



The relationship between ADHD and substance use disorder:

Evidence based treatment and clinical implications

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Conflicts of interest

2009: Have given talks supported by Novartis and Eli Lilly

2010: Received travel support from Eli Lilly

The support was approved by The Danish Medicines Agency





What is ADHD and Hyperkinetic Disorder?

- **ADHD – Attention Deficit Hyperactivity Disorder**
 - DSM-IV diagnosis with three subtypes
 - Combined Type, Inattentive type and Hyperactive/Impulsive type
- **Hyperkinetic Disorder (HKD)**
 - ICD-10 diagnosis identical with ADHD combined type





The core symptoms of ADHD and HKD

- **Inattention**
 - Sustained attention (finishing tasks)
 - Selective attention (ignoring things)
 - Divided attention (shifting focus)
 - Joined attention (multitasking)
 - Executive functioning (planning, prioritizing)
- **Hyperactivity**
 - Running around (leaving seat)
 - Fidgeting (staying in your seat, but still moving)
 - Restlessness
- **Impulsivity**
 - Difficulty waiting turn (impulsive in action)
 - Budding in on conversations (verbally impulsive)



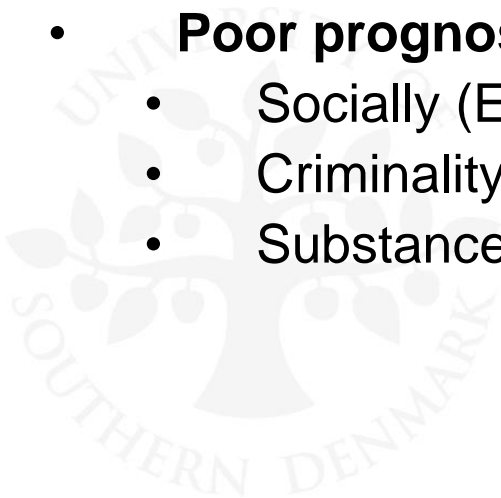
Epidemiology of ADHD / HKD

- **Most common psychiatric disorder in childhood, affecting**
 - 3-5% of school-aged children, 3-4% of adults
- **More common among males than females**
 - In clinical samples 7:1
 - In epidemiological samples 2:1
- **Mainly a genetic disorder**
 - Twin studies have shown concordance rates of around 80%
- **Increasing incidence rates of diagnosis (but maybe not prevalence)**
 - More knowledge on the disorder is available
 - Treatment is more accepted in the public



From childhood to adulthood – with ADHD

- **The core symptoms do change with increasing age**
 - Less hyperactive (especially the “obvious” hyperactivity)
 - Increasing problems with executive dysfunctions (higher demand)
- **Change in comorbidity**
 - Anxiety disorders, affective disorders and personality disorders
- **Poor prognosis in several domains**
 - Socially (Education, job, sexuality, relationships)
 - Criminality
 - Substance use problems (alcohol, drugs, smoking)





Stroop

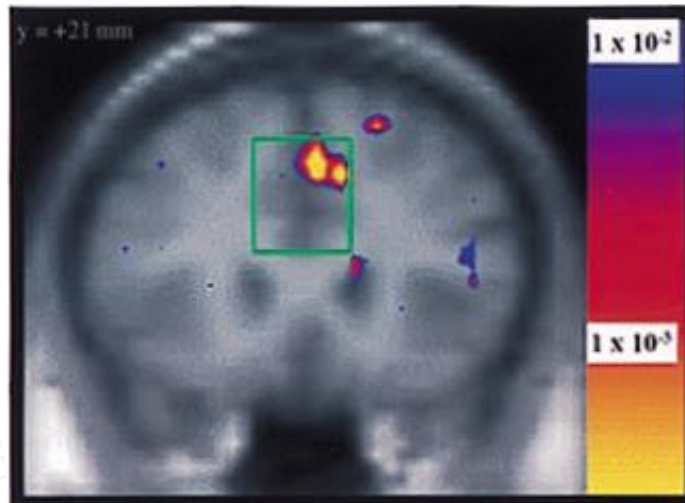
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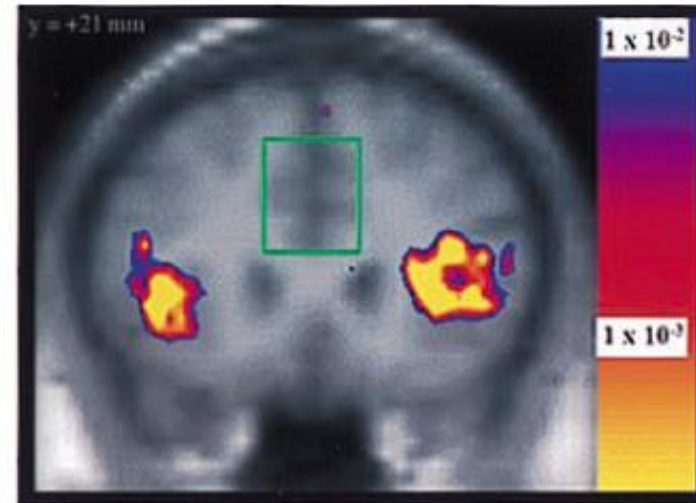
Activation during Stroop, fMRI

