstate Medical University, Syracuse, NY 13210, USA

# Verlauf

N=110 Jungen mit ADHS, N=105 Kontrollen

6-17 (M=11)J zu Studienbeginn und 15-31 (M=22)J  
bei Verlaufsuntersuchung

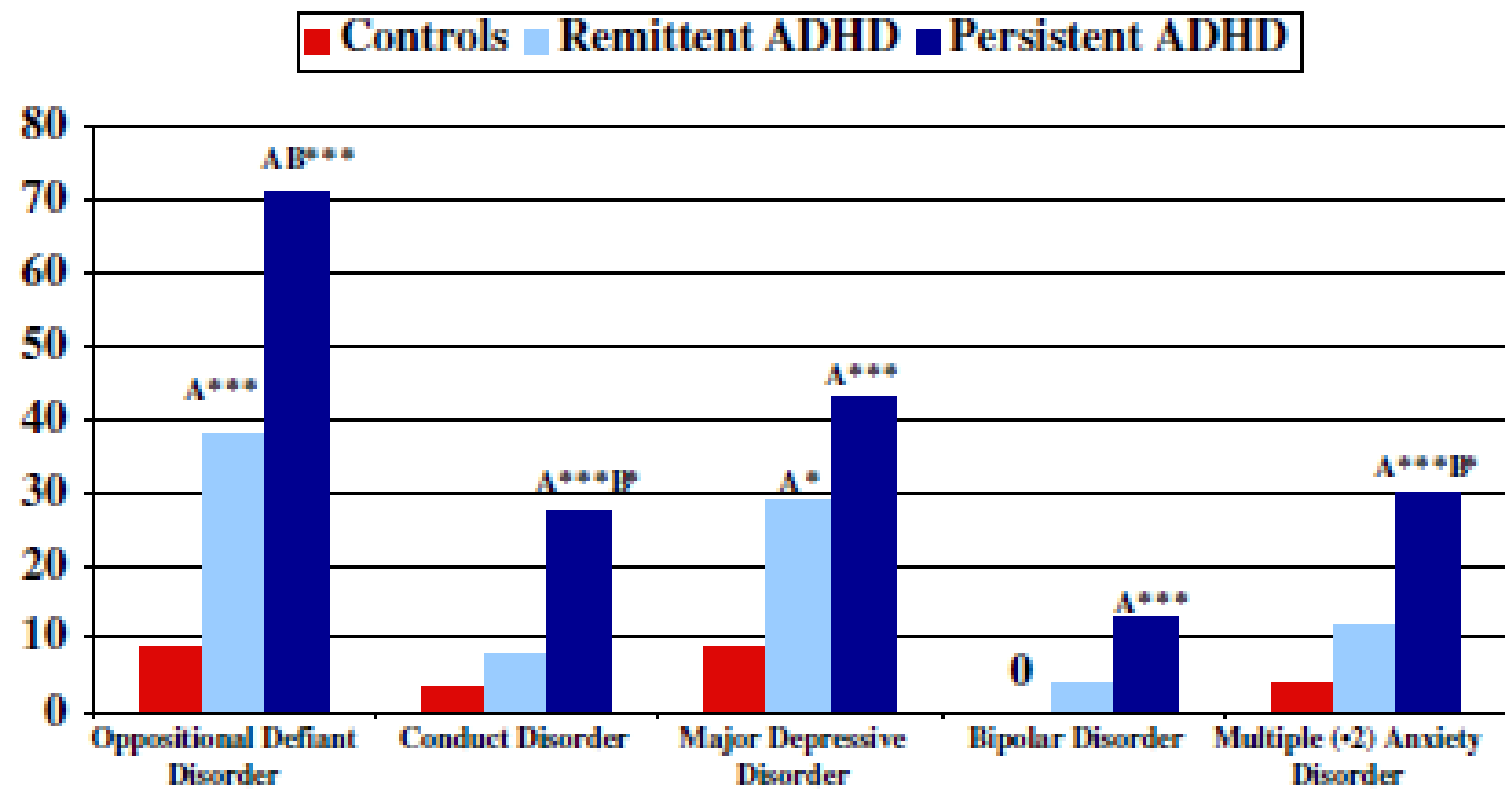
78% der ADHS - Pbn. hatten zu

- 35% ein ADHS-Vollbild
- 22% eine subsyndromale ADHS
- 15% eine beeinträchtigte Funktionstüchtigkeit
- 6% eine remittierte ADHS mit Behandlung

Prädiktoren der Persistenz

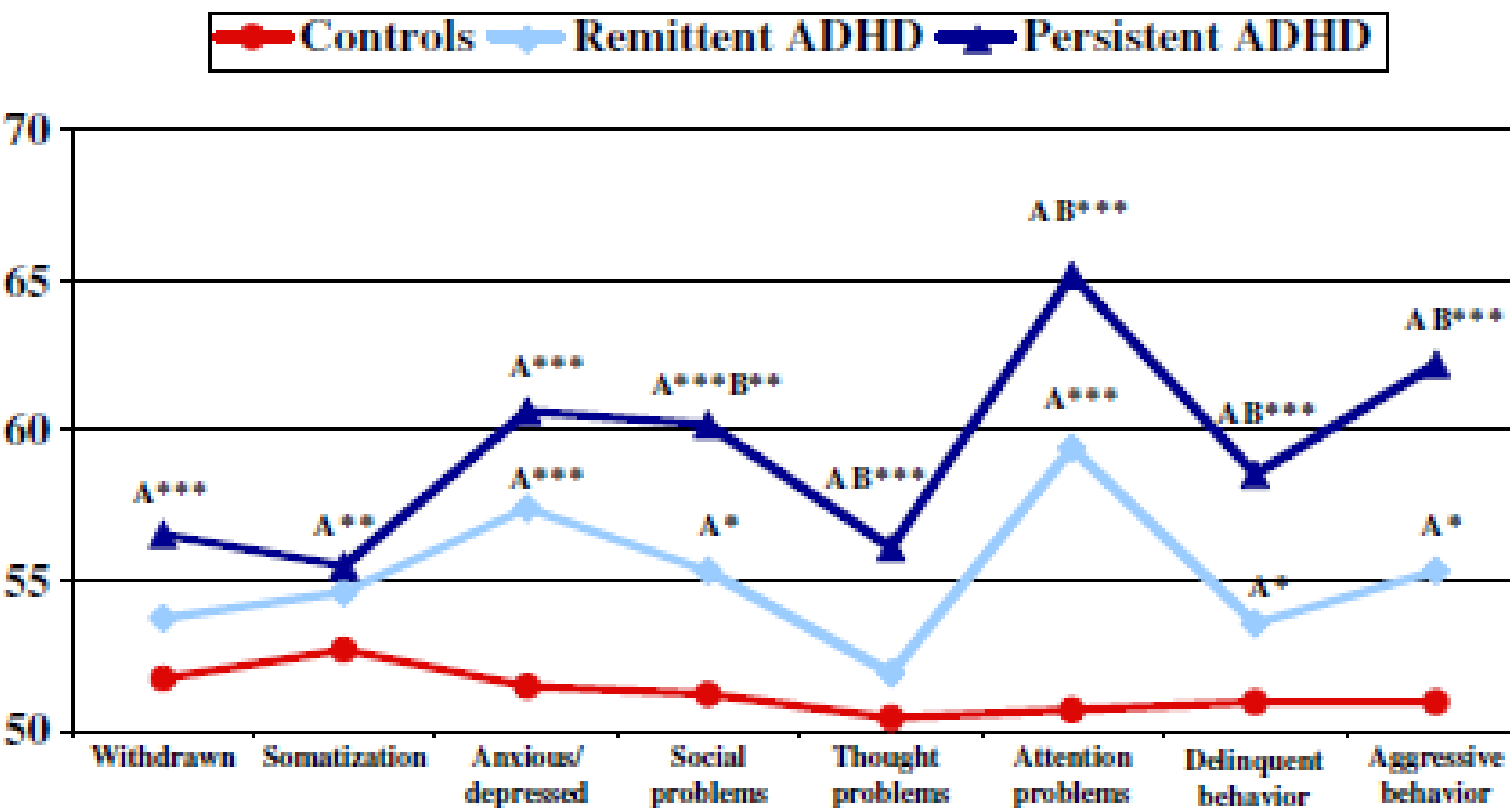
- starke Beeinträchtigung durch ADHS
- psychiatrische Komorbidität

# Verlauf



A=vs. Controls, B=vs. Remittent ADHD; \* $p \leq 0.05$ ; \*\* $p \leq 0.01$ ; \*\*\* $p \leq 0.001$

# Verlauf



=vs. Controls, B=vs. Remittent ADHD; \* $p \leq 0.05$ ; \*\* $p \leq 0.01$ ; \*\*\* $p \leq 0.001$



# Verlauf

## Adult Psychiatric Outcomes of Girls With Attention Deficit Hyperactivity Disorder: 11-Year Follow-Up in a Longitudinal Case-Control Study

Joseph Biederman, M.D.

Carter R. Petty, M.A.

Michael C. Monuteaux, Sc.D.

Ronna Fried, Ed.D.

Deirdre Byrne, B.S.

Tara Mirto, B.A.

Thomas Spencer, M.D.

Timothy E. Wilens, M.D.

Stephen V. Faraone, Ph.D.

## Verlauf

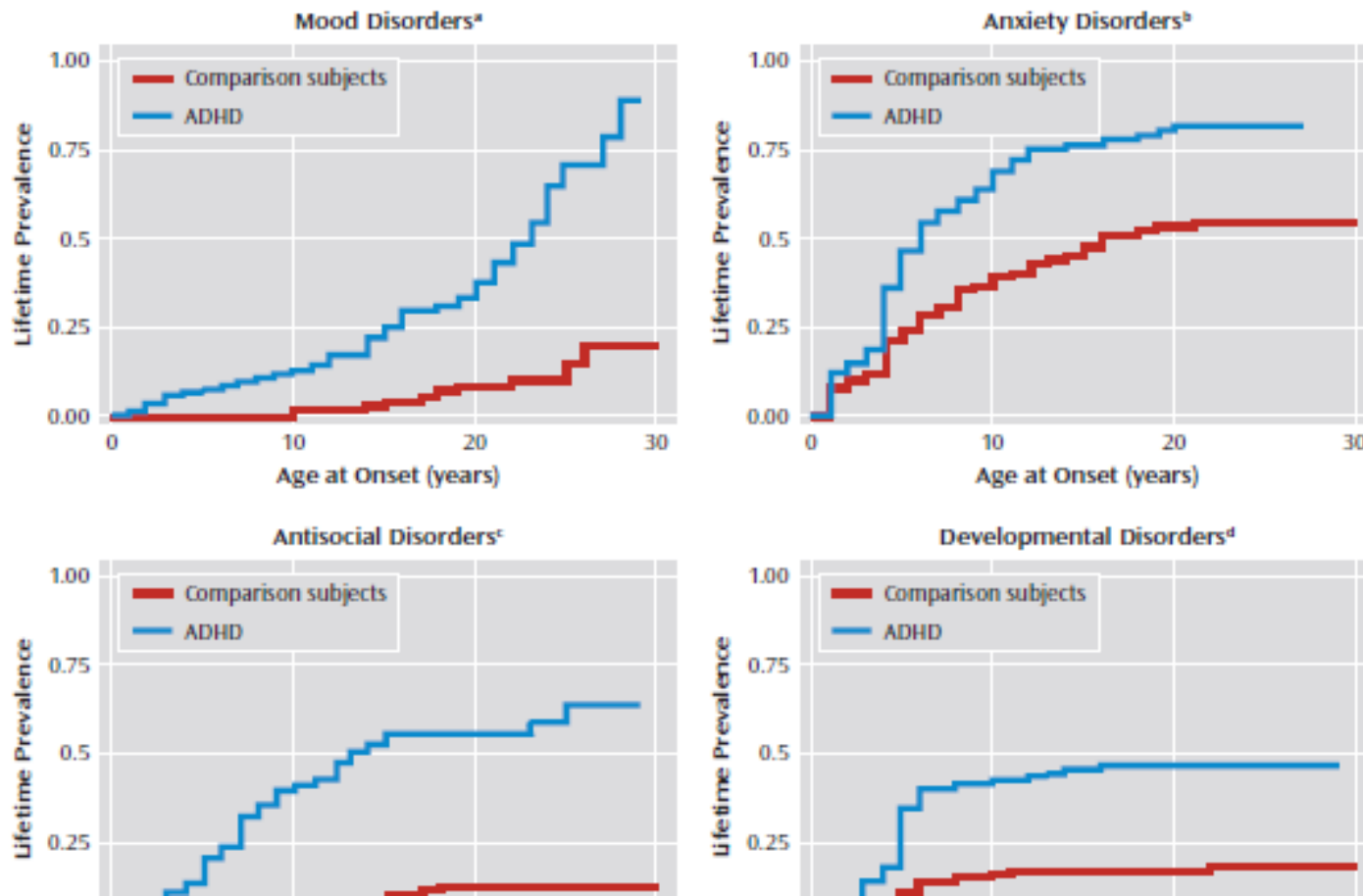
**Methods:** The authors conducted a longitudinal case-control study of 6- to 12-year-old girls with (N=140) and without (N=122) ADHD ascertained from psychiatric and pediatric sources. At the 1-year follow-up, 96 (69%) of the girls with ADHD and 91 (75%) of the comparison girls were reassessed (mean age=22 years). Participants were blindly assessed using structured diagnostic interviews.

**Results:** Lifetime and 1-year risks for all composite categories of psychopathology were significantly greater in girls with ADHD grown up relative to comparison girls. Lifetime hazard ratios were 7.2 (95% CI=4.1-12.7) for antisocial disorders, 6.8

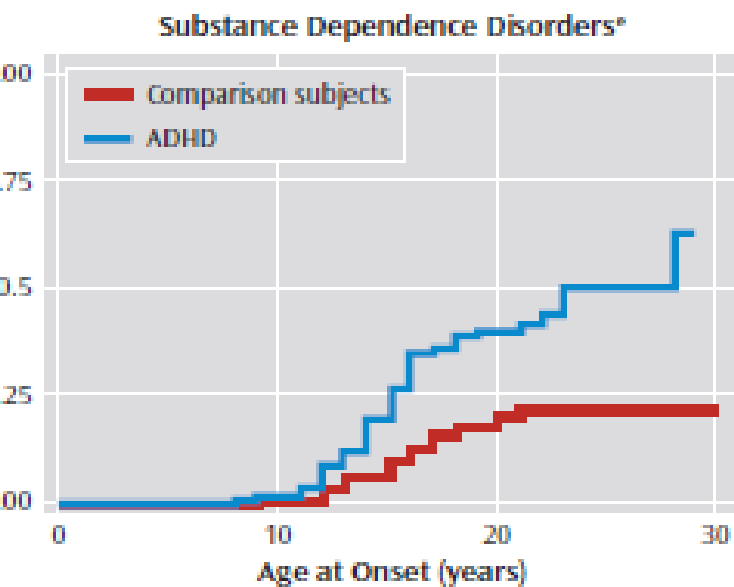
2.1 (95% CI=1.6-2.9) for anxiety disorders, 3.2 (95% CI=2.0-5.3) for developmental disorders, 2.7 (95% CI=1.6-4.3) for addictive disorders, and 3.5 (95% CI=1.6-7.3) for eating disorders. For lifetime psychopathology, all six composite categories remained statistically significant after controlling for other baseline psychopathology. Except for addictive disorders, significant 1-year findings remained significant after controlling for baseline psychopathology. The 1-year prevalences of composite disorders were not associated with lifetime or 1-year use of ADHD medication.