Normal Controls



Anterior cingulate

ADHD



Frontostriatal-insular



ADHD and addiction

People with ADHD have a significant increased risk of developing substance use problems (especially alcohol and cannabis)

Adolescents with ADHD

Earlier onset of substance use than others

More likely to become dependant

More likely to be involved in criminality related to drugs





Registerbased follow-up study in Denmark

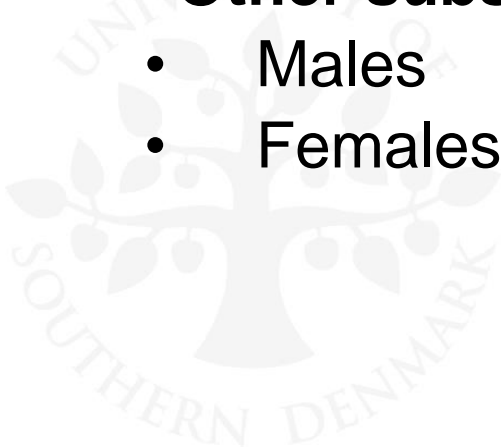
- **Follow-up study of 208 children with ADHD**
 - All been treated with stimulants in the period 1970-1989
 - All been at in-patient treatment
 - Had severe childhood ADHD, lots of comorbidity
- **Followed until a mean age of 31 years, no attrition**
- **Outcomes**
 - Psychiatric admissions to hospitals
 - Criminal convictions
- **Compared a matched control sample from background population (n=1.2 mill)**



Outcomes on addiction

Diagnosis of addiction during psychiatric admission

- **Alcohol abuse, overall** **RR=5.2 (2.6-9.3)**
 - Males RR=4.5 (2.5-8.0)
 - Females RR=21.5 (5.4-85.8)
- **Other substance abuse, overall** **RR=7.7 (3.8-13.7)**
 - Males RR=5.9 (3.3-10.7)
 - Females RR=38.7 (12.5-119.9)





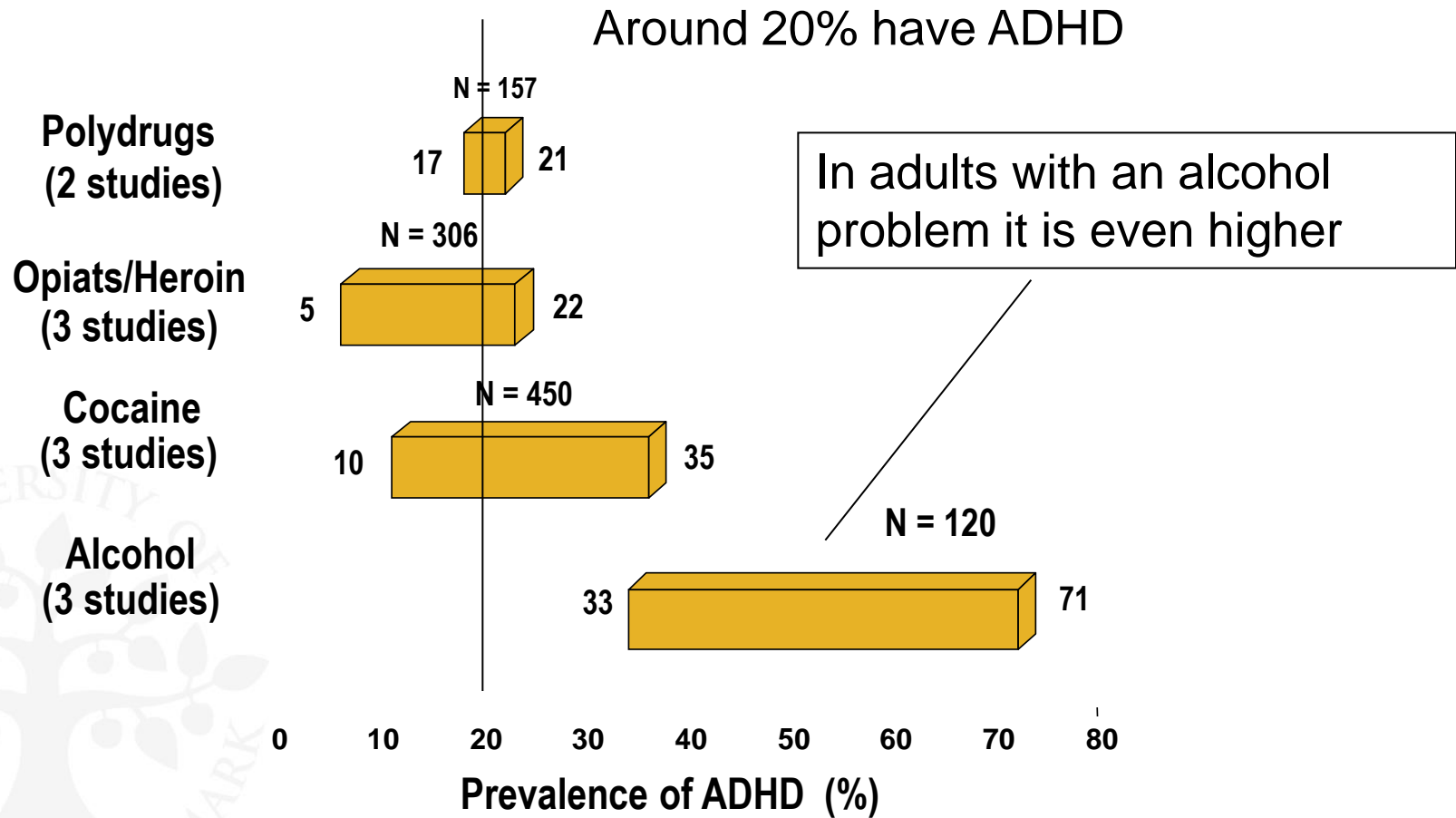
Outcomes on drug related criminality

- **Possession of illicit drugs**
- **6% were convicted (<1% blandt kontroller) RR=7.6**
- **Drunk driving**
- **13% convicted (1% blandt kontroller) RR=12.4**





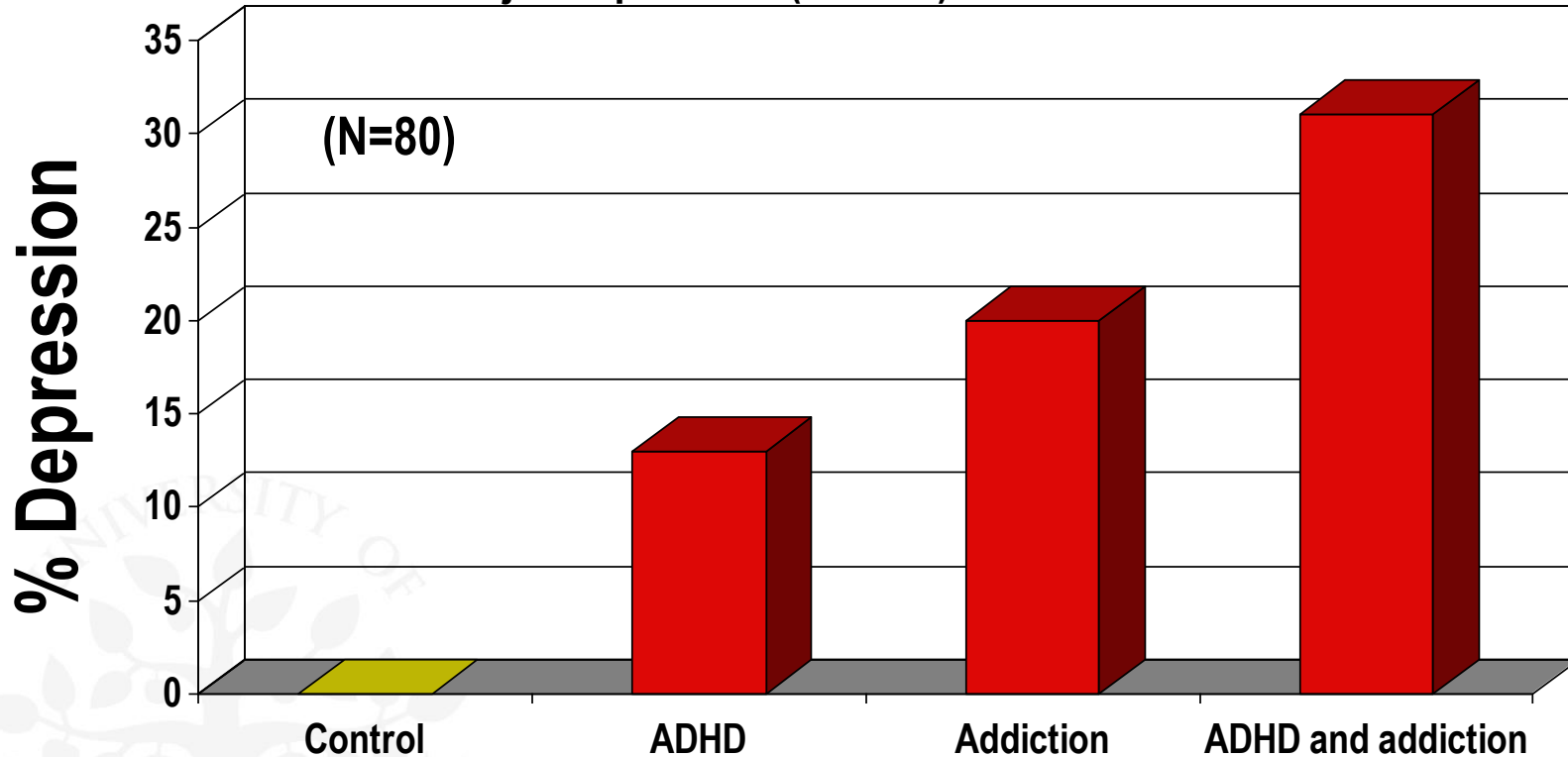
Prevalence of ADHD in adults with addiction





Depression, ADHD and addiction

Major Depression (lifetime)