# Verlauf

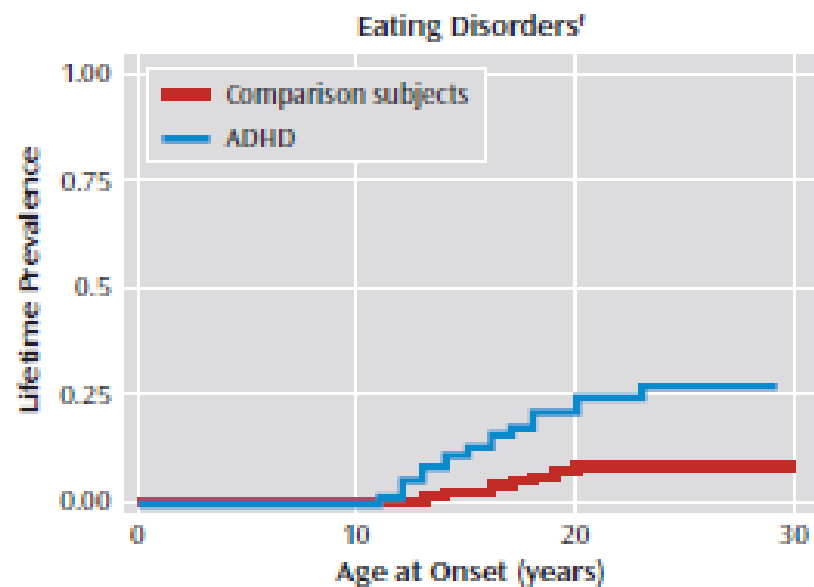
FIGURE 1. Cumulative Risks for Disorders in Girls With ADHD Relative to Comparison Girls for Six Composite Diagnostic Categories



# Verlauf



ratio=6.8, 95% CI=3.7–12.6,  $p<0.001$ .  
ratio=2.1, 95% CI=1.6–2.9,  $p<0.001$ .  
ratio=7.2, 95% CI=4.0–12.7,  $p<0.001$ .  
ratio=3.2, 95% CI=2.0–5.3,  $p<0.001$ .  
ratio=2.7, 95% CI=1.6–4.3,  $p<0.001$ .  
ratio=3.5, 95% CI=1.6–7.3,  $p=0.001$ .



# Verlauf

predictors of persistence in girls with attention deficit hyperactivity disorder: results from an 1-year controlled follow-up study

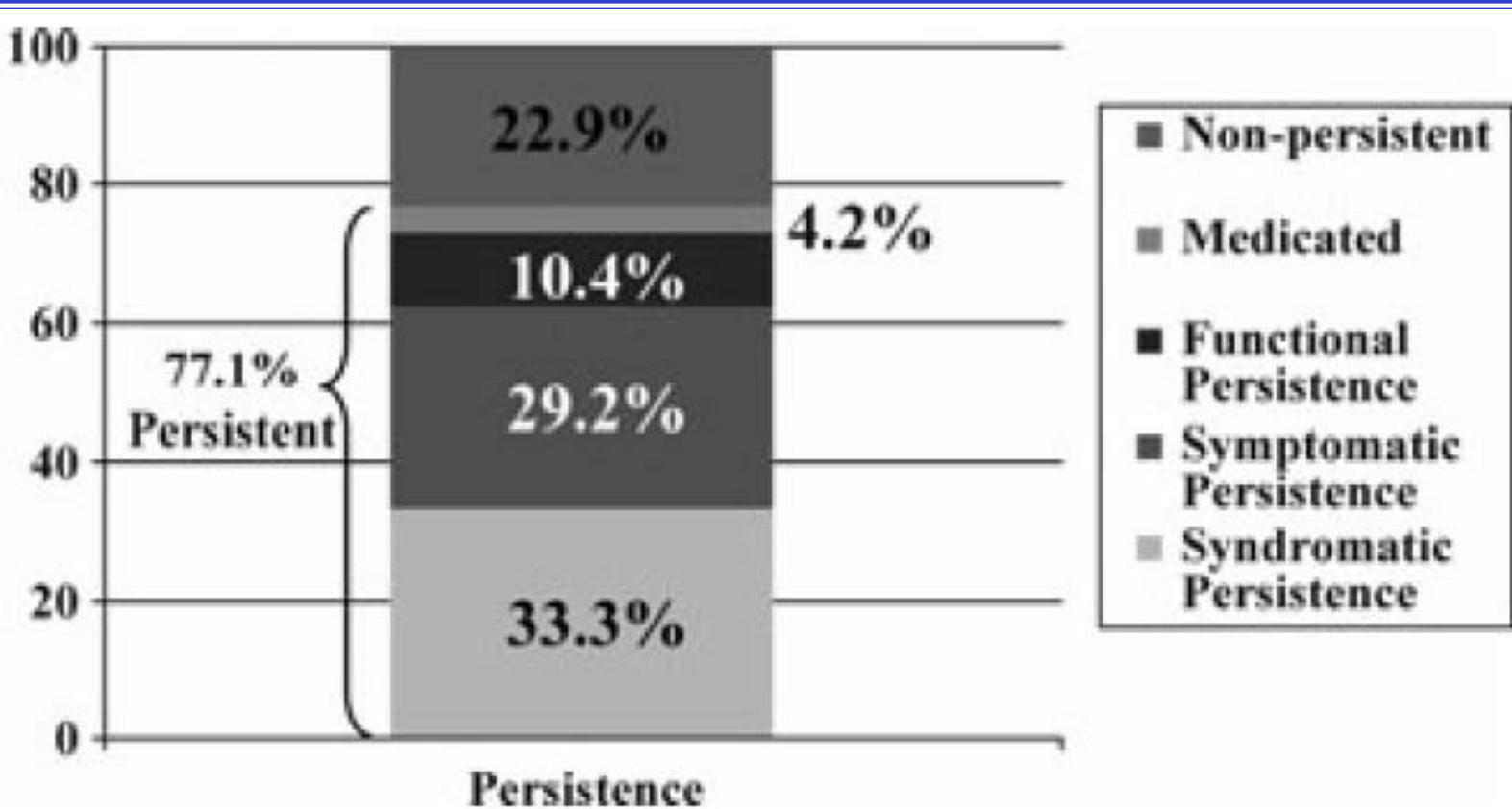
**J. Biederman<sup>1,2</sup>, C. R. Petty<sup>1</sup>,  
K. B. O'Connor<sup>1</sup>, L. L. Hyder<sup>1</sup>,  
S. V. Faraone<sup>3</sup>**

## Verlauf

**Method:** Participants were girls with ( $N = 96$ ) and without ( $N = 91$ ) ADHD and were 6–17 years old at the baseline assessment (mean age, 10.5 years) and 15–30 years old at the follow-up assessment (mean: 22.5 years). Participants were comprehensively and blindly assessed with structured diagnostic interviews and assessments of cognitive, social, and family functioning.

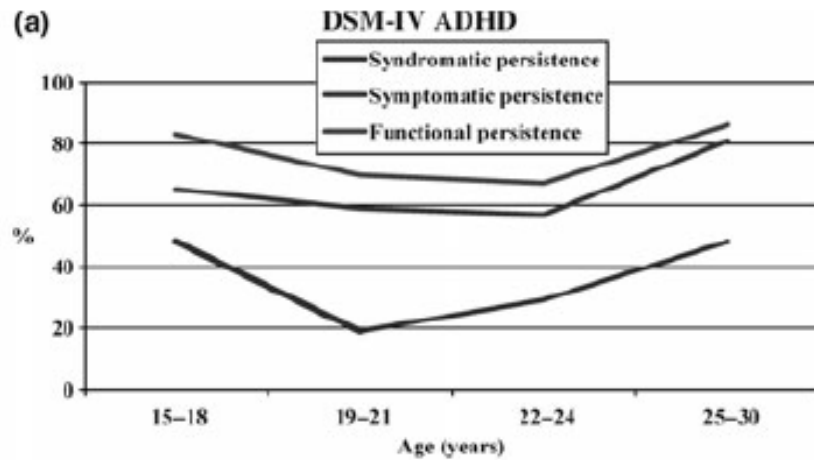
**Results:** At the 11-year follow-up, 33.3% met full criteria for ADHD, 25.5% showed partial persistence of the disorder, 10.4% had impaired social functioning, and 4.2% were remitted but treated (77.1% of the sample). Predictors of persistence were psychiatric comorbidity, family history of psychopathology, and family and school functioning at baseline.

# Verlauf

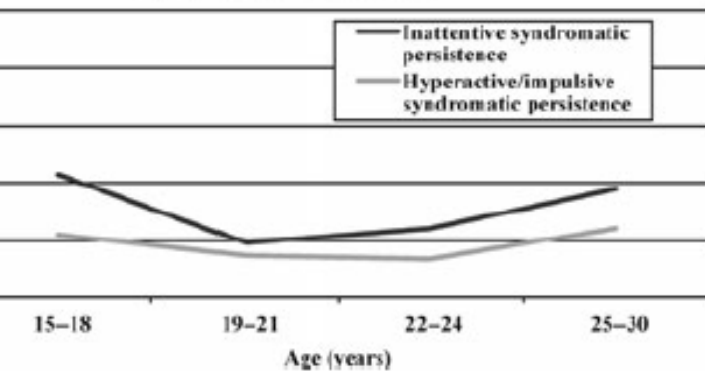


1. Persistence of attention deficit hyperactivity disorder at

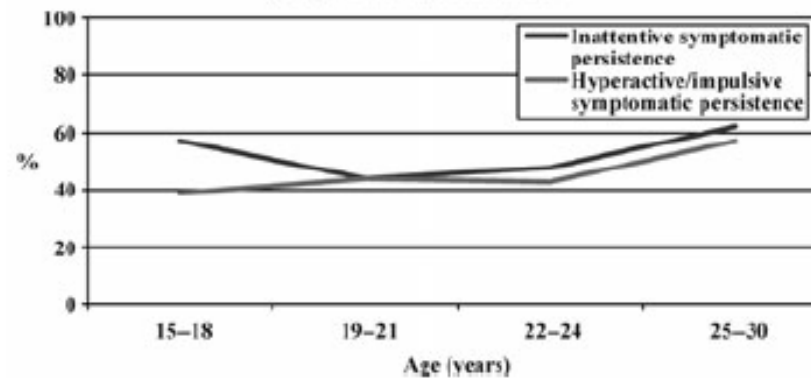
# Verlauf



**Inattentive and hyperactive/impulsive - syndromatic persistence**

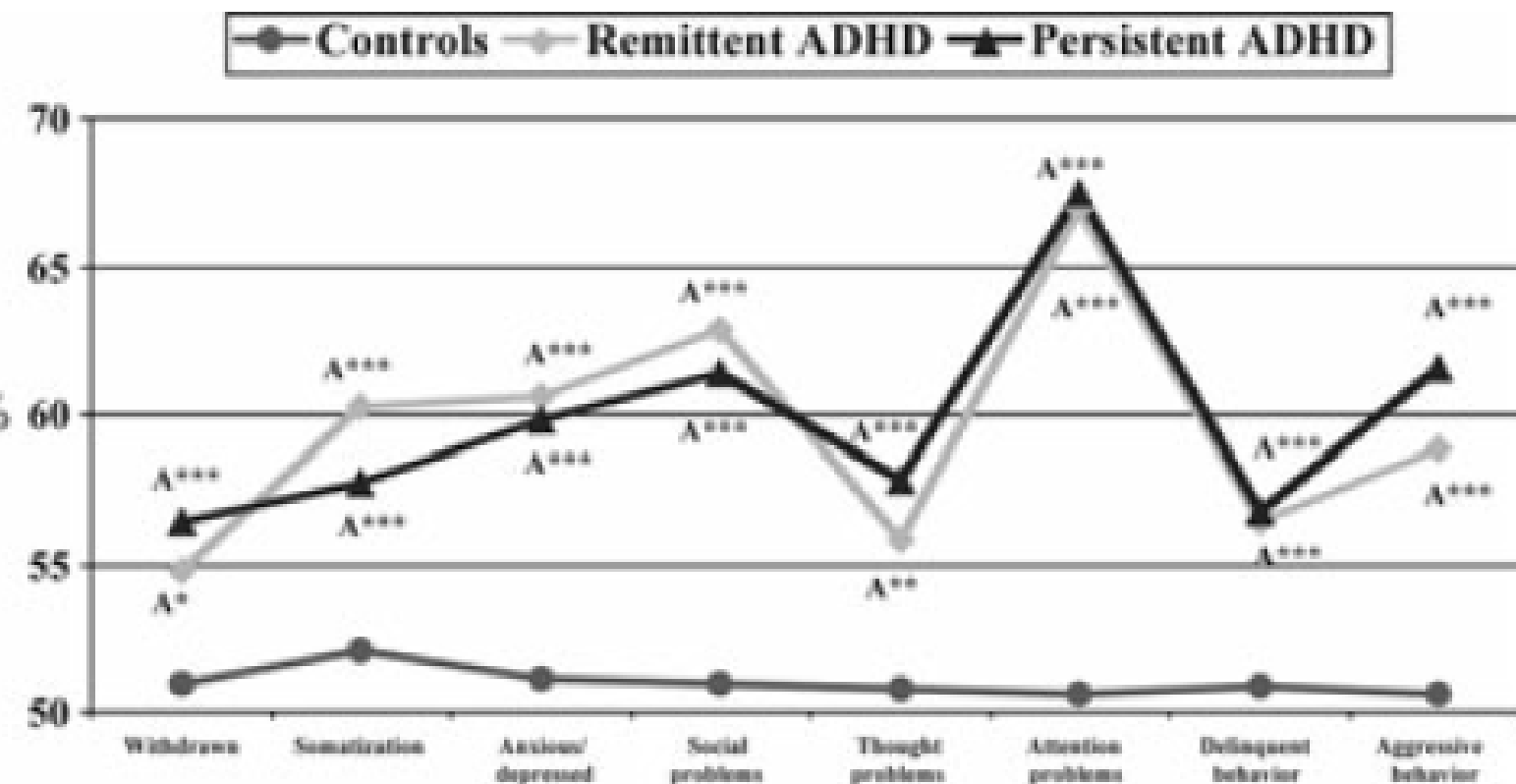


(c) **Inattentive and hyperactive/impulsive - symptomatic persistence**





# Verlauf



A = vs. Controls, B = vs. Remittent ADHD; \* $P \leq 0.05$ ; \*\* $P \leq 0.01$ ; \*\*\* $P \leq 0.001$

# Verlauf

**Ult Outcome of Attention-Deficit Hyperactivity  
Disorder: A controlled 16-Year Follow-Up Study**

Berman, J. et al., Journal of Clinical Psychiatry, 2012, 73:  
950

# Verlauf

## ETHOD

Case-controlled, 16-year (15-19 years) prospective follow-up study of ADHD. 140 boys with and 120 without DSM-III-R ADHD.