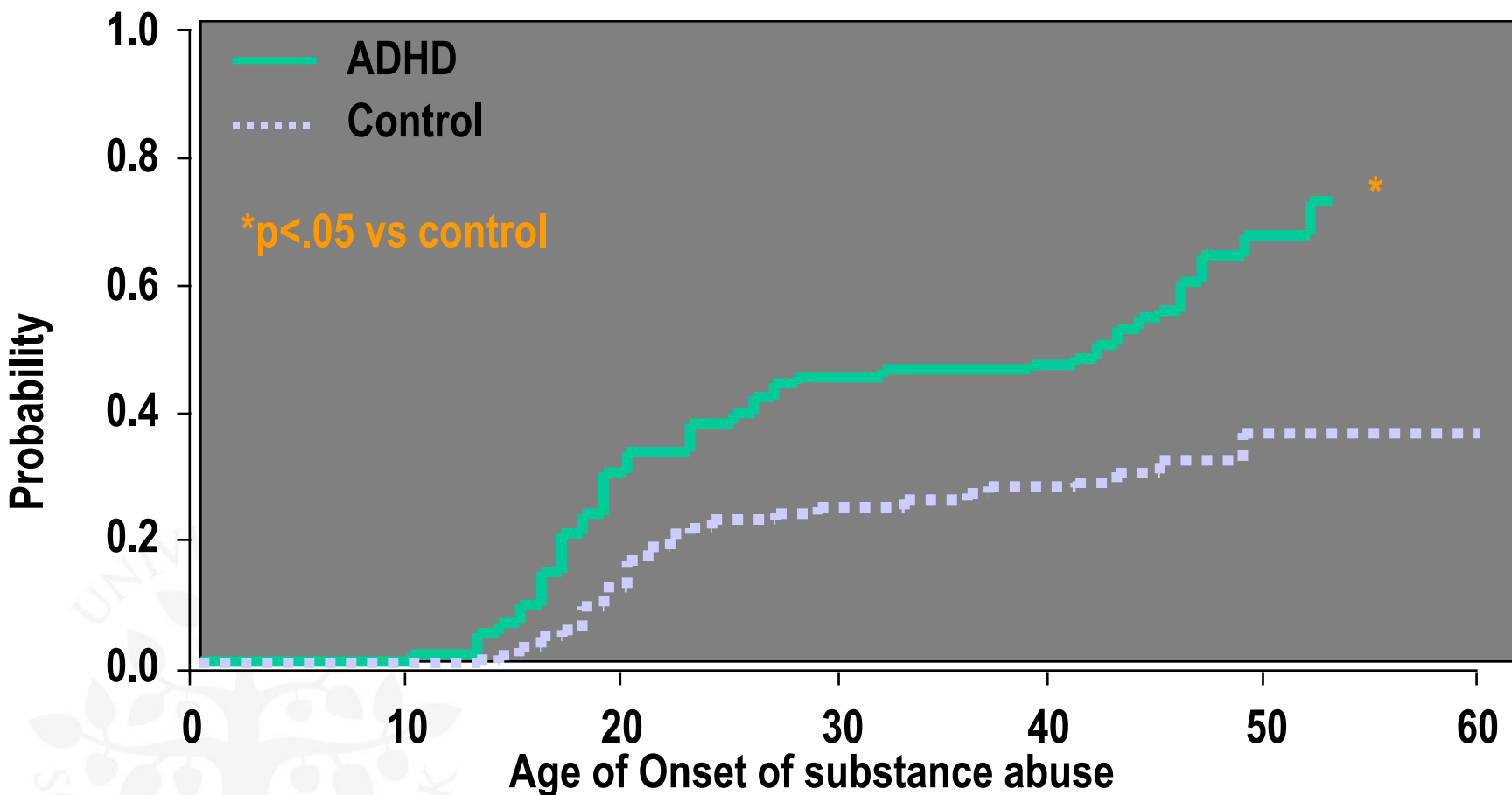


Prevalence of depression in adults

(Wilens et al., Am J Addiction:2005)

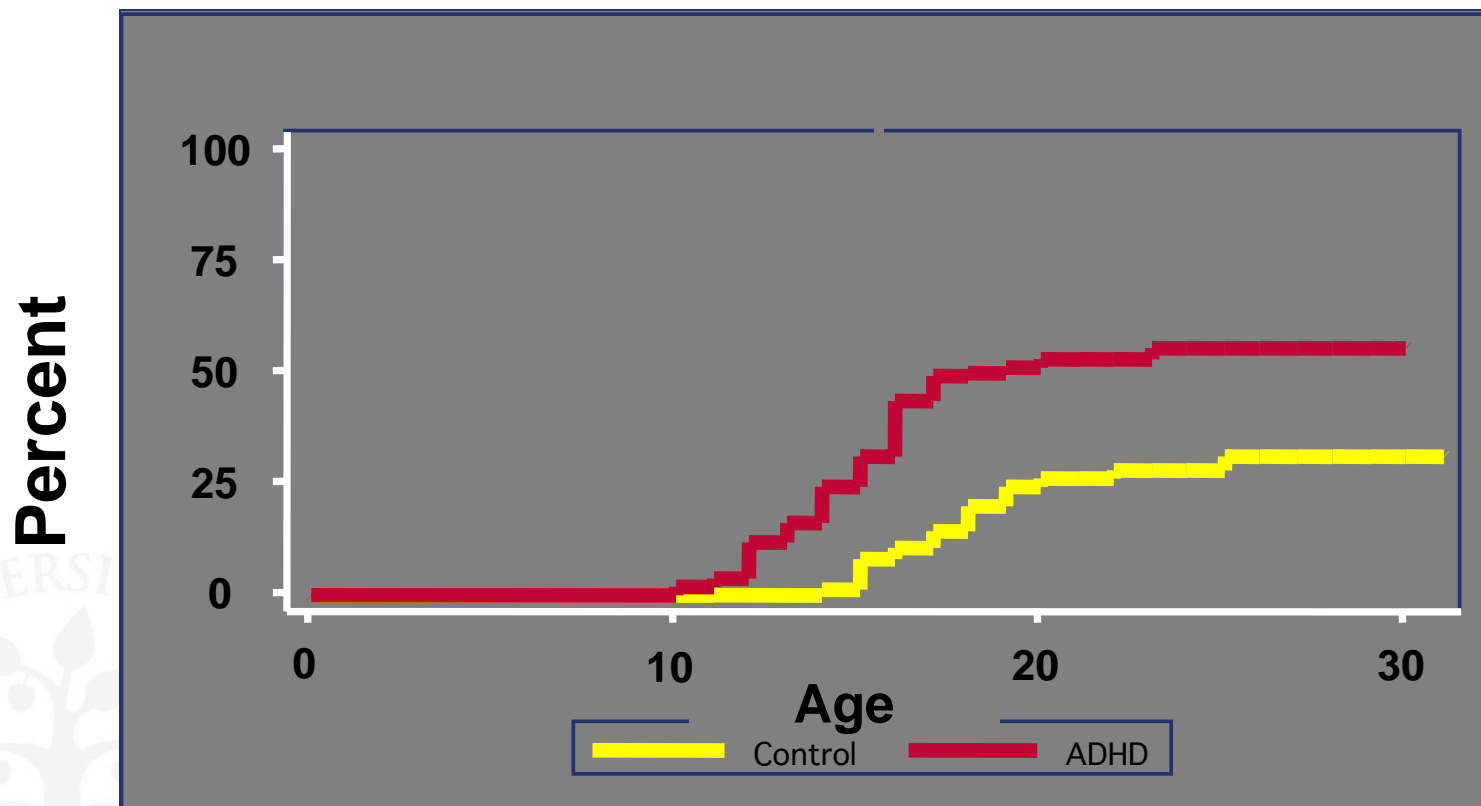


Age of onset of addiction





Nicotine dependence in adolescents



Biederman, et al. *Psych Med*, 2006.



Cigarettes and addiction

Nicotine

Increases attention and executive functions

Stimulates the release of neuro-transmitters

Acetylcholin, Serotonin, Dopamin

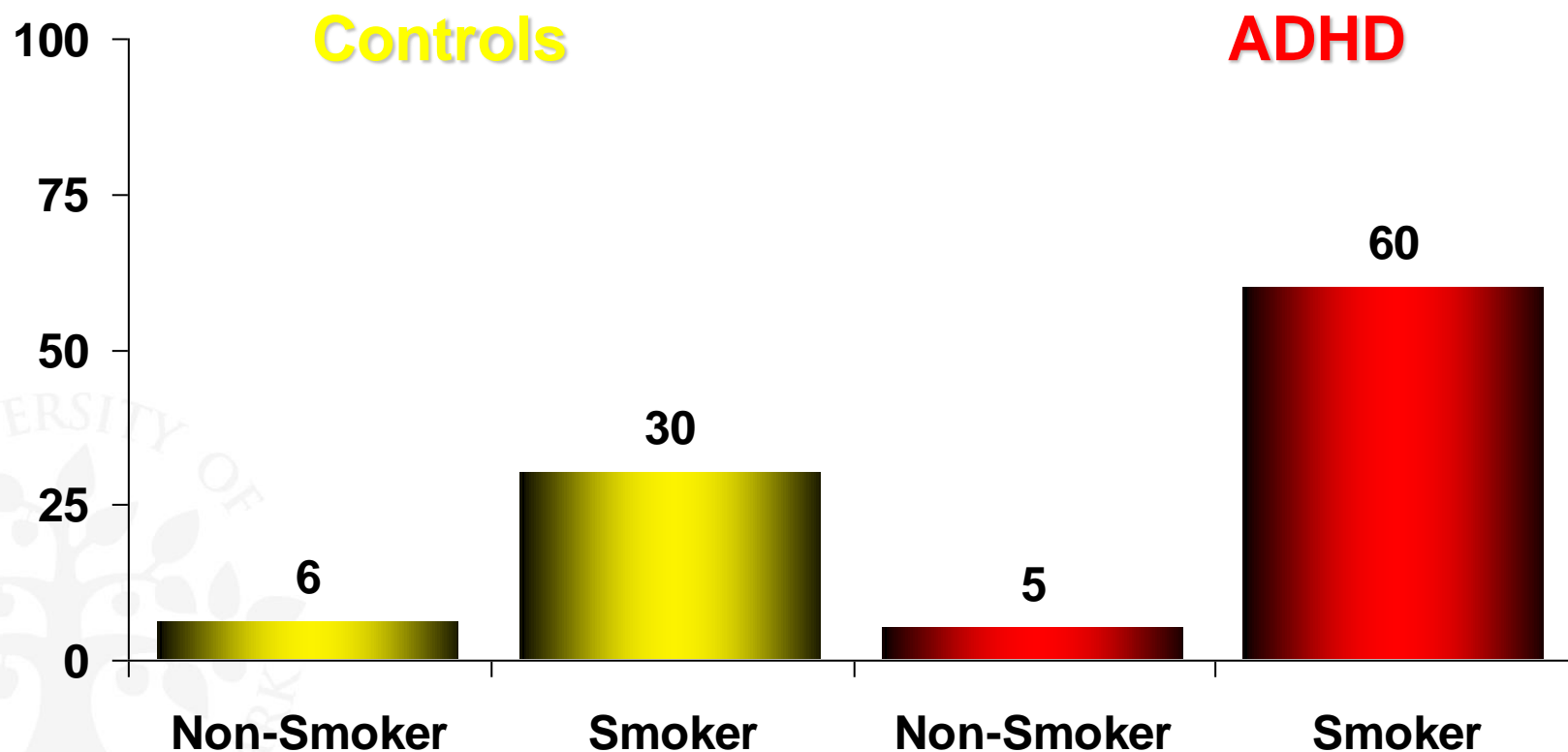
May also act as a "gateway" to addiction