The main outcome measures were structured diagnostic interviews and measures of psychosocial, educational, and neuropsychological functioning.

Data were collected from 1988 to 2006.

# Verlauf

## RESULTS

At the 16-year follow-up, subjects with ADHD continued to significantly differ from controls in lifetime rates of antisocial, mood, anxiety, and addictive disorders, but with the exception of a higher interval prevalence of anxiety disorders (20% vs 11%) and smoking dependence (27% vs 11%), the incidence of individual disorders in the 6-year interval between the current and prior follow-up did not differ significantly from controls.

At the 16-year follow-up, the ADHD subjects compared with controls were significantly more impaired in psychosocial, educational, and neuropsychological functioning, differences that could not be accounted for by other active psychopathology.

# Prädiktoren des Verlaufs

## Jugendalter

niedrige Sozialschicht korreliert mit Schweregrad ADHS

niedriger IQ → ungünstiger Schulverlauf

ausgeprägte frühe Probleme mit Gleichaltrigen →

Beziehungsprobleme im Jugend- und Erwachsenenalter

komorbide SSV → Belastung der psychosozialen

Anpassung und des Schulverlaufs, Substanzmissbrauch,

SSV und Delinquenz

frühe mütterliche Psychopathologie (ADHS, Dissozialität,

Substanzmissbrauch) → psychische Störungen beim

Jugendlichen

frühe feindselige E-K-Interaktionen → spätere E-J-

# Prädiktoren des Verlaufs

*Psychiatry*. 2009 January 1; 65(1): 46–54. doi:10.1016/j.biopsych.2008.10.005.

## Good predictors of adult ADHD: Results from the WHO World Health (WMH) Survey Initiative

Maria Elena Medina Mora, MD, PhD<sup>1</sup>, John Fayyad, MD<sup>2</sup>, Ron de Graaf, PhD, MSc<sup>3</sup>, Ronald C. Kessler, MD, PhD<sup>4</sup>, Sergio Aguilar-Gaxiola, MD, PhD<sup>5</sup>, Matthias Angermeyer, MD<sup>6</sup>, Koen Demyttenaere, MD, PhD<sup>7</sup>, Giovanni de Girolamo, MD<sup>8</sup>, Josep Maria Haro, MD, MPH, PhD<sup>9</sup>, Robert Jin, MD, PhD<sup>10</sup>, G. Karam, MD<sup>2</sup>, Jean-Pierre Lépine, MD<sup>10</sup>, Maria Elena Medina Mora, PhD<sup>11</sup>, Johan van den Brink, MD<sup>12</sup>, José Posada-Villa, MD<sup>13</sup>, and Nancy Sampson, BA<sup>4</sup>

# Prädiktoren des Verlaufs

Childhood history of ADHD DSM-IV in ten countries in the WHO World Mental Health Survey

Estimated adult persistence of ADHD: 50% (84.1% Italy – 32.8% Mexico) with no respondent or gender difference in persistence rate

Predictors of persistence

- ADHD symptom profile (combined type)
- Symptom severity
- Comorbid MDD
- High comorbidity ( $\geq 3$  disorders)
- Paternal anxiety - mood disorders

# Prädiktoren des Verlaufs

## Synopse

Kognitive Merkmale (niedrige Intelligenz)

Emotionale Instabilität (Aggressivität, niedrige Frustrationstoleranz)

Familienmerkmale (psychische Störungen KE, emotionales Klima, defizitäre Erziehung, niedrige Sozialschicht)

Schweregrad ADHS (speziell Hyperaktivität/ Impulsivität)

Komorbidity (speziell SSV)

Soziale Funktionseinschränkung



# Verlauf

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Therapie und Verlauf

# MTA

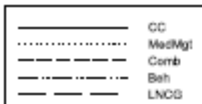
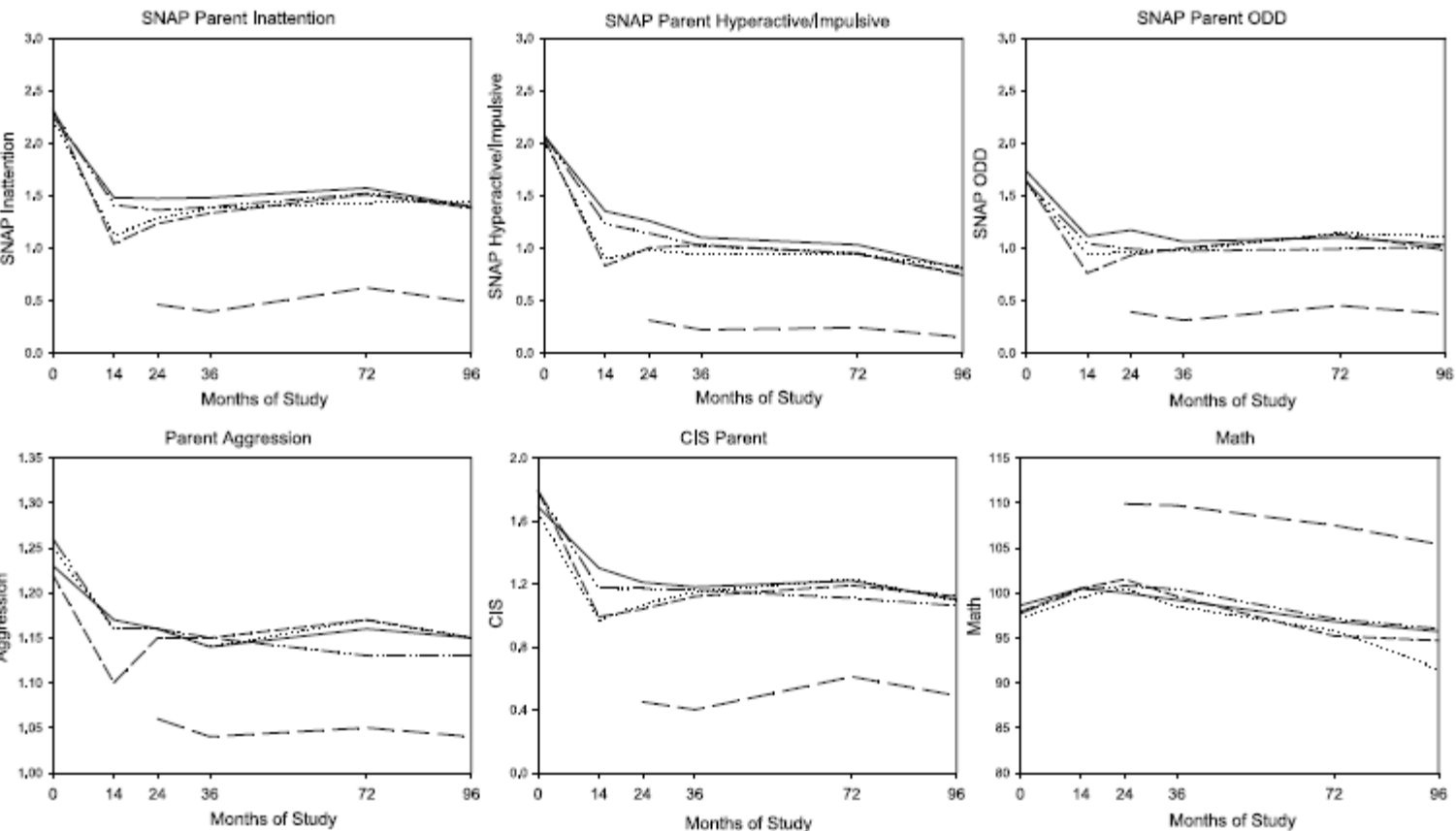
## 8 Year Follow-up

### MTA at 8 Years: Prospective Follow-up of Children Treated for Combined-Type ADHD in a Multisite Study

E. S.G. MOLINA, Ph.D., STEPHEN P. HINSHAW, Ph.D., JAMES M. SWANSON, Ph.D.,  
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PETER S. JENSEN, M.D., JEFFERY N. EPSTEIN, Ph.D., BETSY HOZA, Ph.D.,  
HECHTMAN, M.D., HOWARD B. ABIKOFF, Ph.D., GLEN R. ELLIOTT, Ph.D., M.D.,  
NANCE L. GREENHILL, M.D., JEFFREY H. NEWCORN, M.D., KAREN C. WELLS, Ph.D.,  
TIMOTHY WIGAL, Ph.D., ROBERT D. GIBBONS, Ph.D., KWAN HUR, Ph.D.,  
PATRICIA R. HOUCK, M.S., AND THE MTA COOPERATIVE GROUP

# MTA

## 8 Year Follow-up



# MTA

## 8-Jahres-Verlauf

nahezu allen Analysen unterschieden sich die ursprünglich randomisierten Gruppen nicht signifikant.

Medikation nahm um 62% nach dem kontrollierten 14-Monate-Versuch ab; keine Veränderung der Resultate nach Randomisierung für diesen Faktor.

Verlauf der ADHS Symptome in den ersten 3 Jahren prädizierte 55% der Verlaufsergebnisse.

Teilnehmer der MTA zeigten bei 91% der untersuchten Variablen schlechtere Befunde als die lokale Vergleichsgruppe.

Typ oder die Intensität der 14-Monate-Behandlung der ADHS in der Kindheit prädiziert das Funktionsniveau nach 6-8 Jahren nicht

# MTA

## 8-Jahres-Verlauf

### Schlussfolgerungen

Kinder mit weniger komplexen Verhaltensproblemen und aus besserem sozialen Milieu, mit dem besten Ansprechen auf jegliche Therapie haben die beste Langzeitprognose.

Trotz anfänglicher Verbesserung unter Therapie, die weitgehend nach Therapie aufrechterhalten bleibt, haben Kinder mit ADHS (Comb) deutlich mehr Beeinträchtigungen in der Adoleszenz.

Innovative Therapieansätze mit Ziel auf bestimmte Bereiche der Funktionstüchtigkeit von Jugendlichen

# MTA

## 8-Jahres-Verlauf

ründe für das Verschwinden der Gruppenunterschiede:

- Die Medikation war nicht weiter effektiv oder
- alle Teilnehmer profitierten von der Behandlung und diese Verbesserung wurde aufrecht erhalten oder
- der natürliche Verlauf war für die Verbesserung verantwortlich oder
- die Daten waren konfundiert and Schlussfolgerungen lassen sich schwer ziehen.

# Therapie und Verlauf

BMC Medicine 2012, 10:99  
biomedcentral.com/1741-7015/10/99



RESEARCH ARTICLE

Open Access

Systematic review and analysis of long-term  
outcomes in attention deficit hyperactivity  
disorder: effects of treatment and non-treatment

Law<sup>1†</sup>, Paul Hodgkins<sup>2\*†</sup>, Hervé Caci<sup>3</sup>, Susan Young<sup>4</sup>, Jennifer Kahle<sup>5</sup>, Alisa G Woods<sup>6</sup> and  
Arnold<sup>7</sup>

# Therapie und Verlauf

**d:** In childhood, attention deficit/hyperactivity disorder (ADHD) is characterized by age-inappropriate inattentiveness/disorganization, hyperactivity/impulsiveness, or a combination thereof. Although the symptoms of ADHD are well defined, the long-term consequences in adults and children need to be more extensively understood and quantified. We conducted a systematic review evaluating the long-term consequences (defined as 2 years or more) of ADHD with the goal of identifying long-term outcomes and the impact of treatment (pharmacological, non-pharmacological, or multimodal) has on ADHD long-term outcomes.

Studies were identified using predefined search criteria and 12 databases. Studies included were peer-reviewed primary studies of ADHD long-term outcomes published between January 1980 to December 2010. Inclusion was agreed on by two independent researchers on review of abstracts or full text. Published statistical analyses of outcome results were summarized as poorer than, similar to, or improved versus comparators, and presented as percentage comparisons of these categories.

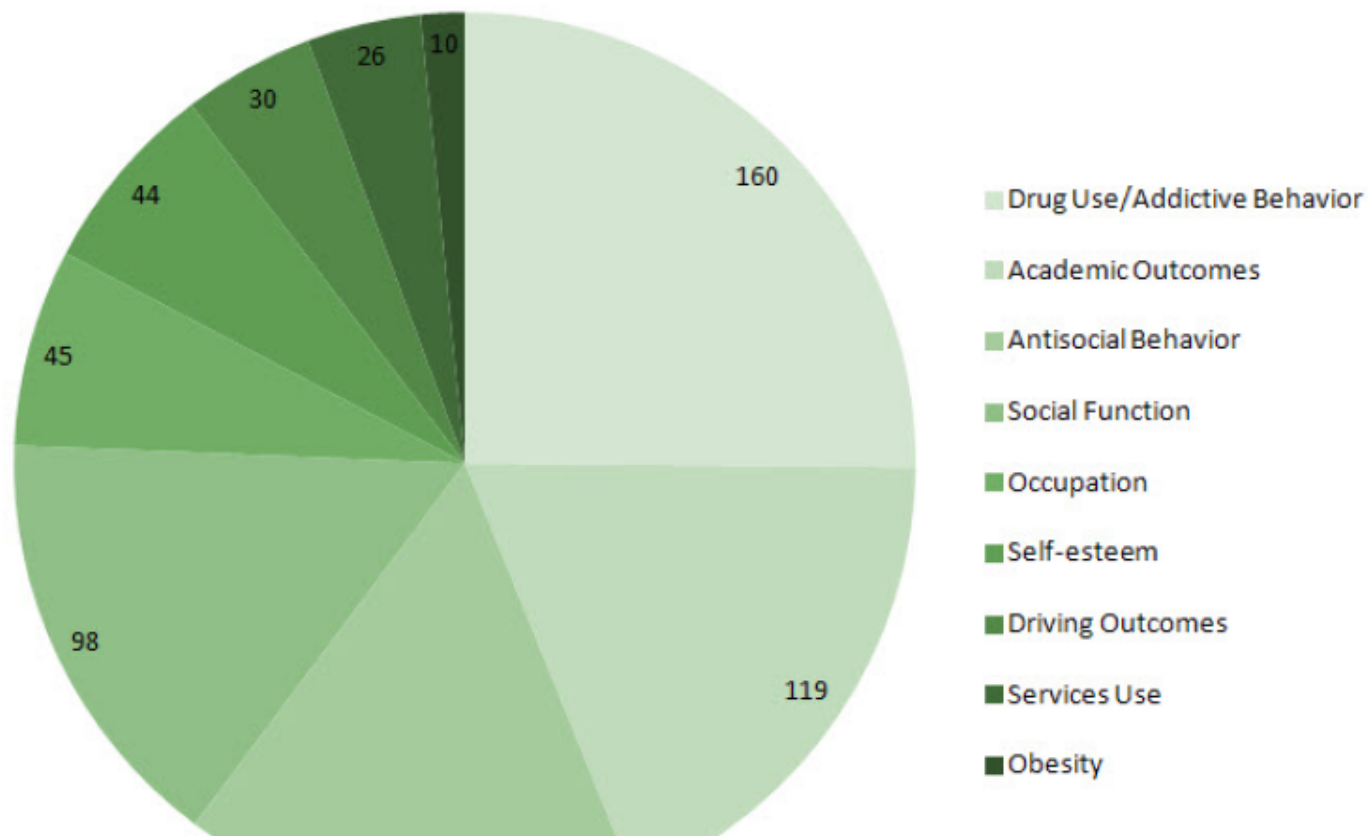
Outcomes from 351 studies were grouped into 9 major categories: academic, antisocial behavior, driving, substance use/addictive behavior, obesity, occupation, services use, self-esteem, and social function. The following broad trends emerged: (1) without treatment, people with ADHD had poorer long-term outcomes in all categories compared with people without ADHD, and (2) treatment for ADHD improved long-term outcomes compared with untreated ADHD, although not usually to normal levels. Only English-language papers were included and databases may have omitted relevant studies.