(Retzvani and Levin, 2001)





Smoking and substance use

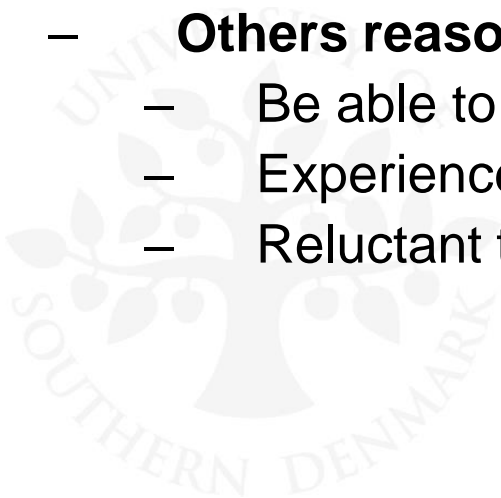


(Biederman, Wilens, Monuteaux Bio Psych:2006 Feb 1;59(3))



Adolescents and adherence

- **Teenagers tend to think:**
 - "Medication = I'm sick"
 - "No medication = I'm well"
 - "I wanna be like other teenagers"
 - "So, I will stop taking the medication"
- **Others reasons for wanting to discontinue treatment:**
 - Be able to drink alcohol
 - Experience the naturalistic reduction in hyperactive symptoms
 - Reluctant to come to the clinic (or to listen to adults in general)





Why is adherence important?

- **Continuation of ADHD treatment is important, because it:**
- **Reduces ADHD core symptoms**
- **Reduces impairment**
- **Reduces level of conflicts with**
 - parents, peers and teachers
- **Methylphenidate probably reduces the risk of SUD**
- **Meta-analysis of RCT**
 - With a factor 6 in adolescence
 - With a factor 2 in adulthood



What is the evidence on treatment and risk of SDU?

- **1 study shows an increased risk of SDU in subjects with ADHD treated with stimulants**
 - Lambert et al 1998
- **3 studies shows no effect of treatment on risk of SDU**
 - Dalsgaard et al 2002
 - Barkley et al 2003
 - Molina et al 2007 (the MTA study, 36 month follow-up)
- **5 studies and a meta-analysis shows a protective effect**
 - Biederman 1999
 - Huss 1999
 - Wilens 2003 (meta-analysis)
 - Katusic 2005
 - Wilens 2008
 - Dalsgaard et al (in prep)



The adolescent study in Denmark

Questionnaire survey of 219 adolescents 13-18 years of age in The Region of Southern Denmark

117 adolescents with ADHD

All in pharmacological treatment for ADHD

Having shown **good compliance** within the last 12 months

102 adolescents without ADHD (the control group)

Matched for age, gender and region



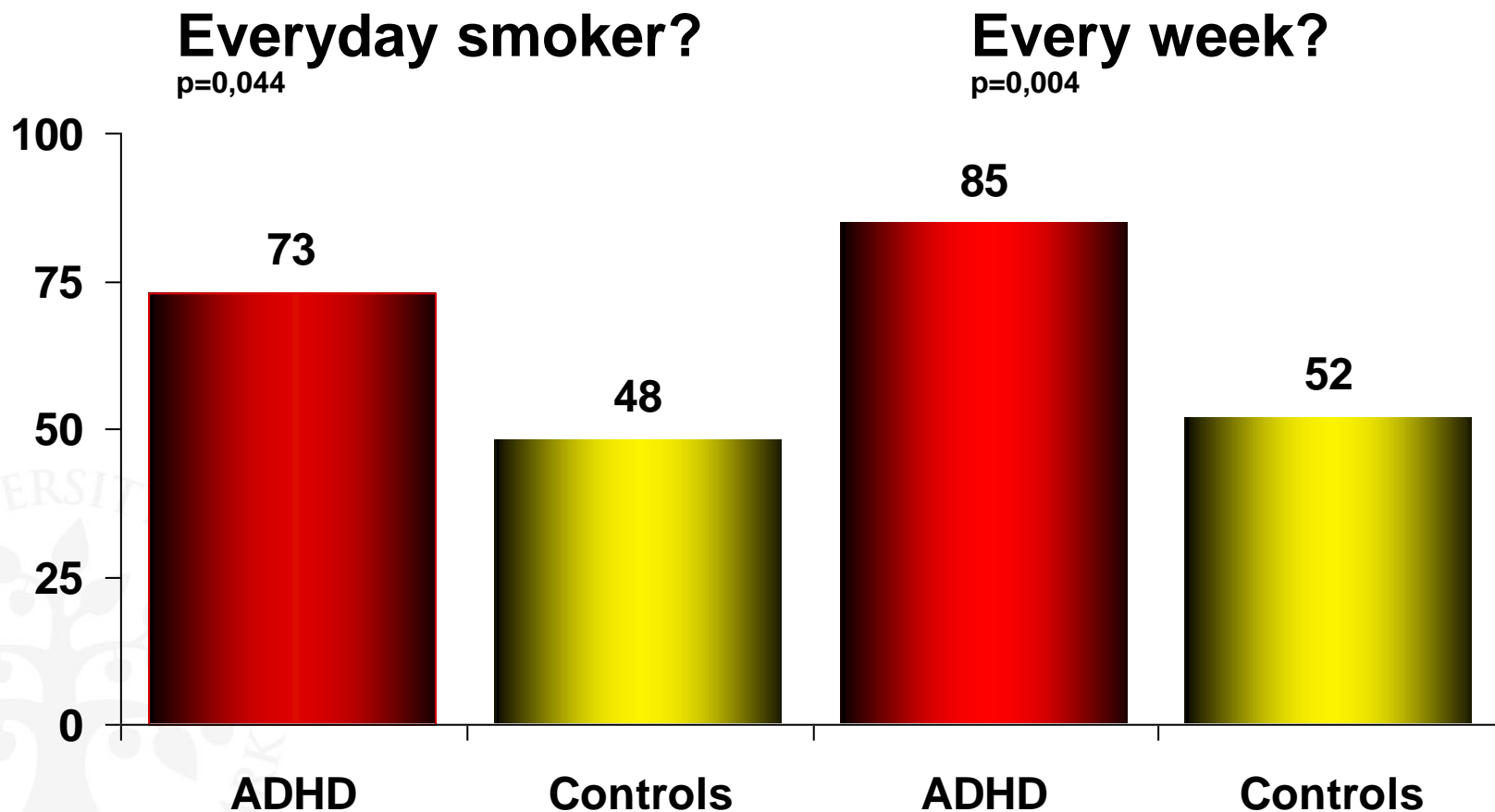


Adolescents with good compliance

	Adolescents with ADHD (N=117)	Controls <i>without</i> ADHD (n=102)	Significant difference?
Ever tried smoking cigarettes?	51%	55%	ns
Ever tried drinking alcohol?	79%	89%	ns
Ever tried cannabis?	19%	21%	ns
Ever tried any of these?	83%	92%	0,041