**s:** This systematic review provides a synthesis of studies of ADHD long-term outcomes. Current



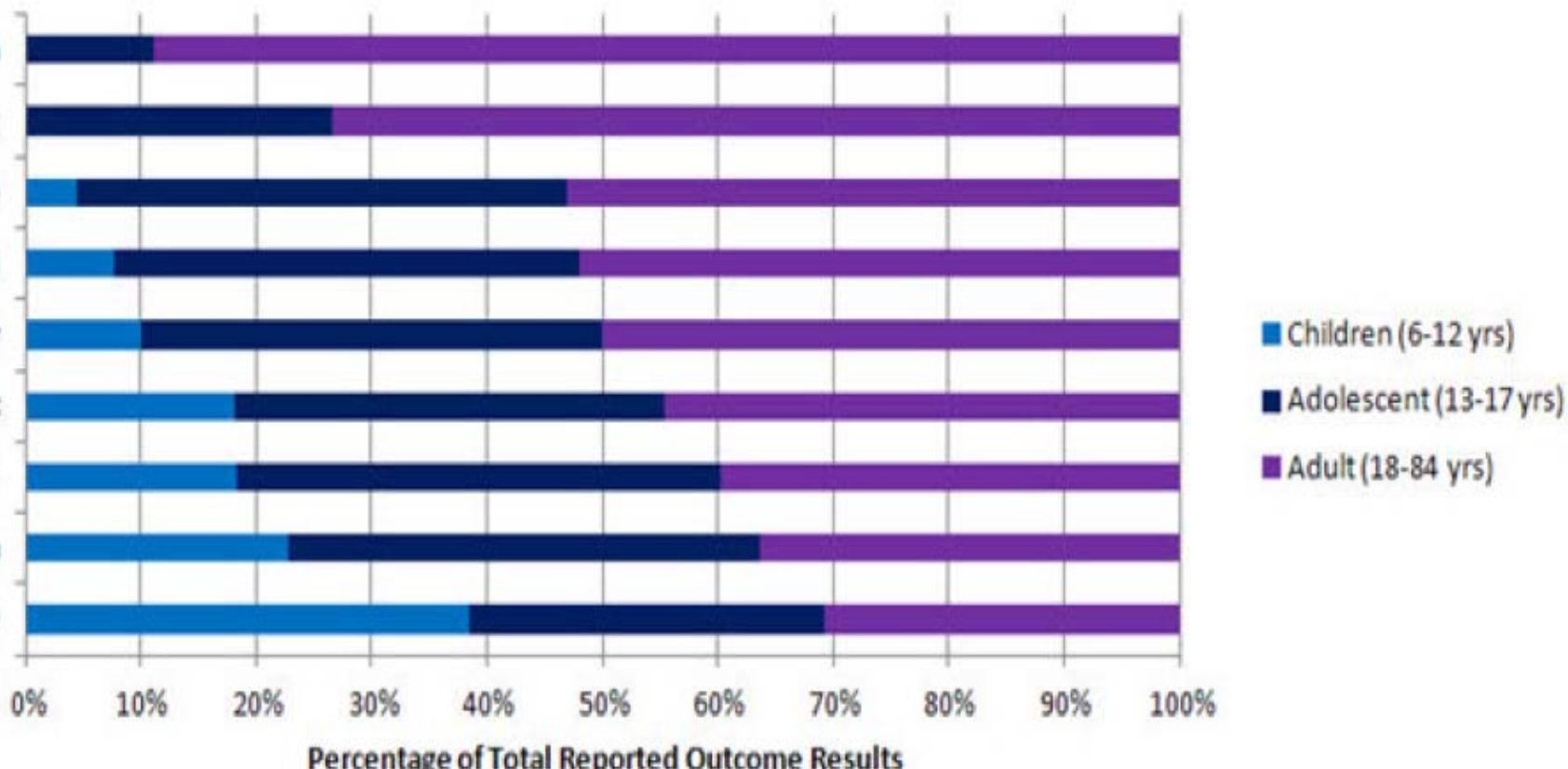
# Therapie und Verlauf

Outcome Groups



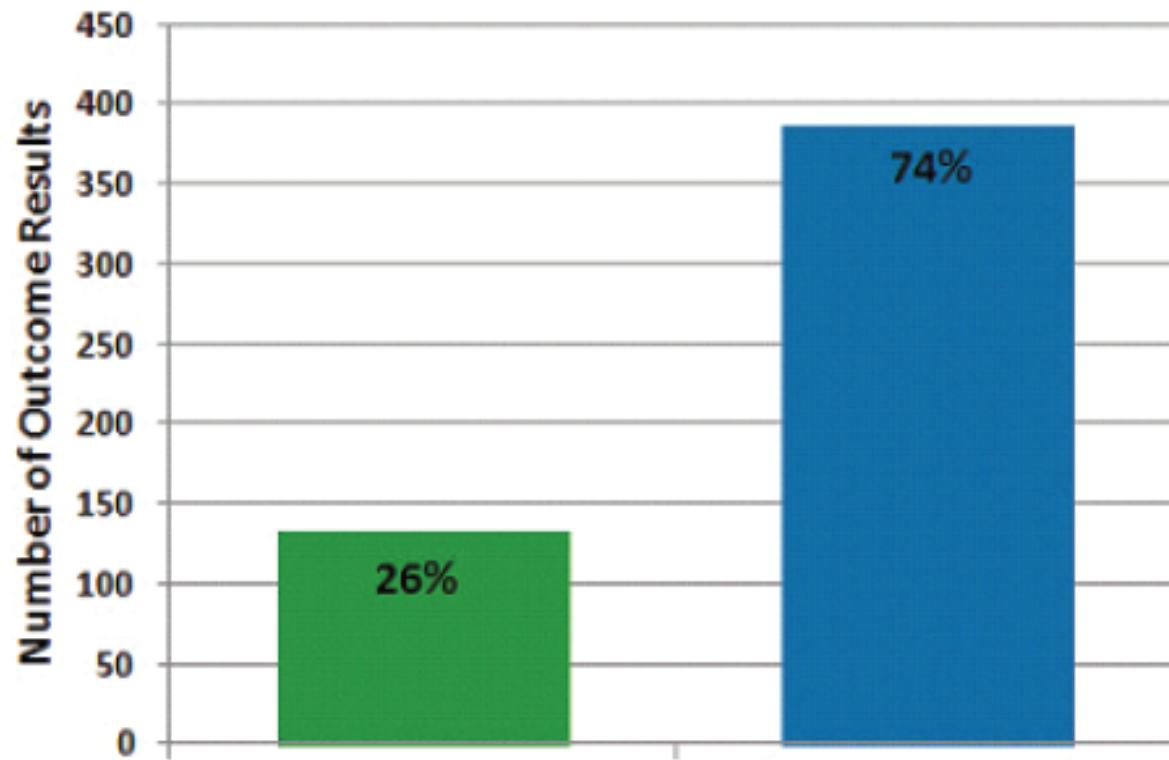
# Therapie und Verlauf

## Outcome Groups by Participant Ages

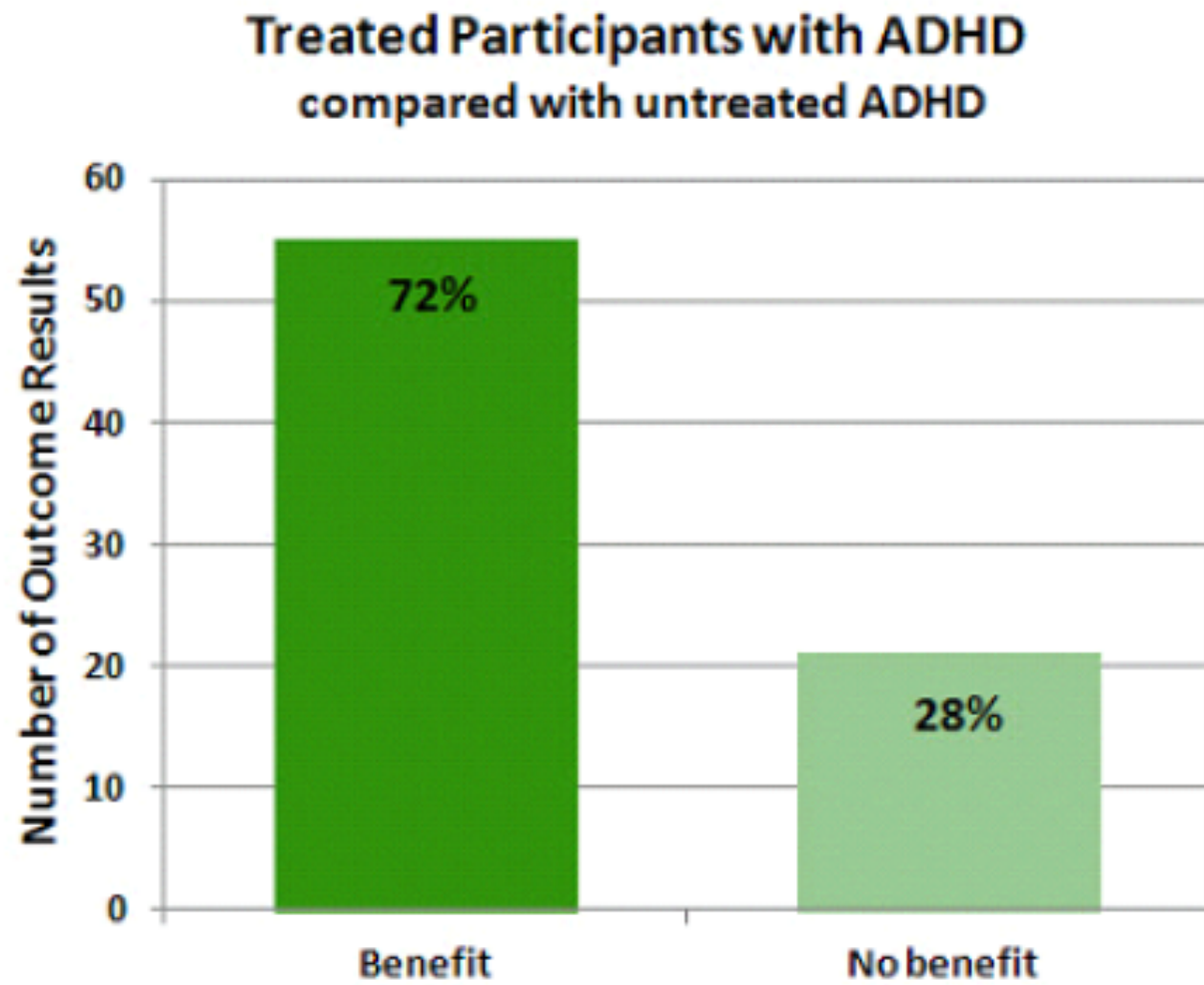


# Therapie und Verlauf

**Untreated Participants with ADHD**  
compared with non-ADHD participants

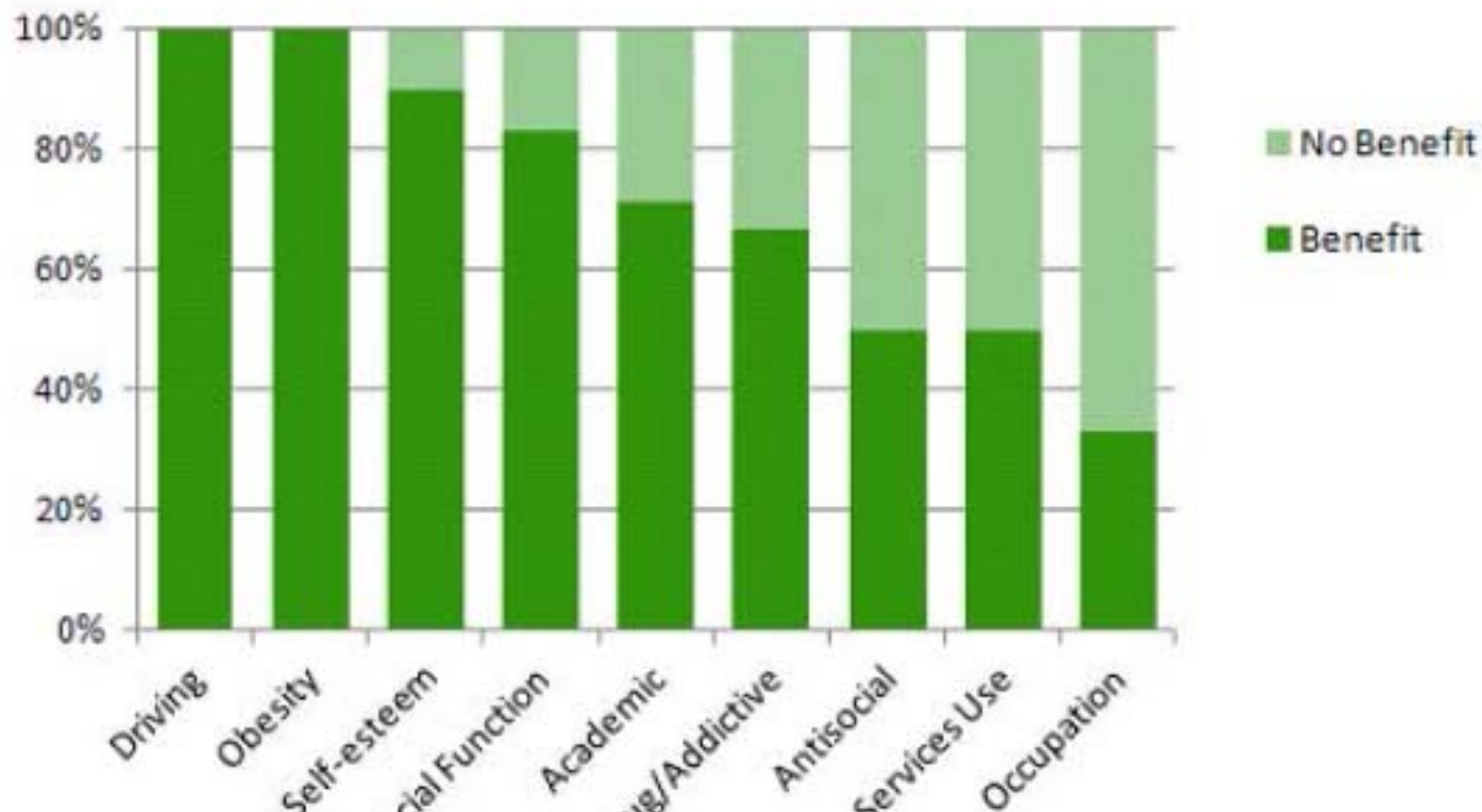


# Therapie und Verlauf



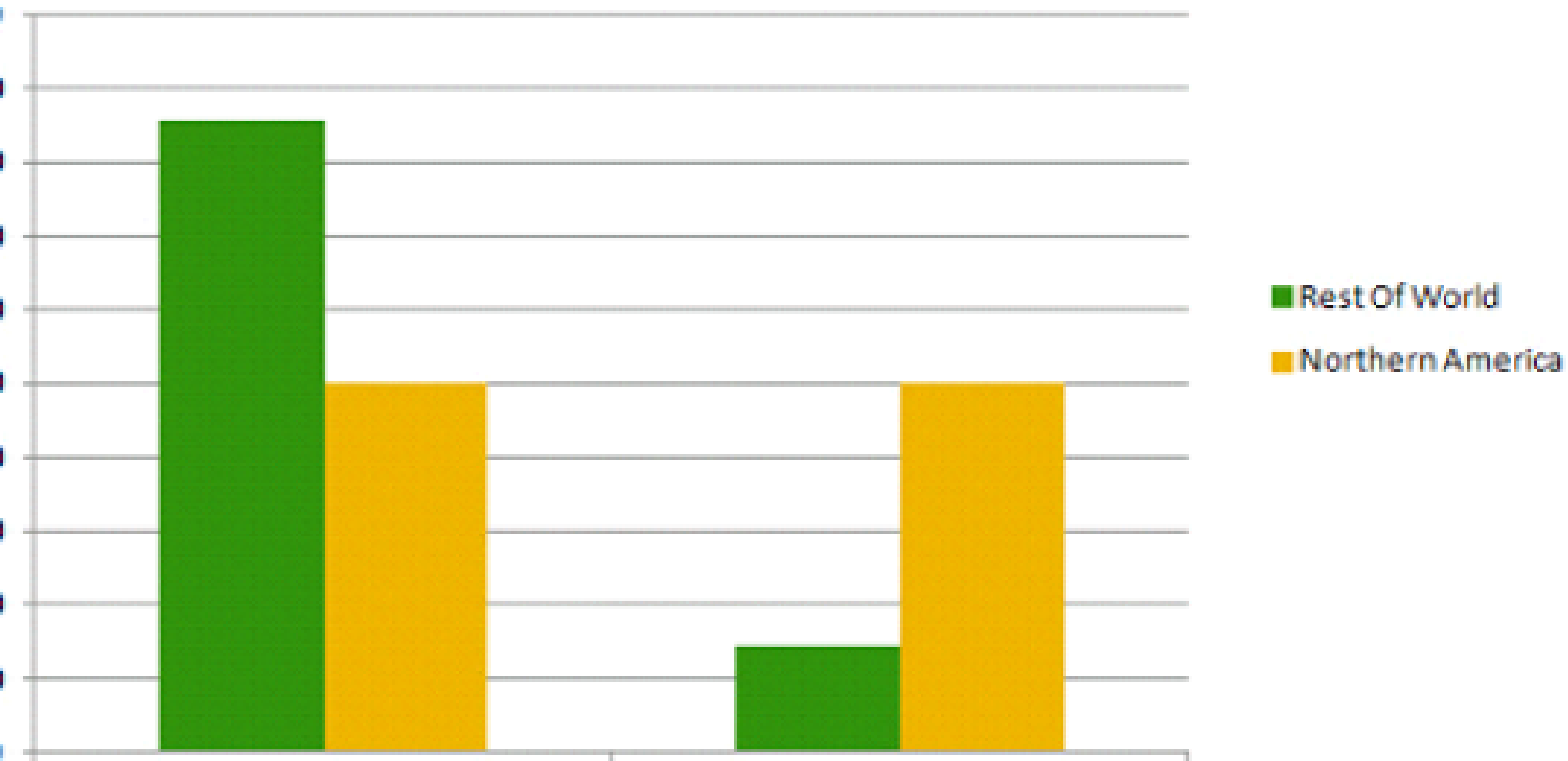
# Therapie und Verlauf

**Treatment Benefit by Outcome Group**  
compared with untreated ADHD



# Therapie und Verlauf

**Treatment Outcomes by Region  
for a Subgroup of Outcome Groups**



# Therapie und Verlauf

## Conclusions

The present analysis supports the premise that without treatment, people with ADHD often experience poorer long-term outcomes and that treatment may improve the long-term outcomes of ADHD for some individuals, but not necessarily to the degree of healthy controls. Further analyses of the present data set will more comprehensively examine the impact of treatment on specific outcomes, as well as the impact of specific types of treatment modalities. The question remains as to whether the short-term benefits demonstrated by short-term drug or non-pharmacological treatment studies translate directly into long-term outcomes. Associations between specific short-term symptoms need to be examined as possible predictors for long-term outcomes, particularly because long-term studies are not always feasible. Future research should focus on the association between short-term symptom relief and long-term consequences and include longer-term follow-

# Therapie und Verlauf

*N Engl J Med.* 2012 November 22; 367(21): 2006–2014. doi:10.1056/NEJMoa1203241.

## Medication for Attention Deficit-Hyperactivity Disorder and Anxiety

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# Therapie und Verlauf

—We gathered information on all individuals with a diagnosis of ADHD (N=25,656), pharmacological treatment, and subsequent criminal convictions in Sweden during 2006 to 2012 using Swedish national registers. We used stratified Cox regression analyses to compare the criminality while on ADHD medication, compared with the rate for the same individual without medication.

—Compared to non-medication periods, the criminality rate while on medication was significantly decreased by 32% (stratified Cox Regression hazard ratio: 0.68; 95 % confidence interval: 0.63-0.73) for men and 41% (hazard ratio: 0.59; 95 % confidence interval: 0.50-0.70) for women. The rate reduction remained between 17-46% in sensitivity analyses among males, across different exposures (e.g., type of treatment – stimulant and non-stimulant) and outcomes of crime - less severe, violent, and substance-related conviction).

**Conclusions**—We found statistically significant associations between ADHD medication and criminality in within-individual comparisons, with lower rates of criminality observed during medication treatment. These findings raise the possibility that medication treatment reduces the criminality among patients with ADHD.



# Therapie und Verlauf

European Journal of Neuropsychopharmacology (2014) 24, 232-241



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Substance use disorders in association  
with attention-deficit/hyperactivity disorder,  
comorbid mental disorders, and medication  
in a nationwide sample

Andreas Steinhausen<sup>a,b,c,\*</sup>, Charlotte Bisgaard<sup>a</sup>



# Therapie und Verlauf

## Abstract

**Background:** The association of substance use disorders (SUD) with attention-deficit disorder (ADHD), co-morbid mental disorders, and medication has only been studied in isolation and in rather small samples.

**Procedure:** Data were based on four Danish national registers covering a total of 20,742 patients with ADHD, their dispensed medications, co-morbid mental disorders, and associated SUD between 1994 and 2010. The analyses considered the risk of various medications (methylphenidate only, antidepressants only, antipsychotic only, mixed medication) in comparison to a control group of non-medicated patients with ADHD, various co-morbid disorders, duration of medication, age at diagnosis, year of birth, and sex for developing SUD.

**Results:** The observation period of the cohort ranged between 2.25 and 66.21 years and the prevalence for SUD was 9.51%. The SUD rates were significantly higher prior to, compared to following the onset of medication in the methylphenidate and the mixed medication subgroup, whereas they were significantly higher following onset of medication in the antidepressants and the antipsychotics subgroups. However, the SUD rates were significantly higher in all drug conditions except for methylphenidate after onset of medication compared to the non-medicated subgroup. Risk factors obtained by regression analysis did not include methylphenidate but did include antidepressants, antipsychotics, and mixed medications, in combination with co-morbid mood, anxiety, personality, and conduct disorders, and older age at diagnosis. Longer duration of medication and female sex were protective factors.

**Conclusions:** This representative study based on a large nationwide psychiatric sample provides solid evidence into the patterns of SUD in patients with ADHD based on medication use and co-

# Therapie und Verlauf

Age at diagnosis onset, duration of treatment with defined daily dose (DDD), and observation periods in various subgroups.

subgroup	Age at diagnosis		Years on DDD		Period prior to Onset of medication (years)		Period following Onset of medication (years)		$z^a$	$p$	
	$N$	Mean	SD	Mean	SD	Mean	SD	Mean			SD
idate	7314	11.11	5.68	2.69	3.04	11.35	5.45	3.50	3.23	69.98	<0.001
ants	952	27.46	10.56	1.54	2.47	24.34	8.46	3.24	3.33	26.71	<0.001
ics	483	20.90	10.28	0.61	2.61	18.95	7.67	3.19	3.47	18.96	<0.001
ication	5494	20.29	11.76	5.19	6.36	17.94	9.57	5.44	3.72	60.89	<0.001
ion	6370	13.30	8.88	-	-	14.45	7.38	-	-	-	-

<sup>a</sup> comparing the period prior to medication vs. the period following medication.



# Therapie und Verlauf

Number (percentages) of patients with substance use disorder (SUD) in various medication subgroups prior to and following onset of medication and in comparison to no medication.

	(A) SUD prior to onset of medication (N=553)	(B) SUD following onset of medication (N=1229)	$p^a$	$p^b$	$V^a$	$V^b$
Medication	103 (18.63%)	102 (8.30%)	<0.001	<0.001	0.14	0.26
Antipsychotics	24 (4.34%)	319 (25.96%)	<0.001	<0.001	0.25	0.15
Mood stabilizers	53 (9.58%)	181 (14.73%)	<0.01	<0.001	0.07	0.37
No medication	373 (67.45%)	627 (51.02%)	<0.001	<0.001	0.15	0.16

<sup>a</sup>and Cramér's  $V$  comparing A vs. B.

<sup>b</sup>and Cramér's  $V$  comparing SUD following onset of medication in the various total medication subgroups with the no medication subgroup (N=72/20,742[0.35%]).

# Therapie und Verlauf

Hazard ratios associated with various medication, co-morbid mental disorders, subgroups of ADHD, and age at ADHD relation to substance use disorders stratified on year of birth and sex with medication subgroups treated as time-

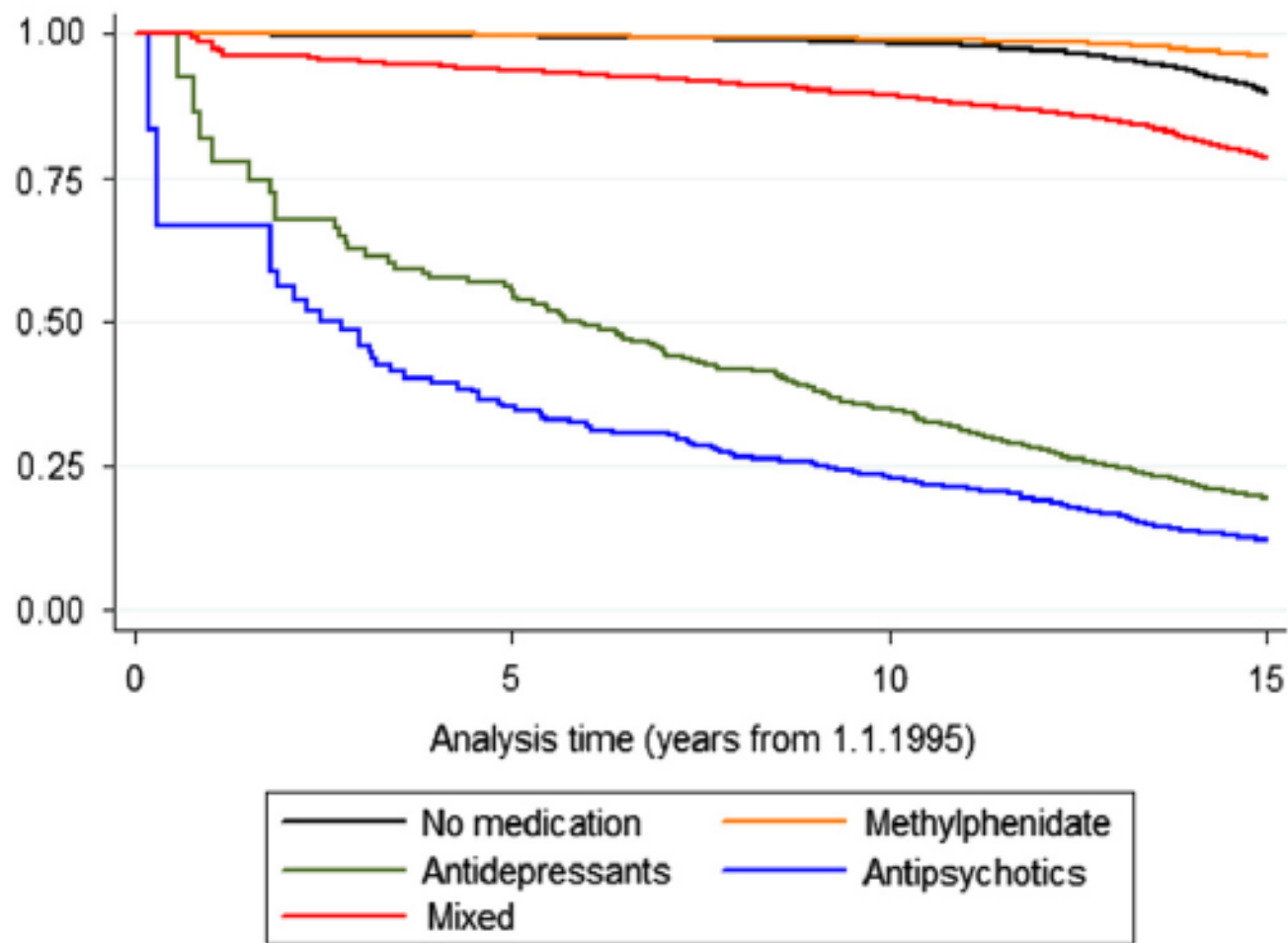
	Hazard ratio	Std. error	p-Value	95% CI
group				
ation	1.00	-	-	(Reference)
enidate	0.92	0.10	n.s.	[0.74;1.15]
essants	6.94	0.52	<0.001	[5.99;8.03]
otics	7.58	0.67	<0.001	[6.37;9.02]
edication	1.48	0.10	<0.001	[1.31;1.69]
mood disorders				
	1.00	-	-	(Reference)
	1.40	0.08	<0.001	[1.25;1.57]
anxiety disorders				
	1.00	-	-	(Reference)
	1.20	0.09	<0.05	[1.04;1.39]
personality disorders				
	1.00	-	-	(Reference)