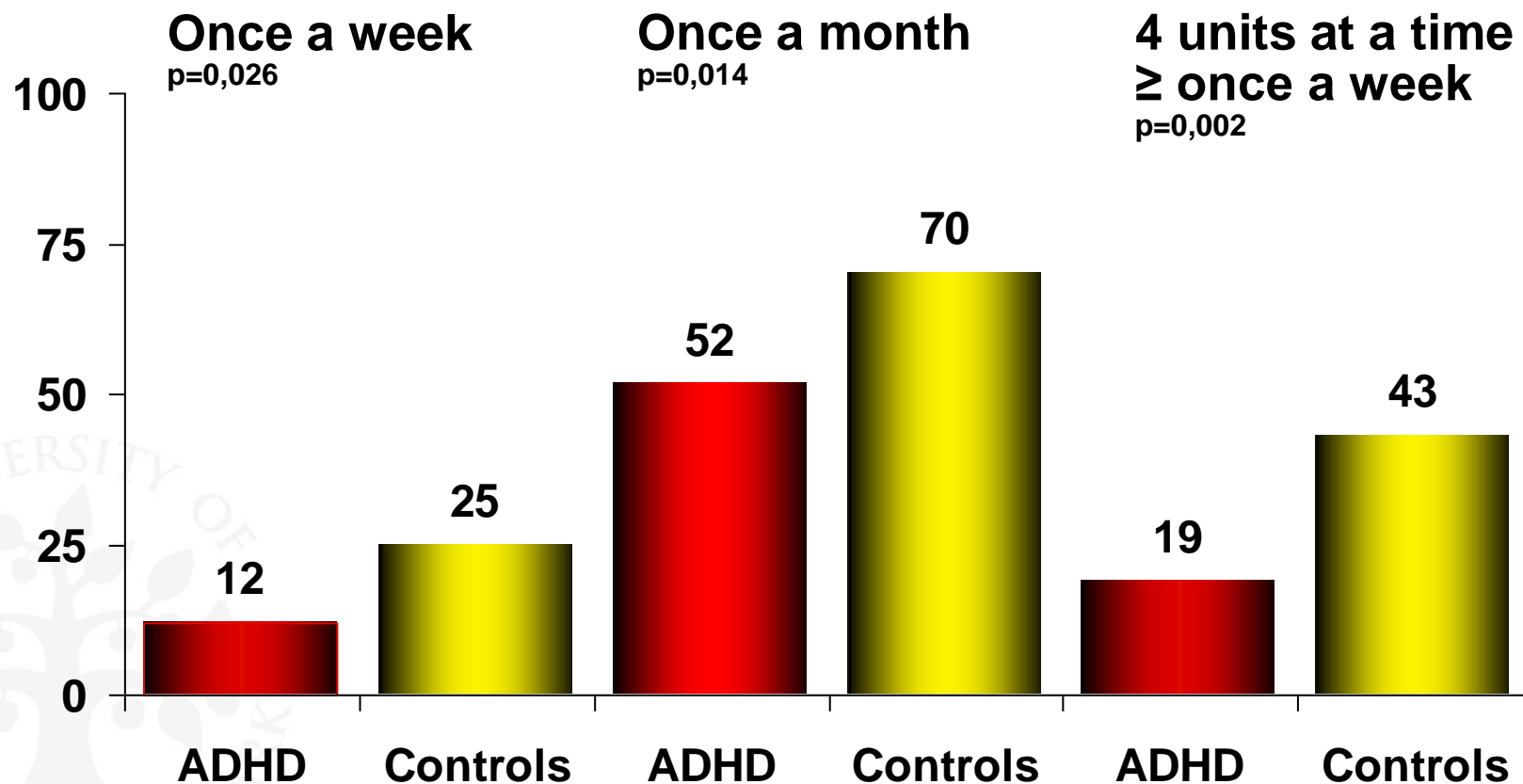


Habits among smokers





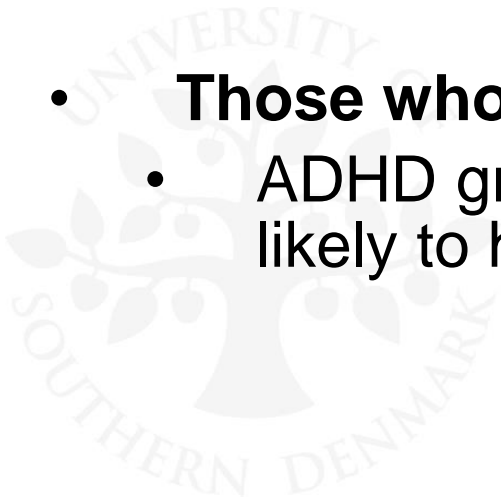
Those having tried alcohol





Adolescents with ADHD with good adherence

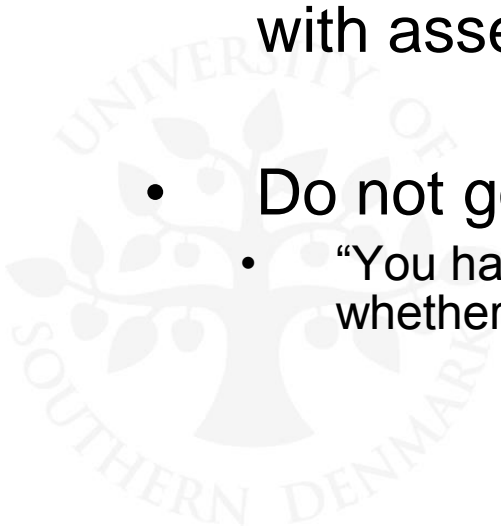
- **Overall ADHD at decreased risk of ever having tried**
 - Smoking cigarettes, drinking alcohol or using drugs
- **Those who do try smoking cigarettes**
 - ADHD group at higher risk of getting addicted, becoming regular smokers
- **Those who have tried alcohol**
 - ADHD group drinks alcohol less frequent and are less likely to have a heavy use of alcohol





Screen populations with SUD for ADHD?

- Might be a good idea, but screening is not a diagnosis
- Some people with SUD will try to get a diagnosis of ADHD to get “ADHD-treatment“
- Collaborate with professionals who have experience with assessing and treating ADHD
- Do not go with the
 - “You have to be abstinent for 6 months before we can assess whether you have ADHD“





Using stimulants in adolescents already at risk of SUD?

- **Make sure they actually have ADHD**
 - Some adolescents with SDU will tell you they have ADHD
- **Evaluate the alliance you have with the adolescent**
 - Do you feel that you can trust him or her?
- **Use a slow-release depot formulation**
- **Keep an eye on the intervals between prescriptions**
 - Do not except explanations like “I dropped them all in the sink“
- **If you suspect current use of substances**
 - Treat with Atomoxetine instead



Assessment of adolescents and adults

Some of the pitfalls

- **High score on a screener (ASRS) = ADHD**
 - No, may be due to a number of other reasons (SUD...)
- **Hyperactive adults most likely have ADHD**
 - No, most adults with ADHD are no longer hyperactive
- **Methylphenidate increases the risk of SUD**
 - No, the evidence seems to suggest the opposite
- **Mental retardation / attachment disorders are very different from ADHD**
 - No, they are the most important differential diagnoses



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Thank you for your attention!

Questions?