# Therapie und Verlauf

Conduct disorders	1.00	-	-	(Reference)
	1.66	0.12	<0.001	[1.44;1.91]
Autism spectrum disorders	1.00	-	-	(Reference)
	0.71	0.07	<0.01	[0.58;0.87]
Deficit of activity and attention	1.00	-	-	(Reference)
	1.13	0.23	n.s.	[0.75;1.69]
Oppositional defiant disorder	1.00	-	-	(Reference)
	1.07	0.24	n.s.	[0.70;1.65]
Conduct disorder, Unspecified	1.00	-	-	(Reference)
	1.35	0.29	n.s.	[0.89;2.04]
Diagnosis	1.00	-	-	(Reference)
ADHD (12 yrs)	1.00	-	-	(Reference)
ADHD (12 yrs)	5.29	0.63	<0.001	[4.19;6.68]



# Therapie und Verlauf



# Therapie und Verlauf

## Control of confounding by indication

Propensity score analyses by

- age at diagnosis of ADHD
- year of birth and sex
- comorbid disorders prior to onset of medication

There was only little difference in propensity scores for the medicated and the non-medicated group, indicating that there was no underlying difference in the groups.

The additional variables in the propensity analyses may still be too limited to detect any underlying systematic similarities in the treated and the untreated groups

# Verlauf

## Schlussfolgerungen

Schwieriges Temperament und Probleme der Selbstregulation als frühe Vorläufer von ADHS. Überlagerung der Kernsymptome durch OTV im VS-Alter

Beeinträchtigte Schullaufbahn als grösstes Risiko im Kindes- und Jugendalter

Komorbide SSV als zweitgrösstes Risiko mit Übergang in Dissozialität und SM

Multiple Beziehungsstörungen als drittes Risiko

Schlechtere Bildungsabschlüsse, beeinträchtigte Berufskarrieren und Probleme der sozialen Anpassung

Häufige Persistenz bzw. inkomplette Remission von ADHS

# Danish ADHD Follow-up Study

## amples

All children and adolescents aged 4-15 years and diagnosed in 1995-2005 with ADHD (F90) in the DPCRR (N=4967).

- A random sample of 387 cases was extracted for the validation study.
- Preliminary results suggest, that at least 87 % have diagnoses consistent with ICD-10 criteria for F90

Case-probands were matched on birth date and sex to at least 5 non-exposed (non-ADHD) individuals at the time of ADHD diagnosis of the case-probands.

- This group was randomly selected from the Danish

# Danish ADHD Follow-up Study

## Outcomes

Mental disorders incl. hospitalization

Delinquent acts and crimes (traffic violations/tickets, convictions, prison sentences etc.)

Educational status (attainments and grades)

Occupational status (income, social benefits, disability pension etc.)

Physical health conditions (pregnancies, diseases etc.)

# Danish ADHD Follow-up Study

## Predictors

### *Individual*

- Comorbid mental disorders
- Psychotropic medication
- Perinatal risk factors (birth weight, gestational age, Apgar scores, maternal smoking during pregnancy etc).

### *Social*

- Parental mental and vocational status
- Parental educational status
- Placement outside the home / social welfare services
- SES of the family

Danke für die Aufmerksamkeit!

Anhang



# **MTA Follow-up**

# MTA Follow-up at 24-Month

Comb / Med Mgt > Beh / CC  
for ADHD and ODD symptoms

Superiority not as great as at 14 months

Superiority partly mediated by continuing medication

Near normalization / excellent responders<sup>1</sup>:

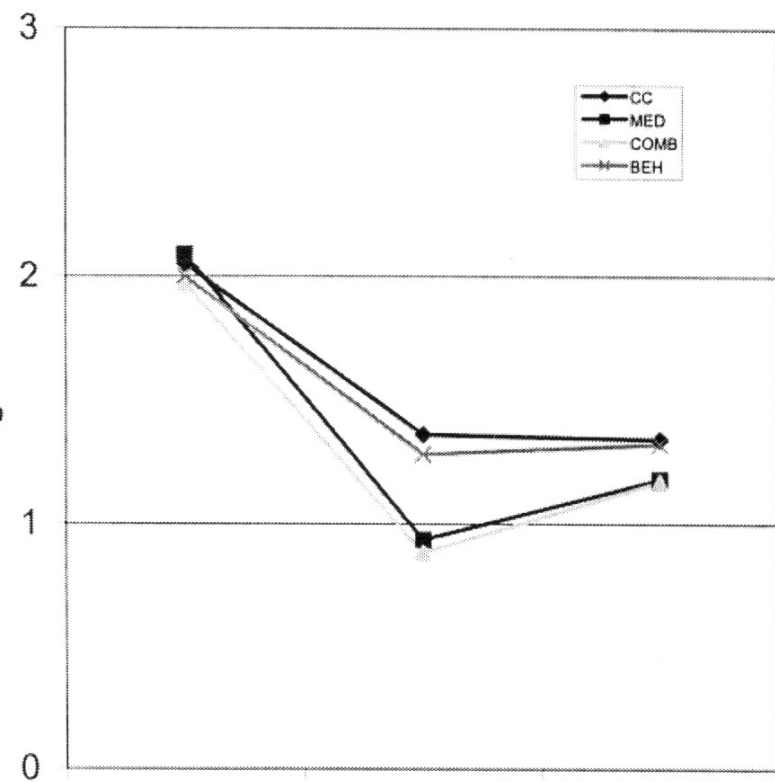
Comb 48%; Med Mgt 37%; Beh 32%; CC 28%

AP item mean  $\leq 1$  “just a little“)

# MTA Follow-up at 24-Month

*Changes in effectiveness*

Comb / Med Mgt deteriorated, but Beh / CC did not



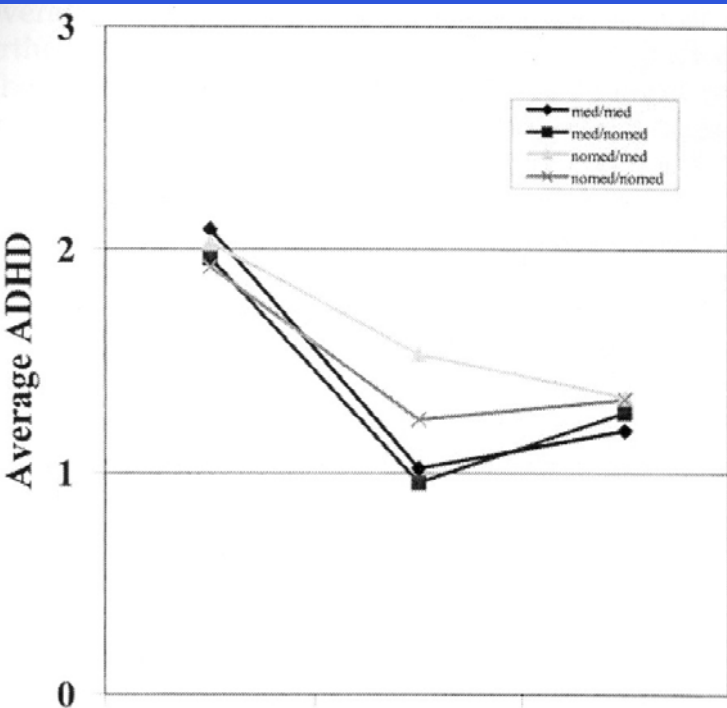
Assigned Treatment (n=521)	Change Scores	
	B-14 months	14-24 months
Comb (n=135)	-1.10	+0.27
MedMgt (n=120)	-1.10	+0.22
Beh (n=135)	-0.75	+0.04
CC (n=131)	-0.67	+0.02

Fig 1. Assigned (randomized) treatment groups: SNAP-ADHD ratings and change scores.

# MTA Follow-up at 24-Month

## Change in effectiveness

Differences in 14- to 24-month deterioration are partially explained by actual medication use in the follow-up period



Naturalistic Subgroups Based on Pattern of Medication Use (n=521)	Change Scores	
	0-14 months	14-24 months
Med/Med (n=255)	-1.10	+0.15
No Med/NoMed (n=139)	-0.68	+0.10
Med/No Med (n=76)	-1.00	+0.33
No Med/Med (n=51)	-0.50	-0.15

Fig 2. Naturalistic subgroups: SNAP-ADHD ratings and change scores.

# MTA Follow-up at 24-Month

## *Changes in Height and Weight*

Growth suppression in the initial 14-month treatment phase for  
Comb / Med Mgt

Dissipation of the initial growth suppression effect in the 10-  
month follow-up

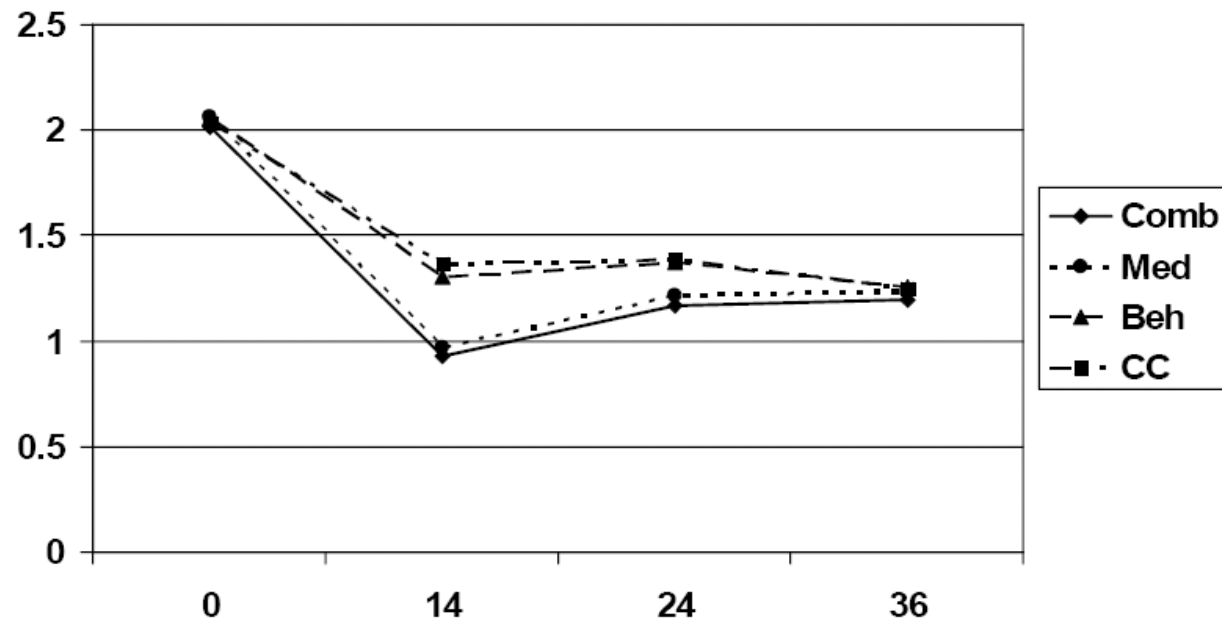
Consistent medication use showed mild growth suppression;  
however, this group was shorter and lighter at baseline

Alternative interpretations: medication-related growth  
suppression vs. Preexisting selection factors (or interaction)

No ultimate growth estimation (subjects were only 9-11 years  
of age)

# MTA Follow-up at 36 months

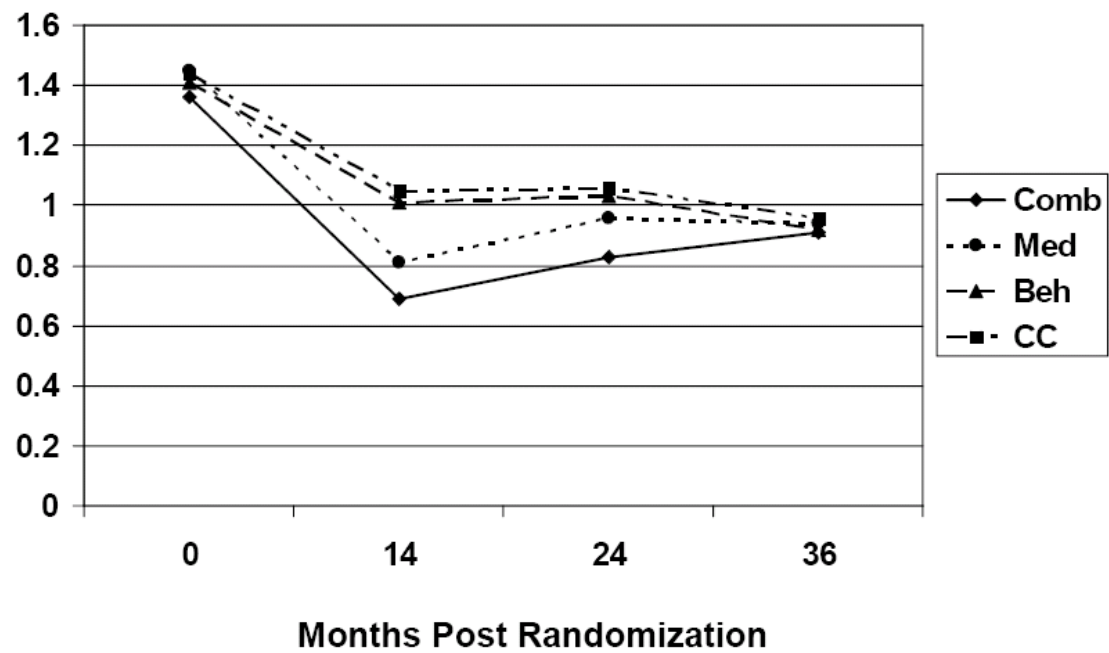
## ADHD Symptoms



Months Post Randomization

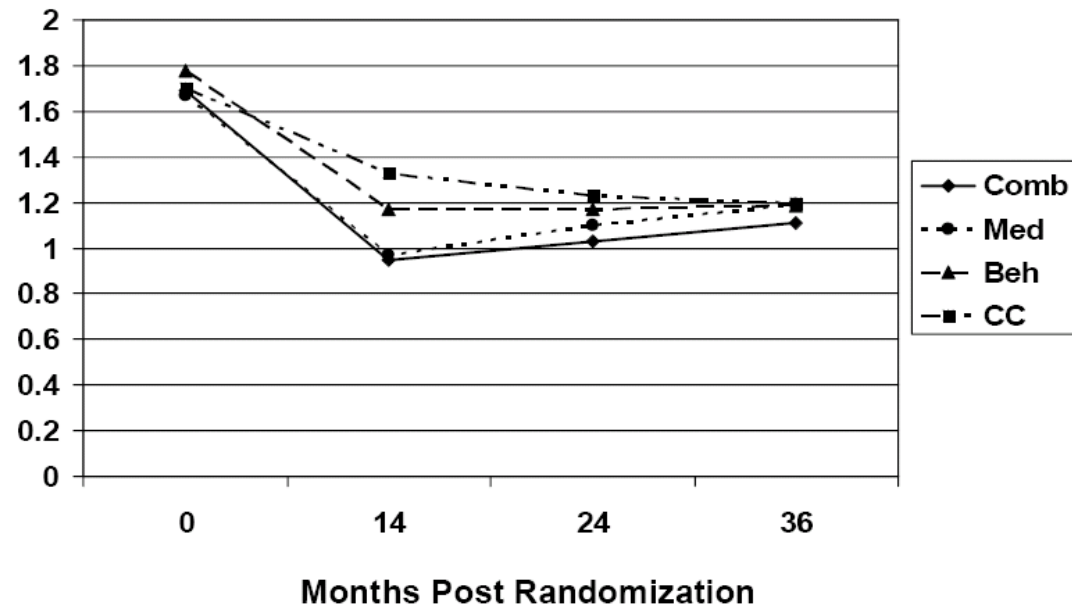
# MTA Follow-up at 36 months

## ODD Symptoms



# MTA Follow-up at 36 months

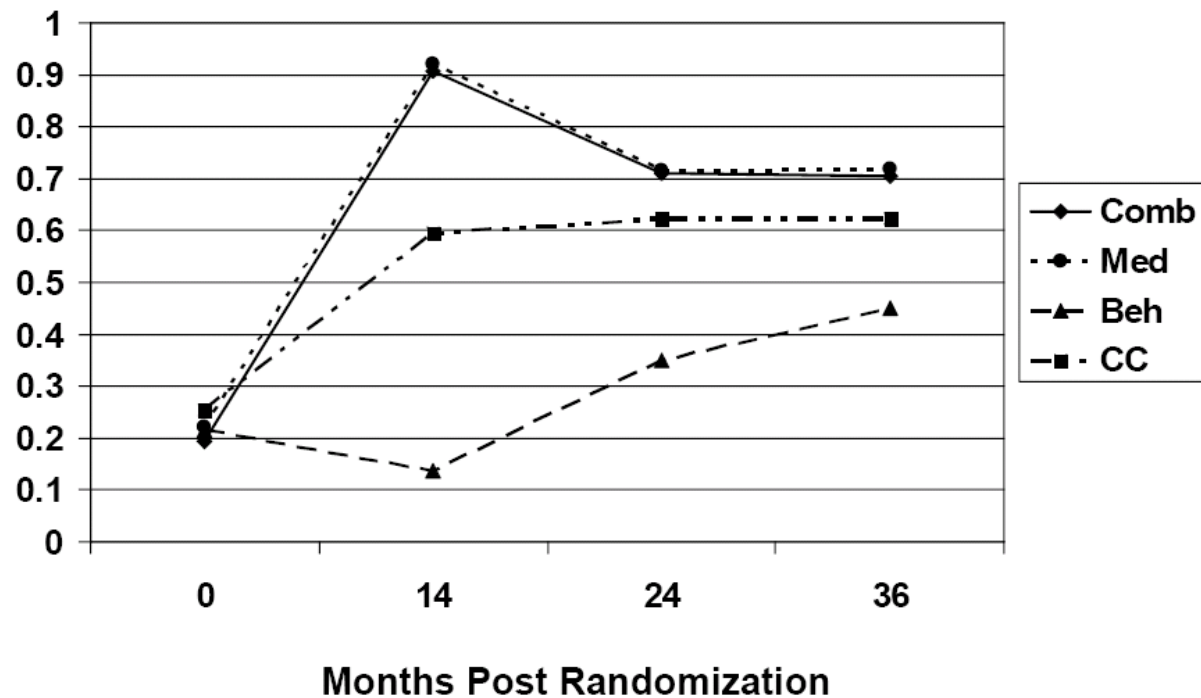
## Columbia Impairment Scale





# MTA Follow-up at 36 months

## Proportion of Subjects Taking Medication



# MTA Follow-up at 36 months

## *condary evaluations*

Test of the self-selection hypothesis that proposes the following:

- Cases with higher severity at entry or during follow-up would be more likely to have adverse outcomes
- would be more likely to receive medication after the initial intervention,
- and the association of severity and long-term medication would result in selective long-term treatment of the most severe cases, potentially masking beneficial long-term effects of medication.

This hypothesis was not confirmed

All five propensity subgroups showed initial advantage of

# MTA Follow-up at 36 months

## *growth rates*

Stimulant-naive subgroups had z scores for height and weight significantly  $>0$  at baseline

The newly medicated subgroup showed decreases in relative size that reached asymptotes by the 36-month assessment (average growth of 2.0 cm and 2.7 kg less than the not medicated group)

No evidence of growth rebound

Inconsistent findings in four other studies based on chart reviews

Consistent finding in the PATS

# MTA Follow-up at 36 months

## *Delinquent Behaviour and emergent substance use*

MTA children relative to local normative comparison group (11-13 yrs.):

- higher rates of delinquency (21.7 vs. 7.4%)
- and substance use (17.4 vs. 7.8%)

Children randomized to intensive BT reported less 24-month substance use than other MTA children

# MTA Follow-up at 36 months

## Discussion

Randomisation ended at 14 months. Subsequent reports have provided details of naturalistic follow-up of the groups at 24 and 36 months.

At the end of randomisation entailed that patients and families selected which intervention was best for them. This may lead to a situation in which each individual gets whatever combination of treatments that suits them best, so all interventions have reasonably good outcomes.

The end of intensive therapy could mean that any effects, that are additional to those of usual good treatment, wane when the intensity is reduced: so that all treatment arms become similar to community treatment.

The absence of an untreated control group makes it impossible to

## Comments

The MTA study initially reported the outcomes at 14 months of four groups, to which young people with combined-type ADHD were randomly assigned.

One group received carefully supervised medication, one an intensive programme of behaviourally oriented psychosocial therapy, one the combination of both, and one was assigned to community treatment (which included medication for about two-thirds).

At 14 months the outcome strongly favoured careful medication (whether or not in combination with behaviour therapy); at that point the randomisation ended, families were free to choose treatment or not, and the intensive interventions (medication monitoring and behavioural work) discontinued.

## Comments

Subsequent reports have provided details of naturalistic follow-up of the groups at 24 and 36 months after randomisation, and conference presentations have outlined preliminary findings at the 8-year point. By the 3-year mark, the outcome was similar for all the four groups.

These results have been widely interpreted as showing no long-term impact of medication or behaviour therapy. While this is one possible reading, it is not demonstrated by the study and other explanations need to be considered

## Comments

(1) The end of randomisation entailed that patients and families selected which intervention was best for them. This may lead to a situation in which each individual gets whatever combination suits them best, so all interventions have reasonably good outcomes.

(2) The end of intensive therapy could mean that any effects, that are additional to those of usual good treatment, wane when the intensity is reduced: so that all treatment arms become similar to community treatment.



## Comments

(3) The absence of an untreated control group makes it impossible to know whether the treatments were better than not intervening. Outcome scores at 36 months remained considerably better than the levels before treatment; the conclusion may be that all treatments work rather than that none do.

(4) The MTA investigators did not report that the treatments had no effect. They agreed that there was some evidence of medication benefit when the results were analysed by growth mixture modelling, which divides the sample into latent classes based on their trajectory over time. The best fit was *3 classes*.

# Comments

- One of the classes, 34% of the sample, showed gradual improvement with continuing benefit from medication over the whole 3 years. The second class, 52% of the sample, had an initial large response, maintained for 3 years; in another 14% a large initial response was followed by deterioration.
- There was, in the second group who responded well, a significant preponderance of children who had been assigned to the intense MTA medication algorithm in the first 14 months - whether or not they continued medication

## Comments

(5) Adverse events at the 24- and 36-month points after randomisation included influences on growth in height and weight – an effect of 0.75 inches at the 2-year mark, with no further loss at the 3-year point and (in conference reports) catch-up growth by the 8-year point, suggesting no growth suppression in that time scale.

## Comments

It would therefore not be correct to regard behaviour therapy or stimulant medication as short-term treatments only.

Our clinical recommendation for longer term medical treatment, in the absence of definitive scientific evidence, is for periodic discontinuation to assess whether a continuing need for medicine is present.

Our research recommendation is for the commissioning of studies on long-term effectiveness and hazards of medication (such as randomised trials of discontinuation).

# MTA

## 8 Year Follow-up

### MTA at 8 Years: Prospective Follow-up of Children Treated for Combined-Type ADHD in a Multisite Study

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# MTA

## 8 Year Follow-up

### ABSTRACT

To determine any long-term effects, 6 and 8 years after childhood enrollment, of the randomly assigned treatments in the NIMH Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder (MTA;  $N = 436$ ); to test whether attention-deficit/hyperactivity disorder (ADHD) symptom trajectory through 3 years predicts outcome in subsequent years; and to examine functioning level of the MTA adolescents relative to their non-ADHD peers (local normative comparison group;  $N = 261$ ). **Method:** Mixed-effects models with planned contrasts at 6 and 8 years tested a wide range of symptom and impairment variables by parent, teacher, and youth report. **Results:** In nearly every analysis, the originally randomized treatment groups did not differ significantly on repeated measures or newly analyzed variables (e.g., grades earned in school, psychiatric hospitalizations, other clinically relevant outcomes). Medication use decreased by 62% after the controlled trial, but adjusting for this did not change the results. ADHD symptom trajectory in the first 3 years predicted 5% of the outcomes. The MTA participants fared worse than the local normative comparison group on 15% of the variables tested. **Conclusions:** Type or intensity of 14 months of treatment for ADHD in childhood (at ages 7-9) does not predict functioning 6 to 8 years later. Rather, early ADHD symptom trajectory regardless of treatment response is prognostic. This finding implies that children with behavioral and sociodemographic advantage, with the best response to any treatment, will have the best long-term prognosis. As a group, however, despite initial symptom reduction during treatment that is largely maintained after treatment, children with combined-type ADHD exhibit

# MTA

## 8 Year Follow-up

In nearly every analysis, the originally randomized treatment groups did not differ significantly

Medication use decreased by 62% after the 14-month controlled trial, but adjusting for this did not change the results.

ADHD symptom trajectory in the first 3 years predicted 55% of outcomes.

The MTA participants fared worse than the local normative control group on 91% of the variables tested.

The dose or intensity of 14-month of treatment for ADHD in childhood does not predict functioning 6-8 years later.

Neither early ADHD symptom trajectory regardless of

# MTA

## 8 Year Follow-up

### Conclusions

Children with behavioural and sociodemographic advantage, with the best response to any treatment, will have the best long-term prognosis.

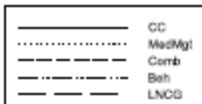
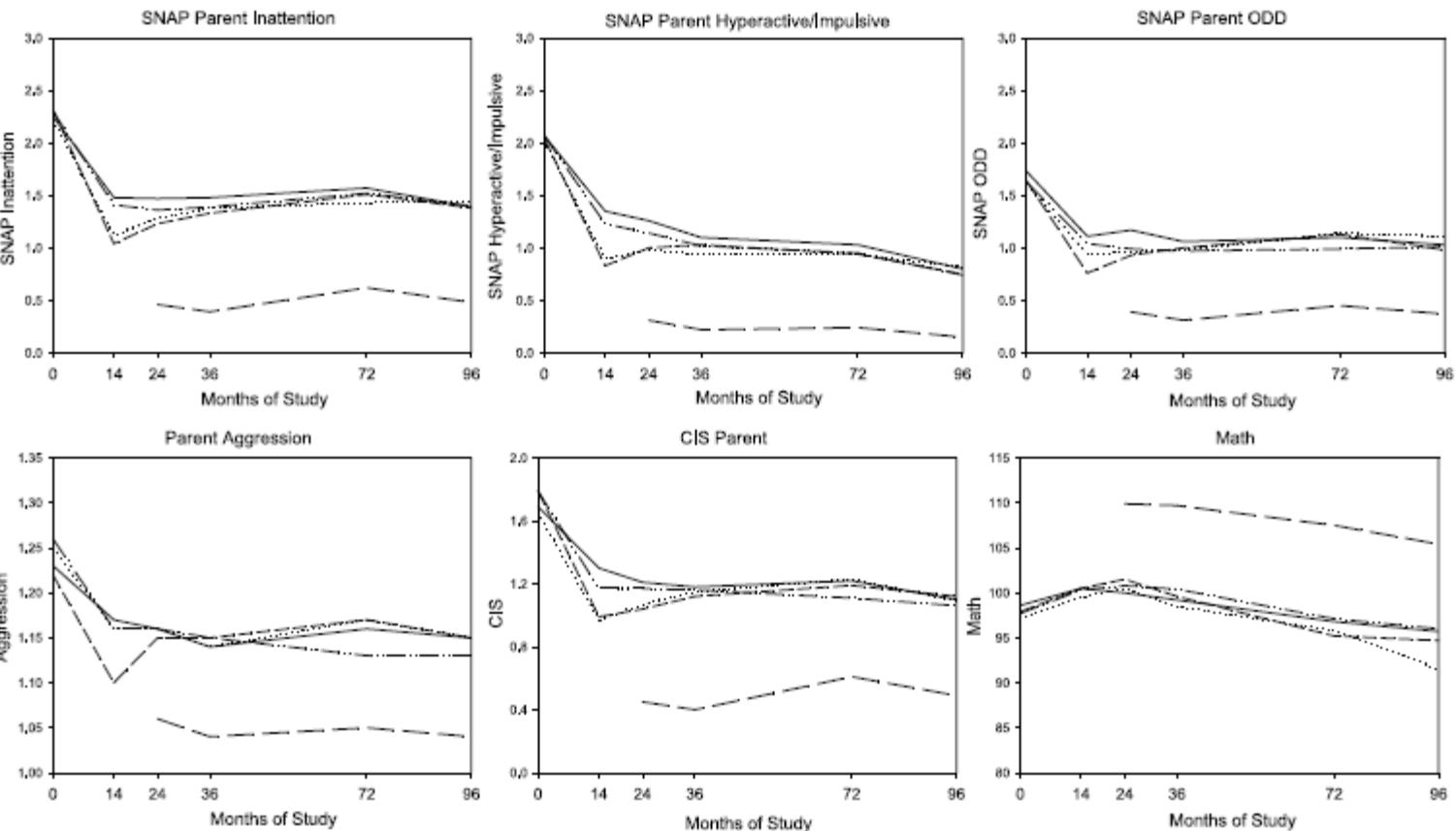
Despite initial improvement during treatment that is largely maintained after treatment, children with combined-type ADHD exhibit significant impairments in adolescence.

Innovative treatment approaches targeting specific areas of adolescent impairments are needed.



# MTA

## 8 Year Follow-up



# MTA

## 8 Year Follow-up

The reasons why the original differences between groups disappeared after 8 years has been extensively debated, with arguments on opposite sides that

- medication was no longer effective or that
- All participants improved from treatment and the improvement was sustained or
- that the natural course of the disorder accounted for the improvement.
- The best interpretation may be that the data were confounded and conclusions difficult to draw.

# MTA

## 8-Jahres-Verlauf

nahezu allen Analysen unterschieden sich die ursprünglich randomisierten Gruppen nicht signifikant.

Medikation nahm um 62% nach dem kontrollierten 14-Monate-Versuch ab; keine Veränderung der Resultate nach Entzug der Medikation für diesen.

Verlauf der ADHS Symptome in den ersten 3 Jahren prädizierte 55% der Verlaufsergebnisse.

Teilnehmer der MTA zeigten bei 91% der untersuchten Teilnehmer schlechtere Befunde als die lokale Vergleichsgruppe.

Typ oder die Intensität der 14-Monate-Behandlung der ADHS in der Kindheit prädiziert das Funktionsniveau nach 6-8 Jahren nicht

# MTA

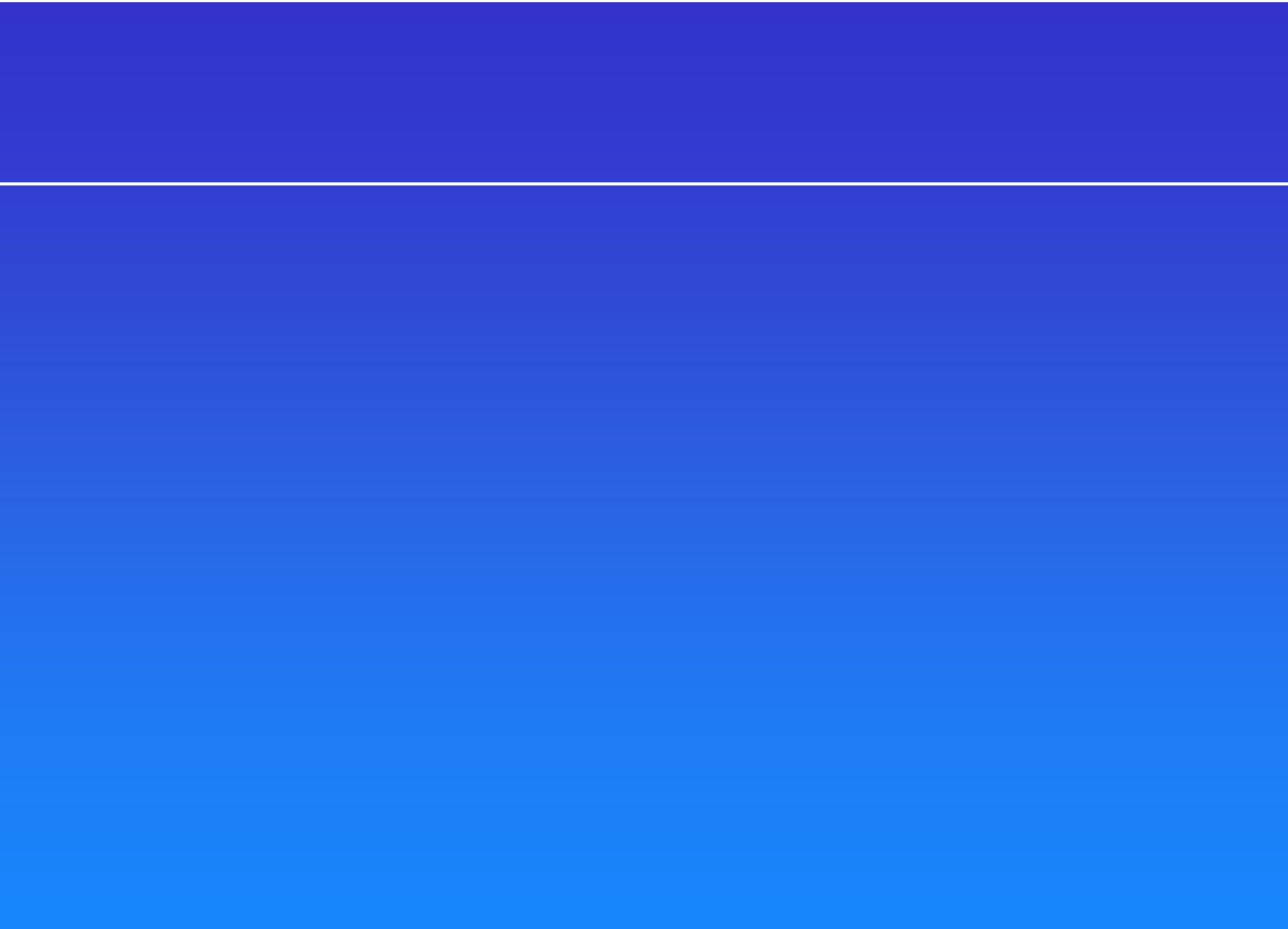
## 8-Jahres-Verlauf

### Schlussfolgerungen

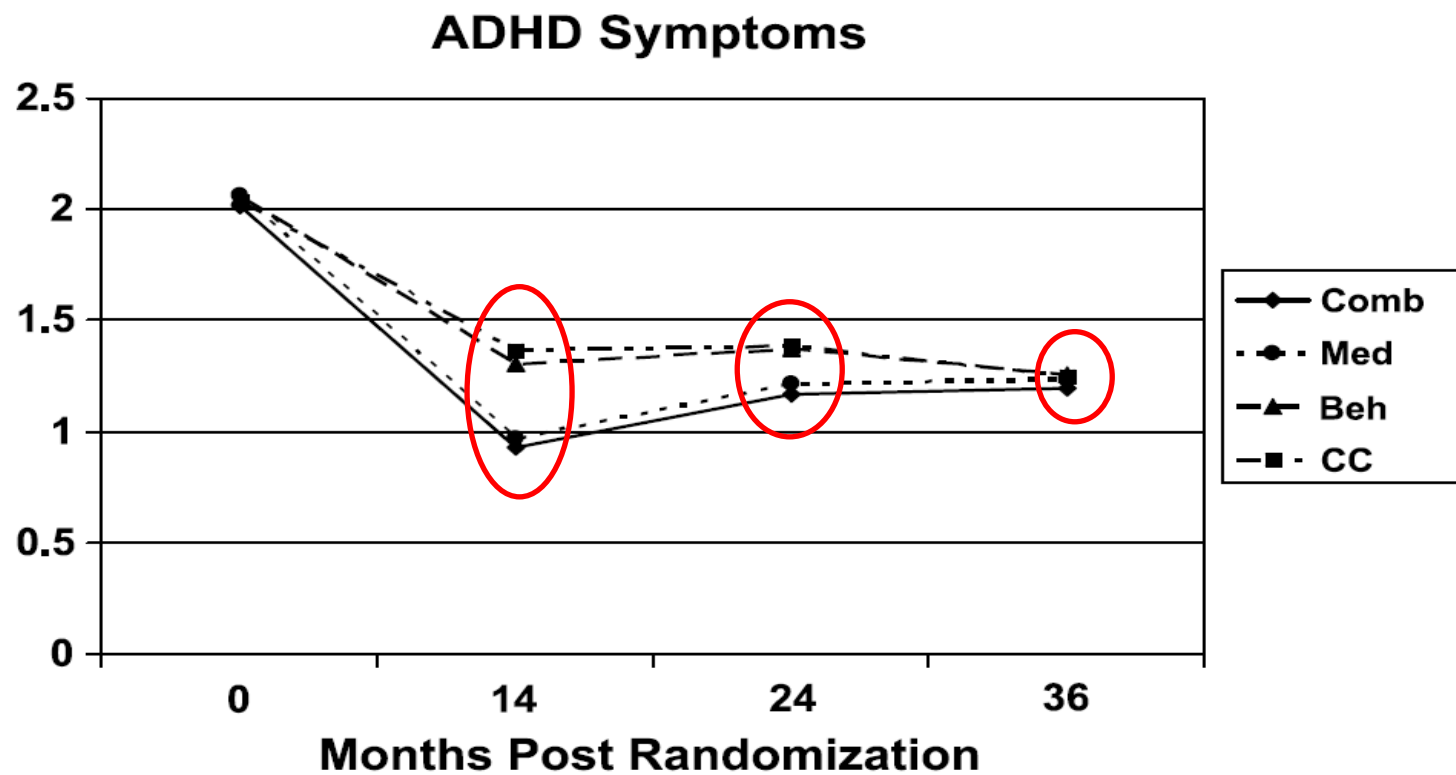
Kinder mit weniger komplexen Verhaltensproblemen und aus besserem sozialen Milieu, mit dem besten Ansprechen auf jegliche Therapie haben die beste Langzeitprognose.

Trotz anfänglicher Verbesserung unter Therapie, die weitgehend nach Therapie aufrechterhalten bleibt, haben Kinder mit ADHS (Comb) deutlich mehr Beeinträchtigungen in der Adoleszenz.

Innovative Therapieansätze mit Ziel auf bestimmte Bereiche der Funktionstüchtigkeit von Jugendlichen



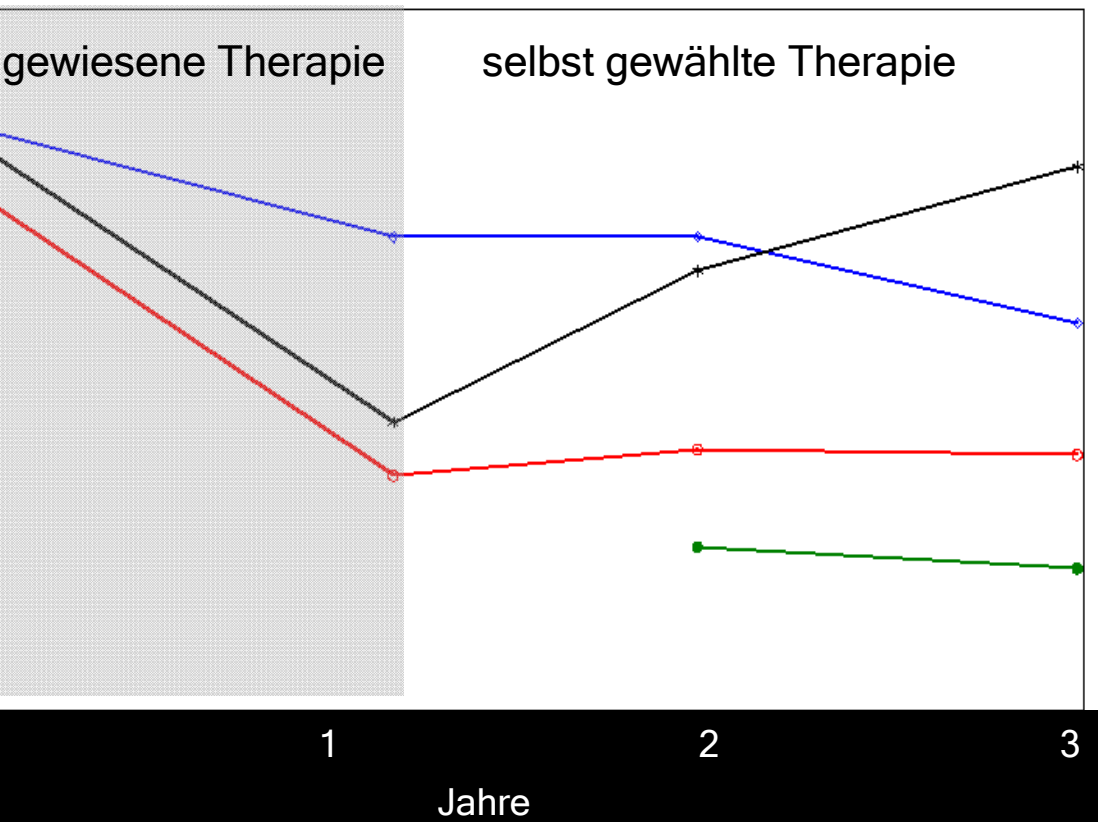
# Zeitverlauf der Ausgangsgruppen (MTA)



- Deutlicher Medikamenteneffekt in den ersten 14 Monaten
- Keine Unterschiede nach 36 Monaten

# Verlaufstypen in der MTA-Studie

Symptomatik



Klasse 3 (14%) Rückfall (MED-)

Klasse 1 (34%) stetige Verbesserung (MED+)

Klasse 2 (52%) Verbesserung gehalten (MED-)

lokale Vergleichsgruppe

MED+: unter fortgesetzter Medikation bessere Effekte

MED- :unter fortgesetzter Medikation keine Effekte

➤ Mehrheitlich positive Langzeitverläufe

# Verlaufsstudien in der Adoleszenz

	Alter (Jahren)		Verlaufsdauer (Jahre)	Persistente ADHD (%)	Störung des Sozialverhaltens %
	M	VB			
rt et al. (1987)	14		5	43	
y et al. (1990),	15		8	72	44
t al. (1995)	13	11-16	4	77	
et al. (1996)		16-18	9	10-29*	3-29*
man et al. (1996)		10-21	9	85	



# Längssstudien im jungen Erwachsenenalter

	Alter (Jahren)		Verlaufsdauer (Jahre)	Persistente ADHS (%)	Antisoziale Persönlichkeit (%)	Substanzmissbrauch (%)
	M	VB				
Hechtman	25	21-33	15	67 <sup>R</sup>	23	
al. (1983)	22	21-23	?		45	
n/Manuzza	18	16-23	9	31	27	16
5, 1989, 1, 1997)	26	24-33	17	8	18	16
t al., 2002; al., 2002;	21	19-25	13+	5 (S) 46 (E)	21	43